The Middle East Journal of Anesthesiology is a publication of the Department of Anesthesiology of the American University of Beirut, founded in 1966 by Dr. Bernard Brandstater who coined its famous motto: “For some must watch, while some must sleep” (Hamlet-Act. III, Sc. ii).

and gave it the symbol of the poppy flower (*Papaver somniferum*), it being the first cultivated flower in the Middle East which has given unique service to the suffering humanity for thousands of years. The Journal’s cover design depicts The Lebanese Cedar Tree, with’s Lebanon unique geographical location between East and West. Graphic designer Rabi Moukalled

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Clinical Update in Anesthesiology, Surgery and Perioperative Medicine
January 17-22, 2010
Paradise Island, Bahamas

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(Deadline – October 16, 2009)

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ANESTHESIOLOGY AT MEMA 2009
(Beirut, April 23-26)

The Middle East Medical Assembly (MEMA) is jointly organized every year by the Faculty of Medicine of the American University of Beirut (AUB), and THE Medical Chapter of the Worldwide AUB Alumni Association (Fig. 1).

MEMA 2009 is the 42nd Middle East Medical Assembly. The front page of the MEMA 2009 announcement was illustrated by a painting of Ibn-El-Razi examining a child suffering from small pox, reminding everybody allover the world of the major contributions of the Arabs to the medical progress and to the renaissance period (Fig. 2).

During the opening ceremony, Professor Ibrahim Salti, the Chairman, considered MEMA 2009 a signal of the spirit of optimism and enthusiasm that renews the grand and pioneering AUB traditions in continuing medical education. In his message, Dr. Salti acknowledged the cooperation and support of the Cleveland Clinic Foundation, the AUB Medical Alumni Association and the National Lebanese Council for Scientific Research (Fig. 3).
In line with the MEMA's tradition, the three-day program was multidisciplinary, which covered the state-of-the-art of the different medical specialties including Anesthesiology. The two-day program of Anesthesiology was organized by Dr. Ghassan Kanazi, the Chairperson of AUB Department of Anesthesiology, in coordination with the Cleveland Clinic, Ohio, and the Columbia University, New York.

Dr. Kanazi delivered the Welcome Keynote, and presented Dr. Anis Baraka, the former Chairman and Emeritus Professor of the Department (Fig. 4).

Dr. Baraka delivered the Keynote address about the role played by the Department of Anesthesiology of the American University of Beirut during the tragic years of Lebanon 1975-1990 (Fig. 5).

Dr. Ibrahim Salti, the Chairman of MEMA 2009 was keen to attend the Keynote welcome and address of Anesthesiology (Fig. 6).

Dr. Armin Schubert, Professor, General Anesthesiology, Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio, USA, reviewed Anesthesia for Minimally Invasive Neurosurgery, as well as what is new about the OR throughput (Fig. 7).

Dr. Maya Jalbut, a graduate of the Department of Anesthesiology AUB, Assistant Professor of Anesthesiology at Columbia University, New York, reviewed the Adult Congenital Heart Disease, and the Bare Metal Versus the Drug-Eluting Stents (Fig. 8).

Dr. Vivek Moitra, Assistant Professor of Anesthesiology, Division of Critical Care, Columbia University, New York, reviewed Oxygen Delivery and
the Use of Dexmetomidine for Sedation.

In addition to the different anesthesia lectures, the program of Anesthesiology at the MEMA 2009 included a full day covering scientific presentations about Cancer Pain Management, Neuropathic Pain, Discogenic Pain, and Intractable Headache, as well as a workshop about the Ultrasound-Guided Nerve Blocks of Upper and Lower Extremities. The pain management sessions and the workshop were coordinated by Dr. Nagy Mekhail, Department Chairman of Pain Management at Cleveland Clinic, Ohio, and Dr. Loran Mounir Soliman, Director Regional Anesthesia Fellowship and Orthopedic Anesthesia at the Cleveland Clinic, Ohio (Fig. 9), as well as by Dr. Danielle Ludwin, Assistant Professor of Anesthesiology, and Dr. Oliver Panzer, Assistant Professor of Anesthesiology and Critical Care, Columbia University, New York.

One of the highlights of the MEMA 2009 was the fundraising Gala Dinner to raise money for scholarships for medical students to ensure outstanding academic training for future generations of medical professionals. The AUB President, Vice President, MEMA Chairman, and the President of the Alumni Medical Association welcomed all participants at the Gala Dinner (Fig. 10). The fabulous Gala Dinner was indeed a happy celebration of a very successful MEMA (Fig. 11).

Anis Baraka, MD, FRCA (Hon)
Emeritus Professor AUB
Emeritus Editor-in-Chief, MEJA
Introduction

The pulmonary circulation is a high flow, low pressure system. Pulmonary hypertension (PH) exists when the mean pulmonary artery pressure (PAP) is >25mm Hg at rest, or >30mm Hg during exercise.

PH has been described as being either primary or secondary. It is termed primary in the absence of secondary causes, such as pulmonary disease (e.g., COPD, ARDS), cardiac disease (e.g., shunts, left ventricular failure), thromboembolic disease, or other pathologic processes. Primary pulmonary hypertension PPH is a rare disease (1 to 2 per million), occurs three times more frequently in women than in men, and has a poor prognosis. Patients with PPH typically have a mean PAP >60mm Hg. Secondary pulmonary hypertension is more common but elevations in PAP are generally less severe (rarely >40mm Hg).

The signs and symptoms of PH are nonspecific and subtle. Left untreated, patients will experience progressive symptoms of dyspnea and right heart failure culminating in markedly curtailed survival.

Causes and Classification

Traditionally, PH has been classified as either primary or secondary. In 1998, the World Health Organization sponsored the 2nd World Symposium on PH where a new more clinically useful classification system was adopted. In 2003, during the 3rd World Symposium on PH, a modified version of the same classification was accepted. This new classification divides PH into five distinct categories (see Table 1) Genetic studies will most likely further refine current classification schemes in the near future.
excess. This chronic vasoconstriction can lead to smooth muscle hyperplasia, which may be the earliest change in PPH. As the disease progresses, the smooth muscle and endothelial cells of the pulmonary vessels undergo marked proliferation, likely due to both hypoxia and a mutation of an inhibitory receptor. This dysregulation is known as vascular remodeling and it causes thickening of the normally thin vessel walls which then increases pulmonary vascular resistance. Other contributors to PPH include increased levels of thrombogenic factors and down-regulation of K+ channels in smooth muscle cells leading to a build up of positive charge inside smooth muscle cells and thus, vasoconstriction.

Clinical Presentation

The most common presenting symptom in PH is dyspnea. Other symptoms may include angina, fatigue, weakness, and syncope. Early in the progression of PH, signs may consist of a loud pulmonic component of the second heart sound (S2), a narrowly split S2, a fourth heart sound, or an early diastolic murmur reflecting tricuspid regurgitation. Jugular venous distention, peripheral edema, cyanosis, a third heart sound, and ascites are all signs seen late in the progression of PH.

Evaluation and Diagnosis (see Table 2)

In the evaluation of a patient with PH, identifying the etiology is essential for appropriate management. The initial screening tool of choice is the echocardiogram. A contrast echocardiogram provides data involving ventricular and valvular function, estimates of PAP, and the presence of shunts. Findings on echocardiogram specific to PH might include right ventricular hypertrophy and/or dilation, left ventricular filling impairment, or paradoxical motion of the interventricular septum. An electrocardiogram of a patient with PH will commonly show right axis deviation, right ventricular hypertrophy (tall R waves in V1-V3), right ventricular strain (T-wave inversion in V1-V3), S wave in V6, and enlarged P waves in II, III, and aVF; though, an electrocardiogram cannot determine disease severity or prognosis. Chest radiograph findings include right ventricular prominence, enlarged hilar

Pathophysiology

Pulmonary vascular tone is normally very low, even when the pulmonary vessels are exposed to hypoxia and vasoconstrictive agents. Several factors have been proposed as contributors to the pathogenesis of PH. One of the earliest factors discovered to play a role is the imbalance between vasoconstrictors (endothelin-1, thromboxane) and vasodilators (prostacyclin, nitric oxide), where vasoconstrictive substances are in excess. This chronic vasoconstriction can lead to smooth muscle hyperplasia, which may be the earliest change in PPH. As the disease progresses, the smooth muscle and endothelial cells of the pulmonary vessels undergo marked proliferation, likely due to both hypoxia and a mutation of an inhibitory receptor. This dysregulation is known as vascular remodeling and it causes thickening of the normally thin vessel walls which then increases pulmonary vascular resistance. Other contributors to PPH include increased levels of thrombogenic factors and down-regulation of K+ channels in smooth muscle cells leading to a build up of positive charge inside smooth muscle cells and thus, vasoconstriction.
pulmonary artery trunk, and hyperlucent peripheral lung fields. Chest radiograph together with pulmonary function tests can demonstrate COPD, pulmonary fibrosis, or thoracic cage abnormalities as causes of PH. Patients who are overweight and have a history of snoring should undergo a sleep study to rule out obstructive sleep apnea, a potentially reversible cause of PH\(^20\). A ventilation-perfusion (V/Q) scan should be done to rule out thromboembolic disease. If abnormal, the V/Q scan should be followed up with a pulmonary angiogram and spiral chest computed tomography. Multiple serological tests, including antinuclear antibody, rheumatoid factor, HIV, and liver function can be used in further diagnostic study\(^21\). Right-sided heart catheterization remains the gold standard for diagnosis of PH as it provides confirmation of increased PAP. It also provides the ability to measure and follow hemodynamic abnormalities which can predict survival\(^22\). In addition, right-sided heart catheterization is used to test for a response to vasodilator drugs.

### Table 2

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Diagnosis of Association Conditions</th>
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<tr>
<td>Echocardiogram</td>
<td>Left ventricular dysfunction</td>
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<tr>
<td></td>
<td>Left sided valvular disease</td>
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<tr>
<td></td>
<td>Congenital heart disease with systemic-to-pulmonary shunt</td>
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<tr>
<td>Chest radiograph and Pulmonary function tests</td>
<td>Chronic obstructive pulmonary disease</td>
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<tr>
<td></td>
<td>Cystic fibrosis</td>
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<tr>
<td></td>
<td>Interstitial pulmonary fibrosis</td>
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<tr>
<td></td>
<td>Thoracic cage abnormalities</td>
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<tr>
<td>Ventilation perfusion scan</td>
<td>Chronic thromboembolic disease</td>
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<tr>
<td>Pulmonary angiogram</td>
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<tr>
<td>Spiral computed tomogram</td>
<td></td>
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<tr>
<td>Sleep study</td>
<td>Obstructive sleep apnea</td>
</tr>
<tr>
<td>Blood tests Serologic (ANA, HIV)*</td>
<td>Lupus, scleroderma, HIV infection</td>
</tr>
<tr>
<td>Liver function</td>
<td>Postpulmonary hypertension</td>
</tr>
</tbody>
</table>

* ANA-antinuclear antibody; HIV-human immunodeficiency virus
Adapted from Gaine\(^2\)

### Treatment of PAP

#### I. Oxygen.
In the 1960s, continuous oxygen administration was found to lower PAP in patients with pulmonary hypertension caused by COPD\(^23\). Subsequent trials showed that supplemental oxygen improved exercise tolerance\(^24\) and consistently increased survival times\(^25\). However, oxygen therapy does not appear to affect vascular remodeling\(^26\). At least 15 hours of daily oxygen therapy is recommended as the benefits increase with longer duration\(^27\). Oxygen works as a selective pulmonary vasodilator, although the exact mechanism by which it lowers mortality is not known.

#### II. Anticoagulants.
In the case of a patient with PH secondary to thromboembolic disease, anticoagulants have an obvious and important role. Anticoagulants also increase survival in patients with primary PH\(^28\) as it has been shown that these patients have abnormalities in blood coagulation and increased thrombotic activity\(^29,30\). Furthermore, patients with PH typically have an inactive lifestyle, venous insufficiency, and compromised pulmonary blood flow, which favors the use of anticoagulation\(^31\). The drug most often used is warfarin, which prevents the formation of vitamin K dependent clotting factors. Heparin, which enhances the action of antithrombin III and inhibits platelet aggregation, is also used.

#### III. Vasodilators.
Vasodilator therapy is very useful in the treatment of PH and represents a majority of options. Generally, vasodilators are most effective in the earlier stages of the disease, before vascular remodeling begins to outweigh vasoconstriction. The ideal vasodilator will decrease PAP, PVR, and cardiac output, without decreasing systemic vascular resistance\(^31\).

A. Calcium channel blockers (CCBs).
CCBs have been used in the treatment of PH since the early 1980s\(^32\). Nifedipine and diltiazem are the CCBs most often used because they are less cardiac depressant than other drugs in this class. They act by blocking calcium channels on smooth muscle cells, thereby inhibiting calcium influx and preventing vasoconstriction. They are most effective in a state of increased vasomotor tone (which involves a high influx of calcium). As such, CCBs are especially useful in patients with PH, where the pulmonary vasculature has elevated vascular tone compared to its normal state\(^33\). High doses of CCBs are necessary to achieve maximum benefit and as such, the drugs should be titrated to each individual’s optimal physiologic response\(^33-35\).

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CCBs appear to be most useful in the treatment of primary PH. One study showed a 94% survival rate over 5 years in patients with primary PH treated with high dose CCBs compared to a 38% survival rate over the same period in patients who were not treated with CCBs.

The effectiveness of CCBs in patients with secondary PH, especially those with PH due to COPD, is less clear and may depend on the initial PAP (the higher the initial PAP, the less effective the drug). It is important to confirm a patient’s response to vasodilators as non-responders may only develop systemic hypotension when given CCBs.

B. Prostacyclin. The vasodilator prostacyclin was first reported to reduce PAP in 1980. It is mainly produced by the vascular endothelium as a product of arachidonic acid metabolism and acts on receptors linked to adenylyl cyclase. This increases levels of cyclic adenosine monophosphate (cAMP), causing vasodilation, increased cardiac output and heart rate, and decreased PAP and right atrial pressure. Prostacyclin is of special benefit to patients with PH because production of prostacyclin is impaired in these patients. Prostacyclin has the added benefit of inhibiting both thrombus formation and vascular remodeling. These added benefits are of major importance as prostacyclin has been shown to improve long term survival in patients with primary PH, even in those patients who do not have an initial acute response to the drug. Prostacyclin also lowers PAP in other causes of PH including adult respiratory distress syndrome, persistent pulmonary hypertension of the newborn, and PH secondary to connective tissue disease. However, like CCBs, it is not effective in patients with PH due to COPD. Prostacyclin is also similar to CCBs in that the patient should be maintained at the highest dose tolerated. One disadvantage of prostacyclin is that it has a very short half life in the circulation (2-3 minutes); therefore long term treatment requires a portable infusion pump. In addition, it is not selective for pulmonary vasculature, and thus it has side effects reflective of systemic vasodilatation. Possible solutions include aerosolized and oral analogues of prostacyclin.

C. Inhaled nitric oxide (INO). Patients with PH were first administered INO in 1991. Like prostacyclin, INO is a vasodilator produced by the vascular endothelium. In addition to the endothelium, small amounts of NO are also produced in the nose. Hence, giving INO to patients who are intubated may substitute for the NO of nasal origin. It acts by directly activating guanylate cyclase which increases cyclic guanosine monophosphate (cGMP) thereby causing vasodilation. It is not inherently selective for pulmonary vasculature, but by virtue of its route of administration and rapid inactivation, INO does not typically reach the systemic circulation. NO is a major contributor to both the naturally low tone in the pulmonary vasculature and in the transition from fetal to adult pulmonary circulation. There are multiple causes of PH that respond to INO including COPD, congenital heart disease, ARDS, and especially persistent pulmonary hypertension of the newborn. NO is also very useful perioperatively for many types of heart and lung surgery including correction of congenital heart defects, heart and/or lung transplantation, and surgeries involving cardiopulmonary bypass. Disadvantages of INO include increased bleeding times due to inhibition of platelet aggregation, negative ionotropic effects, and the formation of potentially toxic products (including methemoglobin, which is of particular concern in preterm infants).

D. Alprostadil (PGE.). Alprostadil is a product of arachidonic acid metabolism and it increases cAMP to cause vasodilation, similar to prostacyclin. When inhaled, it has been shown to be effective in reducing PVR and improving arterial oxygenation in patients with ARDS. It is normally metabolized in the lung and therefore does not have systemic side effects. However, in patients with ARDS, metabolism can be impaired and systemic hypotension may occur. It has also been shown to be more effective than several other drugs for acute reversal of PH in congestive heart failure.

E. Adenosine. Adenosine acts at adenylyl cyclase linked receptors on smooth muscle cells to cause vasodilation. It is administered as a continuous intravenous infusion as it has a very short half life (10 seconds) and therefore has limited use. However, adenosine has been shown to lower PAP and PVR in patients with primary PH and can be used to test the
pulmonary vasculature’s response to vasodilators in patients with PPH. Adenosine can also be of benefit when used as an adjunct to CCBs or to treat pulmonary hypertensive crises perioperatively. Fortunately, due to the small dosing schedule, arrhythmias are rarely observed.

F. PDE inhibitors. Phosphodiesterase (PDE) inhibitors work by inhibiting one or more enzymes responsible for the breakdown of cAMP and/or cGMP. This not only causes pulmonary vasodilation, but also increases left ventricular contractility and may potentiate INO. However, they are not selective for pulmonary vasculature and can cause systemic hypotension. Several different PDE inhibitors have been used with success in lowering PAP in patients with PH secondary to COPD and in patients with PH after cardiac surgery.

G. Magnesium. Magnesium is thought to cause vasodilation by blocking calcium channels. It is also thought to enhance nitric oxide synthase activity, activate adenylate cyclase, and release prostacyclin, which would all augment vasodilation. Magnesium has been used effectively in infants with PH to improve arterial oxygenation and thus could be useful when therapy of short duration and low cost is required.

H. ACE inhibitors. Angiotensin converting enzyme (ACE) inhibitors moderate the formation of angiotensin II and the breakdown of bradykinin. Angiotensin II is a potent vasoconstrictor and smooth muscle mitogen. ACE inhibitors are similar to prostacyclin in that both were more effective with long term treatment compared to short term treatment, emphasizing the importance of minimizing vascular remodeling.

IV. Transplant. Once the only method used to treat PH, transplant is now reserved for patients who do not respond to treatment with vasodilators. Various forms of PH have been treated successfully with transplantation and survival rates of 60-86% for one year and 44-72% for four years have been reported. The two major causes of death after transplantation are obliterative bronchiolitis (which is closely associated with rejection) and infection. As such, transbronchial biopsy is routinely done for early detection of rejection and prophylaxis with trimethoprim-sulfamethoxazole is standard.

Perioperative Management

I. Preoperative management. Surgery for patients with PH is associated with significant morbidity and mortality regardless of which anesthetic technique is utilized; therefore, medical optimization is critical. A thorough history and physical should be done with a focus on the signs and symptoms of PH. An electrocardiogram, chest radiograph, echocardiogram, and possible right heart catheterization should be strongly considered. Evidence of significant right ventricular dysfunction should prompt reevaluation of the need for surgery. All medications for treating the patient’s pulmonary hypertension should be continued until and after surgery, including CCBs, despite any possible interaction with the anesthetics on myocardium or vascular resistance. Warfarin should be changed to heparin before the procedure. If the patient has never been treated for pulmonary hypertension or has a new diagnosis, a PDE inhibitor (50-100 mg sildenafil daily) should be initiated.

II. Intraoperative management:

A. Monitoring. Proper operating room monitoring for patients with pulmonary hypertension is essential. Intra-arterial blood pressure monitoring is necessary for beat to beat blood pressure monitoring to ensure adequate myocardial perfusion pressures and for frequent blood gas analysis. A pulmonary artery catheter allows monitoring of pulmonary artery pressure, right atrial pressure, and assessment of left ventricle by way of pulmonary capillary wedge pressures. Additionally, PVR, SVR, and cardiac outputs can be measures and used as guides for volume, vasodilator, or ionotropic therapy. However, care should be taken in placing these catheters as these patients are at risk for rupture of the pulmonary artery during balloon inflation. In addition, these patients are reliant on atrial contraction for adequate cardiac output, and arrhythmias associated with catheter insertion may not be well tolerated. Finally, transesophageal echocardiography can be useful to assess the preload, contractility of both ventricles, and valvular function. Because of the risks inherent with placing pulmonary artery catheters, proficient use of transesophageal echocardiography can supplant the need for catheterization.

B. Anesthetic techniques. Because the right ventricle is a thin walled, compliant muscle not
intended for pressure work, chronic PH leads to right ventricular hypertrophy and failure. Additional acute increases in pulmonary vascular tone associated with the surgical stress response are poorly tolerated in this population. The goals of management are to optimize PAP, RV preload, avoid RV ischemia and failure. During anesthesia and surgery, there are significant alterations in all the above parameters and appropriate vigilance and monitoring is vital.

Various management techniques have been described with success including regional, general, and peripheral nerve blockade. The choice of technique is not as important as the ability to adhere to the goals mentioned above. In general, the anesthesiologist should strive to use basic physiology to his advantage such as using 100% oxygen for its pulmonary vasodilator effects, and aggressively treating hypercarbia, acidosis, and hypothermia as these all cause pulmonary vasoconstriction. Nitrous oxide has been associated with increases in PVR and should be used with caution. For major surgery, general anesthesia is still the method of choice as it allows for control of ventilation. IV anesthetics have minimal effects on pulmonary vascular tone and oxygenation. Propofol has been shown to reduce PAP, PVR and MAP. It has also been associated with higher PaO2 and lower shunt fraction values; however it may also diminish right ventricular function. Opioids, which have been shown to produce dose dependent vasodilator effects in a number of animal models, reduce the vasoconstriction associated with painful stimuli. Use of volatile anesthetics carries the risk of decreasing systemic vascular resistance, myocardial contractility and potential arrhythmias. A balanced technique utilizing high dose opioids to blunt the cardiovascular response to surgical stimulation and minimal volatile anesthetics can limit the adverse effects. Used in this way, isoflurane has been demonstrated to lower PAP and PVR, and improve CO and is therefore recommended in patients with PH. There is a paucity of data evaluating either desflurane or sevoflurane in pulmonary hypertensive patients.

C. Treating intraoperative PH. Intraoperative PH should first be managed by ensuring that oxygenation, ventilation, fluid volume, and acid/base status are optimized. IV vasodilators will cause dilation of both the pulmonary and systemic vascular beds and can be useful in the setting of combined pulmonary and systemic hypertension. For example, milrinone, a PDE inhibitor, has shown to reduce both pulmonary and systemic vascular resistance in addition to augmenting myocardial contractility. In cases of pulmonary hypertension with systemic hypotension, IV vasodilators may cause worsening of systemic blood pressure and subsequent RV hypoperfusion, ischemia and failure. In this situation, the patient may benefit from therapy selective for the pulmonary vasculature such as inhaled nitric oxide (INO). INO has the benefit of improving ventilation-perfusion matching by increasing perfusion to areas of the lung that are well ventilated. Also, INO has been shown to improve PH in cardiopulmonary bypass settings. Combination therapy with INO and prostacyclin has been shown to augment the effects compared to use of monotherapy. A disadvantage of both INO and inhaled prostacyclin is their cost, which can be prohibitive. In patients who are refractory to the above therapies, right ventricular assist device implantation should be considered.

III. Postoperative management. These patients warrant intensive care monitoring as there is a high mortality in the first postoperative days. As the effects of the anesthetics wear off, patients are at risk for an increase in pulmonary vascular tone, vasospasm, cardiac arrhythmia, increased sympathetic tone, and fluid shifts. Postoperative control of pain should be effective and all precautions should be taken to avoiding hypoxemia, hypotension, and hypovolemia; especially when weaning the patient from the ventilator, stopping or decreasing any vasodilator therapy, and during extubation.

Conclusion

Surgical patients with PH present challenging clinically scenarios and are at an increased risk of significant perioperative complications. Using all available diagnostic techniques to further detail each patient’s particular form of PH is of critical importance to treatment. Recent and ongoing progress in pharmacological treatment ensures that the future will unfold a variety of successful therapies for vasoconstriction, vascular remodeling, and improved
survival for patients with PH. The anesthesiologist’s knowledge of the existing treatment options, pathophysiology, and the implications of various anesthetic agents and techniques is required to ensure the highest level of patient safety and care.

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ANESTHETIC CONSIDERATIONS IN PATIENTS WITH CARDIOMYOPATHIES

-A Review-

PRASHAN H. THIAGARAJAH*, SOMASUNDARAM THIAGARAJAH**
AND ELIZABETH A.M. FROST**

Introduction

Cardiomyopathy literally means “heart muscle disease”, and refers to the deterioration of the function of the myocardium for any reason. Patients with cardiomyopathy are often at risk of dysrhythmias or sudden cardiac death.

Cardiomyopathies can generally be categorized into two groups, based on World Health Organization guidelines: extrinsic and intrinsic. In extrinsic cardiomyopathies the primary pathology is outside the myocardium. Most cardiomyopathies are extrinsic, because the most common cause is ischemia. Intrinsic cardiomyopathies is weakness in the muscle of the heart that is not due to an identifiable external cause. To make a diagnosis of an intrinsic cardiomyopathy, significant coronary artery disease should be ruled out. The term intrinsic cardiomyopathy does not describe the specific etiology of weakened heart muscle.

Anesthetic Implications

Anesthetic management, of patients with cardiomyopathy with reduced systolic function, is challenging and may be associated with high mortality. Tabib and his group presented a retrospective analysis of 1500 autopsies following unexpected deaths and identified 43 deaths possibly related to anesthesia and surgery. Pathological examination revealed cardiac lesions in 40 cases and 20% were due to cardiomyopathy (Table-1).

Table 1 Cardiac causes of death (Tabib et al)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmogenic right ventricular cardiomyopathy</td>
<td>14 cases</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>9 cases</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>8 cases</td>
</tr>
<tr>
<td>Structural abnormalities of the His bundle</td>
<td>7 cases</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>1 case</td>
</tr>
<tr>
<td>Acute myocarditis</td>
<td>1 case</td>
</tr>
</tbody>
</table>

Of note, arrhythmogenic right ventricular cardiomyopathy (ARVC) was identified in 35% in this subgroup series. ARVC is an inherited disease with fatty fibrotic tissue infiltration of the right ventricle which causes ventricular arrhythmias and sudden death. EKG of these patients presents with T wave inversion in the anterior leads.

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The authors and reviewer have no relationships with pharmaceutical companies or manufacturers of products to disclose.
Cardiomyopathies

Cardiomyopathy can be broadly classified as heart muscle disease which decreases cardiac function. It can be classified into four groups: dilated, hypertrophic, and restrictive or Takotsubo type (Table 2).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Types of cardiomyopathies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dilated:</strong></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>Non-ischemic infections, chemotherapeutic agents, drug abuse, alcohol, and peripartum.</td>
</tr>
<tr>
<td><strong>Hypertrophic:</strong></td>
<td>(septal hypertrophy-idiopathic hypertrophic, Secondary to Hypertension)</td>
</tr>
<tr>
<td><strong>Restrictive</strong> (sarcoid)</td>
<td>Takotsubo</td>
</tr>
</tbody>
</table>

Dilated cardiomyopathy (DCM) is defined by a large heart cavity with impaired systolic function of one or both ventricles (Fig. 1). It is characterized by ventricular dilatation and impaired systolic cardiac function. It is defined by the presence of (a). fractional myocardial shortening < 25% and/or ejection fraction < 45%; and (b). left ventricular end diastolic diameter > 117% excluding any known cause of myocardial disease. Familiar dilated cardiomyopathy accounts for 20-48% of all DCM and is defined by the presence of two or more affected relatives with DCM meeting the above criteria or a relative of a DCM patient with unexplained sudden death before the age of 35. The prevalence is 920/100,000. It occurs more frequently in males (3:1) and in African Americans (2.5:1) compared to Caucasians. It may be ischemic or non-ischemic. The ischemic type is related to atherosclerosis and ischemic heart disease. The non-ischemic type may be secondary to infections (HIV, Coxsackie virus, cytomegalovirus, toxoplasmosis, Chagas’ disease, trichinosis, leptospirosis, Lyme disease), chemotherapeutic agents (adriamycin, doxorubicin), drug abuse (alcohol, cocaine, methamphetamines and heroin) or during the peripartum period.

The clinical presentation of dilated cardiomyopathy includes symptoms such as dyspnea, orthopnea, weakness, fatigue and leg edema. Physical findings are similar to those seen in congestive heart failure. Patients may have increased jugular venous distention, rales and pulmonary edema, resting tachycardia, s3 and s4 heart sounds and cardiomegaly.

Hypertrophic cardiomyopathy may occur either related to increased hemodynamic workload or without provocation. The latter is known as hypertrophic obstructive cardiomyopathy (HOCM) and idiopathic hypertrophic subaortic stenosis (IHSS). The former is termed hypertensive hypertrophic cardiomyopathy. IHSS is transmitted in an autosomal dominant pattern with variable penetrance. Echocardiography (ECHO) shows disease in about one fourth of first degree relatives.

Restrictive cardiomyopathy is the least common cause of cardiomyopathy in western countries. It is most frequently due to sarcoid disease.

Recently, Takotsubo cardiomyopathy has been described. It is a transient, reversible, left ventricular dysfunction causing severe hypotension and can mimic an acute coronary event. However, cardiac catheterization often reveals normal coronary arteries. It is rare, usually occurs in postmenopausal women associated with stress and chest pain. EKG may show ST elevation and ECHO and ventriculogram studies demonstrate left ventricular mid and apical ballooning with hypokinesia. The basal segment of the left ventricle may be hyperkinetic. It has been related to anaphylaxis after succinylcholine. Stress induced cardiomyopathy may also follow cephalosporin induced anaphylaxis. Sympathetic discharge can trigger transient cardiomyopathy. In one case report, although vital signs responded favorably to resuscitative efforts after an anaphylactic reaction during general anesthesia, cardiovascular collapse reappeared with transient ventricular tachycardia shortly after transfer to the intensive care unit. There was diffuse regional wall motion abnormalities in the mid ventricular region. Increased MB fractions of creatinine kinase and troponin T levels indicated myocardial necrosis but coronary catheterization indicated normal arteries.
Management

Two key factors exist in the management of patients with cardiomyopathies; one is to improve systolic function and the other is to prevent sudden death due to ventricular arrhythmias.

Several types of treatment for dilated cardiomyopathy aim at improving systolic function. Patients should initially be managed medically. Biventricular pacing, cardioplasty or cardiac transplant may also be required to improve cardiac function. Arrhythmias are managed with amiodarone and/or an automatic implantable cardioverter defibrillator (ICD). Amiodarone prevents life threatening arrhythmias and an ICD promptly treats the arrhythmias with an electrical shock impulse.

Medical management to improve systolic function includes administration of diuretics, beta-blockers, angiotensin converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARB).

In the renin-angiotensin system, angiotensin II causes vasoconstriction, and release of aldosterone, vasopressin and anti diuretic hormone (ADH). All these factors increase the blood volume and cause hypertension. ACE inhibitors prevent angiotensin I from converting into angiotensin II and thus prevent the subsequent hypertensive effects. The net effect is a reduced afterload. In patients with cardiac disease, ACE inhibitors reduce the risk of death. They also slow heart emodling, prevent the heart from becoming less efficient over time and improve ventricular function.

Biventricular pacing devices are often used in patients with cardiomyopathies to improve systolic function (Fig. 2). Biventricular pacing (BVP) is beneficial for patients with severe cardiomyopathy in moderate to severe congestive heart failure with an EF <30% and in ventricular asynchrony. An interventricular conduction defect with a wide QRS complex is indicative of asynchrony of the two ventricles. Biventricular leads are programmed to synchronize the contraction of the right and left ventricles thereby improving the ejection fraction. BVP improves left ventricular (LV) systolic function, decreases LV size, decreases mitral regurgitation, and shortens the prolonged QRS interval. Quality of life is markedly improved.

Right ventricular pacing is achieved by the lead placed in the apex of the right ventricle. This lead in addition to pacing function has arrhythmia detection and defibrillation function. Two shock coils are incorporated in the right ventricular lead for defibrillation. Left ventricular pacing is obtained by a lead placed into the obtuse marginal branch of the coronary sinus (Fig. 2). The pacing of the two ventricles can then be synchronized.

Cardioplasty has been developed in several ways to improve systolic function. In the common type, the latissimus dorsi muscle is placed around the heart as a free flap, and its contraction synchronized to augment

"Fig. 2
Biventricular pacing with ICD. Three leads: right atrial lead, right ventricular lead and 3rd lead via the coronary sinus for the left ventricle. The right ventricular lead has the two shock coils for the ICD

Right atrial lead

Left ventricular lead in the coronary sinus

Shock coil in right ventricular lead"
ventricular systolic function. Mitral valve repair will also improve cardiac function.

Cardiac transplant may be recommended for patients with end stage dilated cardiomyopathy, not amenable to other therapies. Left ventricular assist devices may be used as a “bridge” prior to transplant when a patient is awaiting a donor.

**Antiarrhythmic drugs and ICDs**

In addition to low ejection fraction, patients with cardiomyopathy tend to develop ventricular arrhythmias and sudden death. Therefore, oral administration of amiodarone an antiarrhythmic medication is prescribed, or a cardioverter defibrillator is implanted to treat ventricular tachycardia.

An implantable cardioverter-defibrillator is more effective than amiodarone in reducing mortality in high-risk patients with previous myocardial infarction and is usually the primary treatment. Amiodarone may be used as an adjunct to reduce the frequency of ICD shocks.

A single chamber ICD consists of a generator which contains a battery and a small computer. A ventricular lead with two shock coils is attached to the generator (Fig. 3). The battery life usually ranges from 4 to 6 years. At the tip of the lead are a sensor and a pacer. These devices are able to distinguish between ventricular fibrillation and ventricular tachycardia (VT). If ventricular fibrillation (VF) occurs then a 25 Joules shock is delivered from the ICD right ventricular lead shock coil. If it is VT, then it may pace the heart faster than the rate of VT to override it and break the VT. This is referred to as antitachycardia pacing. When bradycardia occurs pacing function is initiated.

Other indications for ICDs are in patients likely to develop ventricular arrhythmias. These include IHSS, prolonged QT syndrome or Brugada syndrome. Brugada syndrome is an inherited disease with an increased risk of sudden cardiac death due to ventricular fibrillation. The EKG may manifest a right bundle branch block pattern.

**Preoperative preparation (Table 3)**

The preoperative preparation of these patients must be meticulous as they have minimal or no cardiac function.

**Preoperative assessment:**

<table>
<thead>
<tr>
<th>Volume status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue Antiarrhythmic drugs</td>
</tr>
<tr>
<td>Drug interactions with ACEs inhibitors. Electrolytes-Potassium/Magnesium correction</td>
</tr>
<tr>
<td>Hemoglobin optimized</td>
</tr>
<tr>
<td>ICD-deactivation</td>
</tr>
<tr>
<td>Inotropes (Resistance to usual dose)</td>
</tr>
<tr>
<td>Intraaortic balloon pump if necessary</td>
</tr>
</tbody>
</table>

**Fig. 3**

*Chest X-Ray demonstrating the leads of ICD with two translucent segments-shock coils*
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ANESTHETIC CONSIDERATIONS IN PATIENTS WITH CARDIOMYOPATHIES

of electrocautery can be mistaken by the sensor in the ICD as a tachyarrhythmia. The antiarrhythmic function of the ICD is activated and the patient receives an inappropriate shock. This shock, if discharged at the vulnerable phase of the cardiac electrical cycle, may induce ventricular arrhythmia. Also multiple shocks with repeated uses of the cautery, can damage the heart, decrease cardiac function, damage the generator or deplete the battery of the ICD. Therefore, all ICDs should be deactivated prior to surgery if use of cautery is planned. Magnet placement on the generator of some ICDs may deactivate its shock therapy function but not the pacing or sensing capability.

With other ICDs (Angeion, Guidant, St. Jude, Ventritex) placement of a magnet will not have any effect on function. Ideally, in the management of these patients, a cardiologist or the manufacturer representative should be consulted preoperatively. Once the ICD is deactivated, defibrillator pads must be placed on the patient’s chest and connected to an external defibrillator as a stand-by to treat any ventricular arrhythmia that may occur.

**Management of Patients with ICD prior to surgery**

Many patients with cardiomyopathies have an ICD for defibrillating function. Some patients may not be aware of the type, whether it is a simple pacemaker or an ICD. ICDs have larger generators than pacemakers (Fig. 4). The right ventricular lead of an ICD, unlike a pacemaker lead, has two sets of spiral segments which can be identified by chest X-Ray (Figs 3, 5).

The difficulty encountered with ICDs during surgery is that the energy discharged during the use reserve. Any decrease in myocardial contractility, heart rate, or vasodilatation can cause profound hypotension. Preoperatively, patients tend to be dehydrated, as most have been diuresed, a further cause for hypotension during anesthetic care. However this dehydration is generally beneficial for these patients as it improves limited cardiac function. But they easily can become hypotensive with anesthetics which cause vasodilatation. Preoperative hydration may not be desirable as it may lead to congestive heart failure.

Fluid management is critical. To err on the hypovolemic state is prudent. Therefore a vasopressor to mitigate against the vasodilating effect of the anesthetic is a rational approach.

As patients may develop ventricular arrhythmias in the perioperative period, antiarrhythmic medications should be continued. Some patients may already have had an ICD implanted. During the anesthetic care drug interaction resulting in hypotensive episodes requiring vasopressor therapy has been reported when ACE inhibitors are combined with diuretic therapy.

Arrhythmias occur when potassium or magnesium levels are decreased. These electrolytes should be measured preoperatively and corrected as necessary.

Oxygen carrying capacity should be adequate. The main determinants of oxygen carrying capacity are cardiac output and hemoglobin. Therefore, hemoglobin should be maintained at a higher level and 13-14gms/100ml has been recommended. To improve cardiac output, inotropes, biventricular synchronized pacing or an intraaortic balloon pump may be required.

**Comparison of size of ICD generator (left), with pacemaker generator**

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Fig. 4

ICD shock-coils are seen in this chest-X-Ray

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Fig. 5

ICD shock-coils are seen in this chest-X-Ray

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In a critically ill patient with cardiomyopathy, if the planned surgery is complex and absolutely necessary, an intraaortic balloon pump may be placed preoperatively.

**Anesthetic management**

Anesthetic management of patients with severe cardiomyopathies is associated with a high morbidity and mortality and therefore requires careful planning, preparation and monitoring (Table 4). Many of these patients present for ICD or biventricular pacemaker placement. However, they may present emergently or for any type of surgery.

Preoperatively the diagnosis of cardiomyopathy may be lacking or not easily forthcoming. A patient with a history of coronary artery disease with a low EF is usually treated with furosemide, ACE inhibitors and has an implanted ICD. Therefore, in the preoperative evaluation, these four signs (Quadratic sign; CHF, cardiomegaly, ICD, EKG changes) if present, should alert the anesthesiologist to a low EF. If the preoperative diagnosis of cardiomyopathy is missed, routine anesthetic management carries considerable risk. Patients will likely become profoundly hypotensive. Prompt recognition and immediate intervention of hemodynamic instability with appropriate vasoactive or inotropic medications is required to prevent deterioration. Anesthesiologists initially use neosynephrine in incremental doses of 100 µg every 30-40 seconds and initiate a norepinephrine infusion at 4-8µgs/min or dopamine at 5µgs/kg/min and adjust dose range to titrate the systolic blood pressure above 90-100 mmHg.

Patients can also manifest life threatening ventricular arrhythmias. Anesthesiologists should be prepared to use lidocaine, amiodarone or defibrillation to treat the arrhythmia.

**Table 4**

**Presentation of cardiomyopathy patients**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>History of CHF/CAD</td>
</tr>
<tr>
<td>2.</td>
<td>Medications: furosemide, ACE inhibitors, digoxin, beta blocker</td>
</tr>
<tr>
<td>3.</td>
<td>Cardiomegaly on chest X-ray</td>
</tr>
<tr>
<td>4.</td>
<td>ICD/Biventricular pacer with ICD (EF&lt;30%)</td>
</tr>
<tr>
<td>5.</td>
<td>EKG may have conduction defects</td>
</tr>
<tr>
<td>6.</td>
<td>Blood pressure may be low. Heart rate elevated.</td>
</tr>
</tbody>
</table>

In addition to the basic monitoring (BP, pulse oximeter, EKG, end-tidal CO2), direct arterial blood pressure monitoring is required to identify abrupt hemodynamic changes. In situations where the surgery is complex or of long duration, transesophageal echocardiography (TEE) monitoring is also appropriate. When a patient becomes hypotensive during anesthetic management, TEE differentiates the cause of hypotension as due to global hypokinesia, regional ischemic ventricular dysfunction or hypovolemia. These changes may be treated with inotropes, coronary vasodilators or fluids, as indicated. Recently, intraoperative Doppler tissue imaging (DTI) has been added as a valuable diagnostic tool. DTI displays and measures systolic and diastolic velocity from a myocardial region. It is simple to perform and independent of endocardial imaging. Assessment of systolic and diastolic function on regional (detection of ischemia) as well as global levels (ejection fraction, grading of diastolic function) and evaluation of filling pressure can all be derived from DTI signals.

The cardinal feature of dilated cardiomyopathy is the reduction in the systolic function or the left ventricular ejection fraction (LVEF). Patients with LVEF over 45% usually do not require any change in anesthetic technique.

Anesthetics not only depress central nervous system function but also cardiac function. They tend to depress the myocardium, slow the heart rate and dilate the blood vessels. Anesthetic management needs to be customized for those with LVEF below 45%. Therefore, selecting the type and dose of anesthetics with minimal vasodilatation and myocardial depressing effect is prudent. Drugs like ketamine, etomidate and narcotics have minimal depressing effect on cardiac function and are used frequently. Conventional anesthetics like propofol, sodium thiopental or isoflurane in recommended doses depress cardiac function. However, recent laboratory studies indicated that sevoflurane in a porcine model decreased myocardial infarct size after prolonged coronary occlusion. Sevoflurane cardioprotection was substantiated in the juvenile intact organism.

Nerve blocks are a rational approach for appropriate surgery as they have minimal hemodynamic abrasion.
Anesthetic management of the parturient with cardiomyopathy is challenging, as the baby’s welfare must be considered in the management of the critically ill mother. Usually regional techniques are preferred for cesarean section in a normal parturient but may exaggerate the hypotension in a cardiomyopathic parturient. If general anesthetics are indicated in an emergency for a mother who is decompensating, drugs with minimal effect on the baby need to be selected. Etomidate with remifentanil has been successfully used without respiratory depression of the baby. Remifentanil crosses the placenta but is quickly metabolized by the baby’s liver. It must also be borne in mind that most of the cardiac drugs will also cross the placenta and/or be excreted in the mother’s milk and can affect the baby.

Use of vasoactive or inotropic drugs may be required frequently to counteract the negative effects of the anesthetics on cardiac function. Inotropic drugs such as dopamine, epinephrine, dobutamine and milrinone increase the ejection fraction significantly. In clinical reports dopamine is frequently used during the anesthetic care of these patients. Dopamine in the appropriate dose range has positive inotropic, chronotropic and vasoconstrictive effects making it an ideal agent to negate adverse cardiovascular effects of anesthetics.

The beta receptors in the myocardium, B₁ and B₂ receptors, control contractility and B₃ influence relaxation. With cardiomyopathy there is decreased myocardial beta-adrenergic receptor density or sensitivity of these receptors. Therefore conventional doses of beta stimulants may be inadequate and larger doses may be required.

**Conclusion**

Cardiomyopathies as a class are identified increasingly as a result of improved means of detection and an aging population. Also, presentation may be sudden or already well known. Consequently, patients with this underlying condition may present at any time for anesthesia or intraoperatively. It is essential that anesthesiologists understand the underlying pathology to better manage these patients.
References


POSTOPERATIVE ANALGESIA IN CHILDREN: AN UPDATE

GURMUKH DAS PUNSHI*, MOHAMMAD HAMID**
AND MANSOUR AHMED KHAN***

Introduction

Acute pain is one of the most common adverse stimuli experienced by pediatric population as a result of surgery, illness, any injury and necessary medical procedure. Pain is associated with increased anxiety, avoidance, somatic symptoms, and increased parent distress and may lead to long term effects1.

Despite the magnitude of these effects, the acute pain has on a child is often inadequately assessed and treated. Numerous myths, insufficient knowledge among caregivers, and inadequate application of knowledge contribute to the lack of effective management2. Fear of adverse reactions and toxic effects often contributed to the inadequate use of analgesics.

The International Association for the Study of Pain has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage3. Several experts suggest that the neonate’s expression of pain does not fit within the strict definition of the International Association for Study of Pain because of the requirement for self-report. This lack of ability to report pain contributes to the failure to recognize and treat pain aggressively during infancy and early childhood4. Because neonates cannot verbalize their pain, they depend on others to recognize, assess, and manage their pain. Therefore, health care professionals can diagnose neonatal pain only by recognizing the neonate’s associated behavioral and physiological responses.

A large scale survey reported that 40% of pediatric surgical patients experienced moderate or severe postoperative pain and that 75% had insufficient analgesia4. The structural components necessary to perceive pain are already present at about 25 weeks gestation whereas the endogenous descending inhibitory pathways are not fully developed until mid-infancy5. Opioid and other receptors are much more widely distributed in fetuses and neonates6. Fetuses subjected to intrauterine exchange transfusion with needle trans-hepatic access will show both behavioral signs of pain as well as a hormonal stress response7. Significant pain stimulation without proper analgesia, for example during circumcision, will not only cause unacceptable pain at the time of the intervention but also produces a ‘pain memory’ as illustrated by an exaggerated pain response to vaccination as long as six months following the circumcision8. Both neonates and infants are able to mount a graded hormonal stress response to surgical intervention and adequate intra- and postoperative analgesia will not only modify the stress response but has also been shown to reduce morbidity and mortality9-10.
The following guidelines are designed to support quality health care and effective management of acute intraoperative and postoperative pain management. Objective of present guidelines are to recognize pain in children, minimize moderate and severe pain safely in all children, prevent pain if possible, bring pain rapidly under control and to continue pain control after discharge from the hospital.

Assessment Tools

Recognition and assessment of pain is the first and most important step in successful pain management. Pain should be assessed on a regular basis using self-report, behavioral observation and physiologic measures, bearing in mind the age of the child and his or her communication capabilities. There are many different scales that can be used in different age groups. It is of importance to use a scale that is feasible in the clinical setting11.

- Children eight year of age and above can generally use visual analogue pain scales used by adults, which involve rating the intensity of pain on a horizontal scale.

1. "---------------------------------------------10"

- For children from three to eight years old, self reported measures use either face scales (series of photographs or drawings of faces showing increasing degree of distress) or color-analogue scales (rulers with increasing intensity of red color signifying increasing intensity of pain). Good agreement was reported between the results obtained with a photographic face scale and those obtained with a color-analogue scale among three to seven year old children12.

- Behavioral observational scales are the primary methods of pain assessment for neonates, infants, and children under four years of age or for children with developmental disabilities12. Such scales may score facial expressions, limb and trunk motor responses, verbal responses, crying or combinations of behavioral and autonomic measures. Some of these scales record “distress”, which reflects fear and anxiety as well as pain. Behavioral scales may under represent the intensity of persistent pain, as compared with self-reports.

- Physiological indexes of pain are useful and include changes in heart rate, respiratory rate, blood pressure, oxygen saturation, vagal tone, palmer sweating, and plasma cortisol or catecholamine concentrations although they may be nonspecific. For example, tachycardia may be caused by hypovolemia or hypoxemia, rather than pain. Thus, pain assessment in neonates, infants, and children less than four years of age and in children with major disabilities remains a challenge.

Techniques of Pain Control

Combination of pharmacological and non pharmacological techniques have proven to be useful in managing pain in children.

Non pharmacological

A variety of non pharmacologic pain prevention and relief techniques have been shown to effectively reduce pain from minor procedures in neonates. These include use of oral sucrose/glucose, breastfeeding, nonnutritive sucking, “kangaroo care” (skin-to-skin contact), facilitated tuck (holding the arms and legs in a flexed position), swaddling, and developmental care, which include limiting environmental stimuli, lateral positioning, the use of supportive bedding and physical therapy. These measures have been shown to be useful in preterm and term neonates in reducing pain from a heel stick, venipuncture, and subcutaneous injections and are generally more effective when used in combination13.

Pharmacological

Analgesics can be administered through different routes depending on the age, type of procedure, presence of intravenous line, patient preference and severity of pain.

Oral route

Oral route is the preferred approach in routine practice. Alternative routes are necessary for patients who have impaired swallowing or gastrointestinal
Rectal route

Rectal route is particularly useful in immediate postoperative period where patient is not allowed to take oral medication.

Regional (Table 1)

Regional analgesia includes Local infiltration, Peripheral nerve blocks and Central nerve blocks (spinal, epidural, Caudal). The most common regional block in pediatric patient is caudal block.

Non Steroidal Anti Inflammatory Drugs (Table 2)

There are mainly four categories of drugs which are effective in pain management. These are non opioids (Paracetamol, Non steroidal anti-inflammatory drugs, and clonidine), opioids (Morphine, Meperidine, and Tramadol), local anesthetics and adjuvant drugs.

### Table 1

*Maximum local anesthetic doses in infants and children*

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose mg/kg</th>
<th>Continuous epidural analgesia (CEA) mg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine (plain)</td>
<td>5</td>
<td>Not available</td>
</tr>
<tr>
<td>Lidocaine (epinephrine)</td>
<td>7</td>
<td>Not available</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>2: &lt; 3 months 3: child dose</td>
<td>1 (0.5-1.25)</td>
</tr>
<tr>
<td>Levobupivacaine</td>
<td>2</td>
<td>Not available</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>2</td>
<td>1 (0.5-1.25)</td>
</tr>
</tbody>
</table>

### Table 2

*Recommended doses of non-steroids for pediatric patients*

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose</th>
<th>Interval (hours)</th>
<th>Maximum daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>5-15 mg/kg PO</td>
<td>4-6</td>
<td>Children: &lt; 100mg/kg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infants: 75mg/kg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Newborns: (&lt; 32 wks PCA): 60 mg/kg/d</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(28-32 wks PCA): 40 mg/kg/d</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>4-10 mg/kg PO</td>
<td>6</td>
<td>&lt; 40mg/kg/day</td>
</tr>
<tr>
<td>Naproxen</td>
<td>5-10 mg/kg PO</td>
<td>8-12</td>
<td>20 mg/kg/day</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>1-2 mg/kg PO</td>
<td>8-12</td>
<td>Not available</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>0.3-0.5 mg/kg I/V</td>
<td>6-8</td>
<td>&lt; 2mg/kg/day</td>
</tr>
</tbody>
</table>
Acetaminophen (Paracetamol)

Acetaminophen is the most widely prescribed analgesic used for mild type of all pains. It lacks the troublesome side effects of other NSAIDs. Its effects are mediated by central cyclooxygenase III (COX-III) inhibition. Acetaminophen can be given orally or rectally. Acetaminophen is metabolized in the liver primarily by glucuronidation and sulfation.

The recommended oral dosage is 10 to 15 mg per kilogram every four hours for children. Rectal administration produces delayed and variable uptake; single bolus dose of 35 to 45 mg per kilogram generally produces therapeutic plasma concentrations, with prolonged clearance. Subsequent rectal doses should be smaller (e.g., 20 mg per kilogram), and the interval between doses should be extended to at least six to eight hours.

Single rectal doses of 20 mg per kilogram produced safe plasma concentrations in preterm neonates. Daily cumulative acetaminophen doses by the oral or rectal route should not exceed 100 mg per kilogram per day for children, 75 mg per kilogram for infants, 60 mg per kilogram for term and preterm neonates beyond 32 weeks of postconceptional age, and 40 mg per kilogram for preterm neonates from 28 to 32 weeks of postconceptional age.

Acetylsalicylic acid (Aspirin)

Because of its association with Reye’s syndrome, aspirin is now used only rarely in pediatric patients suffering from rheumatologic conditions can be prescribed as 10-15 mg/kg PO.

NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) are used for the management of mild to moderate pain. They are used alone or in combination with opioids. Main advantage of NSAIDs is lack of respiratory depression and sedation. Their mechanism of action is through the inhibition of cyclooxygenase (COX), the enzyme responsible for metabolizing arachidonic acid. When arachidonic acid is released from traumatized cell membranes, it is metabolized by COX to form prostaglandins and thromboxanes, which in turn sensitize peripheral nerve endings and vasodilate vessels, causing pain, erythema, and inflammation. There are two COX isoenzymes. The constitutive form of COX (COX-1) is present throughout the body and the prostaglandins and thromboxanes that are produced are essential for functions such as gastric mucosa protection, renal blood flow regulation, and platelet aggregation. Potential complications of COX-1 inhibition include gastric ulceration, bleeding, altered renal function, and bronchoconstriction. COX-2 is called an “inducible COX” and is present only in traumatized cells or inflamed tissue. Most NSAIDs are nonselective COX inhibitors, but the potential attraction of selective COX-2 inhibition in the reduction of side effects is apparent. Presently, the future of COX-2 inhibitors in children is uncertain. Ibuprofen can be administered 6-8 hours interval in doses of 8 mg/kg PO and 20 mg/kg rectally. Ketorolac in doses of 0.4 to 1.0 mg/kg is useful for mild to moderate pain in children when parenteral administration is required.

Opioids (Tables 3, 4, 5)

Opioids are morphine-like substances. The term opioid is derived from opium (from the Greek term for juice) which is extracted from the poppy plant. Opioids are used for moderate to severe nociceptive pain. Opioids bind to pre- and postsynaptic cell membranes in the central nervous system through the specific opioid receptors, resulting in neuronal inhibition by decreasing excitatory neurotransmitter release from presynaptic terminals or by hyperpolarizing the postsynaptic neuron. Opioid receptors are classified as mu, kappa, delta, and sigma. The mu receptor is further subdivided into subclasses mu1, which mediates supraspinal analgesia and dependence, and mu 2, which mediates respiratory depression, intestinal dysmotility, sedation, and bradycardia. Opioids are classified as agonists, partial agonists, agonist-antagonists, and antagonists. Examples of the mu1 agonists include morphine, hydromorphone, meperidine, methadone, fentanyl, sufentanil, remifentanil, codeine, oxycodone, and hydrocodone.
Morphine

Morphine is the standard opioid with which all other opioids are compared. It has a rather poor oral bioavailability (25-40%), which necessitates a larger oral dose when converting from i.v. to enteral administration. Morphine is metabolized in the liver to morphine-3-glucuronide (inactive) and morphine-6-glucuronide (active), which are both excreted by the kidneys. Generally, the elimination half-life is longer and the clearance is decreased in newborns compared with older children and adults. This difference is especially pronounced in preterm neonates. In addition, less morphine is protein bound in neonates, allowing a greater proportion of unbound

Table 3
Recommended single doses of opioids for pediatric patients

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Single dose</th>
<th>Interval (hours)</th>
<th>Potency (relative to morphine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>0.5-1 mg/kg PO</td>
<td>4-6</td>
<td>Not available</td>
</tr>
<tr>
<td>Meperidine</td>
<td>0.5-1.0 mg/kg I/V</td>
<td>2-3</td>
<td>0.1</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.05-0.15 mg/kg I/V 0.3 mg/kg PO</td>
<td>2 3-4</td>
<td>1</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.5-1 mcg/kg I/V</td>
<td>1-2</td>
<td>50-100</td>
</tr>
<tr>
<td>Tramadol</td>
<td>1-2 mg/kg I/V</td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>25-50 mcg/kg I/V</td>
<td>2-4</td>
<td></td>
</tr>
</tbody>
</table>

Table 4
Recommended continuous infusion dose of opioids for pediatric patients

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Continuous infusion rate doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine</td>
<td>0.1 0.3 mg/kg/hr</td>
</tr>
<tr>
<td>Morphine</td>
<td>10-40 mcg/kg/hr</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.5 mcg/kg/hr</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>10-15 mcg/kg/hr</td>
</tr>
</tbody>
</table>

Table 5
Recommended PCIA dose of opioids for pediatric patients

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Bolus dose mcg/kg</th>
<th>Lockout interval min</th>
<th>Continuous infusion mcg/kg/hr</th>
<th>1 hour limit mcg/kg/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>20</td>
<td>8-10</td>
<td>0-20</td>
<td>100</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.5</td>
<td>6-8</td>
<td>0-0.5</td>
<td>25</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>20</td>
<td>8-10</td>
<td>0-20</td>
<td>100</td>
</tr>
</tbody>
</table>

Agonist-antagonist opioids, which are agonists at one receptor type and antagonists at another receptor, include nalbuphine and pentazocine. Analgesia by agonist-antagonists is mainly kappa & sigma-mediated, with antagonism or partial agonism at the mu receptor.

A partial agonist such as buprenorphine exerts less than full response at a receptor site.

Opioid antagonists include naloxone and naltrexone.

Side-effects common to opioid agonists include respiratory depression, sedation, nausea, vomiting, pruritus, urinary retention, ileus, and constipation. Less common effects are dysphoria, hallucinations, seizures, and myoclonic movements. Opioids can be used as oral, sublingual, transdermal, intranasal, and rectal routes.

Morphine

Morphine is the standard opioid with which all other opioids are compared. It has a rather poor oral bioavailability (25-40%), which necessitates a larger oral dose when converting from i.v. to enteral administration. It can be given through multiple routes (intravenous, oral, subcutaneous, intrathecal, epidural, and intra-articular). Morphine is metabolized in the liver to morphine-3-glucuronide (inactive) and morphine-6-glucuronide (active), which are both excreted by the kidneys. Generally, the elimination half-life is longer and the clearance is decreased in newborns compared with older children and adults. This difference is especially pronounced in preterm neonates. In addition, less morphine is protein bound in neonates, allowing a greater proportion of unbound
morphine to penetrate the brain, thus increasing the risk for respiratory depression. The elimination half-life and clearance reach adult values within 2 months of age\textsuperscript{16}.

Recommended single intravenous dose is 0.08-0.1 mg/kg while epidural and caudal are given as 50 mcg/kg and 120-150 mcg/kg respectively\textsuperscript{15}. If morphine is given by PCA, start with bolus dose of 20 mcg/kg, lockout interval 5 min with or without background infusion 4 mcg/kg/h (especially first 24 h)\textsuperscript{4}.

**Pethidine (Meperidine)**

Meperidine is a synthetic opioid derived from phenylpiperidine. It has 1/10\textsuperscript{th} the analgesic potency of morphine and is metabolized in the liver by hydrolysis and N-demethylation. It has an elimination half-life of approximately three hours. It offers no advantage over morphine in terms of side effects. The primary metabolite, normeperidine, can cause hallucinations, agitation and seizures, when meperidine is used for an extended period\textsuperscript{11}. It can be used intramuscularly & intravenously. It is used in single doses for postoperative shivering\textsuperscript{17} Meperidine should also not be used in conjunction with monoamine oxidase inhibitors or in patients with hyperthyroidism\textsuperscript{14}.

Recommended intravenous dose is 1-1.5 mg/kg with 2-3 hour interval after titration while usual intramuscular dose is 0.8-1 mg/kg with 3-4 hour interval\textsuperscript{15}.

**Fentanyl**

Fentanyl is a synthetic opioid that is 100 times more potent than morphine. It is highly lipophilic, resulting in significant brain penetration. Fentanyl has a short duration of action because of redistribution out of the plasma into body tissues\textsuperscript{14}. Metabolism is through glucuronidation in the liver to inactive metabolites that are excreted by the kidney. Because of its potency, hemodynamic stability, and brief duration of action in small doses, fentanyl is an attractive analgesic for short painful procedures in children, especially in an intensive care unit setting\textsuperscript{16}. Fentanyl can be given through multiple routes: intravenous, epidural, intrathecal, nasal, transmucosal, and transdermal. With repeated dosing or with prolonged infusions, fentanyl may accumulate in the body and leads to longer duration of action.

Transmucosal fentanyl permits rapid onset of analgesia for brief, painful procedures in hospitalized children in whom intravenous access is not available. Transmucosal is more efficient than oral administration because it bypasses the hepatic first pass metabolism of the oral route, which reduces the availability of fentanyl by 25% to 33%\textsuperscript{14}.

Transdermal fentanyl provides a consistent analgesic effect for selected patients, such as children with severe pain due to cancer. Transdermal fentanyl administration is available in patches of 25, 50, 75, and 100 mg/h for use lasting 2 to 3 days. It has a long onset time but also a long duration that persists after the patch is removed\textsuperscript{14}. Fentanyl can be given intravenously as a single bolus of 1-1.5 µg/kg or infuse continuously at 2-4 µg/kg/hr\textsuperscript{15}.

**Codeine**

Codeine is used to treat moderate pain\textsuperscript{11}. Codeine is a mu agonist and a derivative of morphine. It is a commonly used oral opioid most often combined with acetaminophen in liquid or tablet form. Codeine is 0.10 times as potent as morphine. Its bioavailability is 60% after oral administration, with an onset time of 20 minutes and an elimination half-life of 2.5 to 3 hours. Codeine is metabolized in the liver and then excreted in the urine\textsuperscript{18}. Five to ten percent of codeine is metabolized by O-demethylation in the liver by a P-450 oxidase pathway (CYP2D6) to produce morphine. This conversion is necessary for analgesia to occur after codeine administration. When the codeine and acetaminophen combination is used, care must be taken to stay within safe dosage ranges of acetaminophen\textsuperscript{14}. Recommended doses: 0.5-1 mg/kg PO with 4-6 hr interval\textsuperscript{15}.

**Nalbuphine**

Nalbuphine is a kappa agonist and a mu antagonist. It has an analgesia equivalent to morphine up to a dose of approximately 200 mg/kg, at which point it has a ceiling effect of analgesia. Kappa mediated side effects of sedation, dysphoria, or euphoria are likely at higher doses. Nalbuphine is metabolized mainly in the liver and has a half-life of approximately 5 hours. It is usually given intravenously. When given orally, it has
a bioavailability of only 20% to 25%. Care is needed when using nalbuphine in opioid-dependent children in order not to induce opioid withdrawal\textsuperscript{14}.

\textit{Naloxon}

Naloxone is antagonist at all opioid receptors. It is used for opioid induced side effects, like respiratory depression. It also is used in smaller doses for pruritis (1-2 mcg/kg IV). Naloxone is metabolized in the liver and has an elimination half-life of 60 minutes\textsuperscript{14}.

\textit{Tramadol}

Tramadol a synthetic cyclohexanol, 4-phenyl-pipridine chiral racemic analog of codeine, is a centrally acting analgesic that possesses weak affinity for the mu opioid receptor and modifies transmission of nociceptives impulses through inhibition of monoamines (norepinephrine and serotonin) reuptake, but not production. Tramadol is approximately 1/10 as potent an analgesic as morphine\textsuperscript{15}. In general, tramadol is a safe and effective analgesic for mild to moderate pain in children\textsuperscript{19}. The recommended dose of tramadol is 1 to 2 mg/kg (maximum 100 mg) every 6 hours, with a maximum daily dose of 8 mg/kg/d or 400 mg/d\textsuperscript{14}.

\textit{Ketamine}

Ketamine is a phencyclidine derivative and a dissociative anesthetic. It is a potent analgesic in subanesthetic doses and is often used for short painful procedures in children in the emergency room and ICU settings. It can be administered intravenously, orally, rectally, and intramuscularly\textsuperscript{14}. In the postoperative period a low-dose continuous infusion can offer an improved pain situation while minimizing side effects. Because of increased secretions and possible dysphoric effects, ketamine is often combined with an anticholinergic agent and a benzodiazepine. The analgesic effects of ketamine are mediated by NMDA receptor antagonism. Oral bioavailability is 20% to 25%. Ketamine is highly lipid soluble, with rapid redistribution. Ketamine is N-demethylated in the liver by the cytochrome P-450 system Intravenous doses of 0.25 to 0.5 mg/kg can produce intense analgesia for 10 to 15 minutes, although the elimination half-life is 2 to 3 hours. A dose of 1 to 2 mg/kg IV may be needed for more painful procedures such as fracture reduction.

\textbf{Conclusion}

Despite several advances in assessment and management of acute pediatric pain, significant number of children still suffer from moderate to severe pain in the postoperative period. There is a need for education and training of care provider, evidence based research, development of easily applicable assessment tool and effective treatment of pain by pharmacological and non pharmacological means. Institutions should develop and implement guidelines and protocols for pediatric pain prevention, assessment and management according to local environment.
References

ANESTHESIA OUTCOME PREDICTION

Zhibin Tan*, Romeo Kaddoum**, Le Yi Wang***, and Hong Wang****

Abstract

This paper studies the problem of outcome prediction in anesthesia procedures. Anesthesia depth and blood pressures are used as typical outcomes in this study. Traditional diagnosis and control in anesthesia focus on a one-drug-one-outcome scenario. It is well understood, however, that consideration of multiple outcomes is necessary and beneficial for anesthesia managements. This paper introduces a method of modeling that significantly reduces the complexity of the problem and yet retains model accuracy. Utility of the modeling method is demonstrated in the areas of anesthesia outcome prediction and decision assistance.

Introduction

Real-time anesthesia decisions are exemplified by general anesthesia for attaining an adequate anesthetic depth (consciousness level of a patient), ventilation control, etc. One of the most critical requirements in this decision process is to predict the impact of the inputs (drug infusion rates, fluid flow rates, etc.) on the outcomes (consciousness levels, blood pressures, heart rates, etc.). This prediction capability can be used for control, display, warning, predictive diagnosis, decision analysis, outcome comparison, etc. The core function of this prediction capability is embedded in establishing a reliable model that relates the drug or procedure inputs to the outcomes. Typically, an anesthesia drug influences more than one patient outcomes. For monitoring, diagnosis, and control, it becomes essential that the impact of anesthesia drugs on multiple outcomes be taken into consideration. Several researchers have considered the multivariate models5,6,7, mostly off-line and population based models. Since each patient responses to drug inputs with very different dynamics, it is necessary to establish models in real-time and for individual patients. This paper introduces a method to significantly reduce the number of parameters contained in the model.

This paper is organized as follows. Section 2 presents procedures and systems for clinical data collection. Section 3 concentrates on patient modeling. It shows that a Wiener model structure can be used to simplify model structures quite significantly, subjecting only to minor loss of accuracy. When this approach is applied to multi-input-multi-output (MIMO) systems, one may use physiological insights to combine submodels to reduce model complexity. The models are used in Section 4 for anesthesia output prediction and decision assistance. Finally, Section 5 highlights findings of this paper and also points out some important related issues that are not covered in this paper.

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Data Acquisition

The patient population age group is between 20 and 70 years old. These patients are undergoing upper extremity arterio-venous fistula placement or thrombectomy, under intravenous unconscious sedation. Anesthesia is administered by an experienced anesthesiologist or registered nurse anesthetist. The patient is seen, examined and evaluated in the pre-operative holding area by an anesthesiologist. The anesthesiologist makes sure that the patient is ready for the surgery. Labs are checked in the pre-operative holding area and 1 mg of Midazolam IV is administered to the patient, after receiving full consent for the surgery and the participation in this study. All risks and benefits are thoroughly explained to the patient while obtaining consent.

The patient is, then, taken to the operating room, placed on the OR table, started on face mask oxygen at a rate of 8 liters/min, hooked to the electrocardiogram monitor, noninvasive blood pressure cuff is placed on the contralateral arm, and the cuff cycle is set to measure blood pressure every three minutes. A pulse oximeter is hooked on the patient’s contralateral index.

The patient consciousness levels during anesthesia are measured by a BIS (bi-spectrum) monitor by Aspect Medical Devices, Inc. The monitor provides continuously an index in the range of $[0, 100]$ such that the lower the index value, the deeper the anesthesia state. Hence, an index value 0 will indicate “brain dead” and 100 will be “awake”. A bispectral (BIS) electrode is placed on the patient’s forehead before administering anesthesia to the patient. The electrode is connected to the BIS monitor, which in turn is connected to a special computer system to allow continuous recording and saving of the BIS values.

A baseline BIS value of at least 90 is recorded before the administration of anesthesia. The patient is given 1-2 mcg/kg of bolus IV Fentanyl at the beginning of the surgery and 1 mcg/kg bolus during the surgery, as needed. The patient is started on intravenous Propofol pump at a rate of 50 mcg/kg/min and titrated as needed during the surgery. All measured heart rates, blood pressures and pulse oximetry values are entered and saved manually into the computer every three minutes and following any bolus administration. The Propofol rate, any changes made to the Propofol rate, and any Propofol or Fentanyl bolus given are transmitted to the computer monitoring system automatically and continuously at the sampling rate of 1 Hz (one sample per second). Towards the end of the procedure, and after making sure no more surgical stimuli are applied to the patient, all anesthetics are turned off and the patient is awakened with the BIS value of more than 75. The patient is then taken to the recovery room on oxygen tank for a period of two hours of observation.

Typically, an anesthesia drug influences more than one patient outcomes. Fig. 1 shows a typical recording of a patient’s response to propofol and fentanyl titration and bolus injections. For this patient, the anesthesia drugs not only control the anesthesia depth but also influence significantly blood pressures. For outcome prediction and decision assistance, it becomes essential that the impact of anesthesia drugs on both anesthesia depth and blood pressures be taken into consideration.

MIMO Patient Modeling for Anesthesia Monitoring and Control

A basic information-oriented model structure (a special case of Wiener models), for patient anesthesia depth responses to propofol infusion as an SISO system was introduced in 2002. This model can also be applied to relate other patient outcomes, such as blood pressure and heart rate, to input drugs. Its basic idea is summarized below.

The patient dynamics is a nonlinear system. Although the actual physiological and pathological

\[ \text{Drug inputs influence many patient outcomes} \]
features of the patient require models of high complexity, for prediction or control purposes it is not only convenient but essential to use simple models as long as they are sufficiently rich to represent the most important properties of the patient response. Understanding the information used by anesthesiologists in infusion control, we characterize the patient response to propofol titration with three basic components: (1) Initial time delay \( \tau_p \) after drug infusion: During this time interval after a change of the infusion rate, the BIS value does not change due to time required for drugs to reach the target tissues, to complete volume distribution. (2) Dynamic reaction: This reflects how fast the BIS value will change once it starts to respond, and is modeled by a transfer function \( G_p(s) \). (3) A nonlinear static function for sensitivity of the patient to a drug dosage at steady state: This is represented by a function or a look-up table \( f \). The meaning of these system blocks is illustrated in Fig. 2. Combined with infusion pump and monitor models, this model structure for titration response is a special case of the Wiener models shown in Fig. 3.

\[ \text{Fig. 2} \]
Simplified patient model structure

\[ \text{Fig. 3} \]
Wiener model structure

The linear patient dynamics can be well approximated by a continuous-time system that consists of a pure time delay and a first-order dynamics, sampled with sampling interval \( T = 1 \) second. Let a continuous-time system be

\[ P(s) = e^{-\frac{0.93}{73} \cdot \frac{0.93}{s} + 1}. \]

The step responses of the original system and the simplified system \( P(s) \) are shown in Figure 4. Since this model contains only three parameters, it is much easier to be identified in real time. It is also possible to use a simplified nonlinear function which has only three parameter \( r, \alpha, b \) to represent the sensitivity function \( f \):

\[ y = r \left( v \pm \frac{erf(aw)}{erf(aw)} - v \right). \]

Although in principle the above SISO method can be employed in MIMO models, by considering an \( m \)-input and \( n \)-output system as a collection of \( m \times n \) subsystems, each of which represents one input and one outcome relationship. For example, if two drugs (propofol and fentanyl) are present and three outcomes (depth, blood pressures, and heart rates) are considered, we may view this as a collection of 6 subsystems, including propofol-to-depth, propofol-to-BP, propofol-to-HR, fentanyl-to-depth, fentanyl-to-BP, fentanyl-to-HR subsystems. This approach, however, involves many model parameters and encounters high system complexity in modeling processes. For example, if each submodel contains only \( l \) parameters, the over system will have \( 6l \) parameters that must be updated in real time, which is a substantial complexity in this application.

\[ \text{Fig. 4} \]
Step responses of the original system and the simplified system

Modifications to the above approach are made to reduce modeling complexity by the following.
Modifications of the above approach are made to reduce by the following combination method. Since both propofol and fentanyl go through similar propagation and metabolism to influence blood pressure and heart rate, it is reasonable to use the same time delay and same dynamic response speed for both models. They, however, demonstrate very different sensitivity. As a result, it is reasonable to use only one scaling factor to represent the difference between propofol and fentanyl in their impact on the blood pressure and heart rate. Furthermore, fentanyl does not have influence on BIS index. This method reduces significantly the number of model parameters. These complexity reductions are substantial in making real-time MIMO modeling a feasible option in anesthesia applications which are not data rich.

**Multi-Objective Anesthesia Predictive Diagnosis**

Here, we consider a special case that involves two outcomes: the anesthesia depth $y_B$ and mean blood pressure $y_P$. The continuous control is provided by propofol titration whose rate is denoted by $u$. Propofol or fentanyl bolus injections can be used when necessary to assist. Also, blood pressures may also be reduced by vasodilation agents or other means if necessary.

From a system viewpoint, we have a system with two types of control inputs: one main control variable $u$ that is continuously managed, and another pulse type of control $u$ that is used only when it is necessary. The system has two outputs $y_B$ and $y_P$. The basic strategy is to use $u$ to achieve control objectives as much as possible. When $u$ alone cannot achieve certain control objectives, $u$ can be used to assist $u$ to reach the goal.

This paper is focused only on predictive diagnosis, not feedback control design, aspects of the problem: (1) Given the current input $u$, what will be the outcomes in the near future? (2) If the input is changed to a new value, what will be the impact of this change? (3) If we want the outcomes to settle at a new level, will it be possible to achieve it with assistance from $u$?

We first consider a generic simulated patient whose BIS response to propofol titration rate $u$ (mcg/min) is modeled by

$$x_B = e^{-2s} \frac{2.2}{102s + 1} U(s); \quad y_B = 100 - f_B(x_B(t)) + d_B$$

where $f_B$ is a nonlinear sensitivity function, and $d_B$ is an external disturbance to the BIS value; and whose mean blood pressure response to propofol titration is represented by the simplified delay model

$$x_P = e^{-1.2s} \frac{0.12}{65s + 1} U(s); \quad y_P = 110 - f_P(x_P(t)) + d_P$$

where $f_P$ is a nonlinear sensitivity function, and $d_P$ is an external disturbance to the blood pressure.

We will use $w(t) = [y_B(t), y_P(t)]$ to represent the outputs. In real implementations of our prediction algorithms, the patient models will be generated in real-time, using actual input-output data. Here, for methodology description we use the above models to show how outcome prediction is performed.

Suppose that the output vector $w(t)$ is initially at an equilibrium point with $w(t_0) = [y_B(t_0), y_P(t_0)]$ and input $u(t_0) = u_0$. When $u(t)$ is increased from $u_0$ to $u_0 + \Delta$, we may observe the outcome $w(t)$ starts to change due to this input jump. Outcome prediction shows how $w(t)$ will change in the near future and where it will settle to a new equilibrium. Drug impact prediction is an extension of outcome prediction. The outcome prediction provides future outcome trajectories when a drug decision is made and implemented. Drug impact prediction is an assessment of future outcomes when several drug decisions are being considered.

For example, if an anesthesiologist wants to consider possible decisions of increasing propofol rates by 15, 35, 55 starting at $t = 40$ second and compare their impacts, the models can be used to plot all possible trajectories related to these decisions. These impact predictions are plotted in Figure 5.

Suppose that the output vector $w(t)$ is initially at an equilibrium point $w(t_0) = w_0$. The question here is to determine if the propofol control alone is sufficient to achieve a designated target $w_f$. If the answer is affirmative, then assistance from $v$ is not needed. Otherwise, $v$ must be used such that after applying a bolus injection $u$, $w_f$ becomes reachable.

For example, if the current outcomes are $y_B = 70$ and $y_P = 80$, then the reachable outcomes corresponding to different drug inputs are plotted in Figure 6.
anesthesia outcome prediction

From Figure 6, we can see that different designated targets can be achieved through applying different drug inputs. For example, if we want to depress the patient blood pressure without changing BIS values, then only Fentanyl bolus is needed. But, if we want to push the BIS value to some low levels without much fall of blood pressures (mean arterial pressure of 80 mmHg is usually the desired level during anesthesia), then the propofol bolus can be applied to achieve the goal. Figure 7 and 8 show the outcome time trajectories for different drug inputs.

Conclusions

This paper investigates the problem of real-time monitoring, diagnosing, and predicting multiple outcomes of anesthesia patients. For the enhanced anesthesia management, it is essential to view the anesthesia patient dynamics as an multi-input and multi-output system. For the purpose of control, predictive diagnosis, outcome comparison, etc., a reliable model need to be established in real-time and in individual patient. An information-oriented model, Wiener model, is studied for its suitability in representing the patient responses to drug infusion. Furthermore, a method of consolidating submodels is introduced which can significantly reduce the total number of MIMO system parameters. Based on the constructed model, some new ideas and related simulations of prediction and control oriented multi-objective anesthesia diagnosis, such as outcome predictions, drug impact predictions and reachable sets, are demonstrated. In the future,
we will consider to develop this multivariable real-time patient model through Labview graphical programming software (National Instrument Inc.) and apply it in operating rooms for multi-outcome anesthesia diagnosis.

References


Abstract

Background: To investigate whether there is any chronobiological rhythms in onset of massive pulmonary embolism in Iranian population and to study any time variation in occurrence of this disease in patients’ subgroups.

Methods: This study was conducted in an emergency department of a referral teaching hospital from March 2003 to March 2007. All medical records of patients with definite diagnosis of massive pulmonary embolism were reviewed for chronobiological rhythms in hourly, daily, monthly and season periods.

Results: One hundred and twenty patients (49 women and 71 men) included in the study. The mean age of patients was 63.63 ± 17.21 years. Massive pulmonary embolism showed a statistical increase in onset in the morning period (p = 0.004) with peak of occurrence between 9:00 to 10:00, in the first three day of the week (p< 0.001), and during winter (p = 0.003). In addition, hourly and weekly rhythms in onset of massive pulmonary embolism in diabetic patients is different from non-diabetic patients and occur most frequent in evening hours and in the end of week.

Conclusion: Our findings revealed that massive pulmonary embolism has a peak of onset during morning hours and in the winter. We also found that massive pulmonary embolism also has a weekly rhythm. Circadian and weekly rhythms of massive pulmonary embolism were different in diabetic patients and this is a novel finding of this study.

Keywords: Chronobiology, Circadian Rhythm, Pulmonary Embolism

Introduction

Pulmonary embolism (PE) is an important cause of morbidity and mortality in the world. This disease is a common health problem, with an annual incidence of about 60-70 per 100,000 in general population. Pulmonary embolism is divided into 1) massive: with a systemic hypotension, 2) sub-massive: right ventricular hypokinesis with no systemic hypotension, and 3) small to moderate: normal systemic arterial pressure without any signs of right ventricle dysfunction.
Acute massive PE is a rare disease with a high risk of death in the first hours of onset because of right ventricle failure. It is obvious that primary embolectomy or thrombolytic therapy can be lifesaving approaches in treatment of massive PE and survival from this disease depends on rapid reduces in the pressure of right ventricle. If untreated, massive PE is a fatal disease. Thus, early diagnosis is vital element in treatment of massive PE and finding any patterns in onset of it can help early diagnosis and prevent many deaths from this fatal disease.

It has previously been demonstrated that many of biological processes and functions of the body are well organized in time named as chronobiologic rhythms, as evidenced by the expression of circadian (approximately 24-h), circamensual (approximately monthly), and circannual (approximately yearly) rhythms. Previous studies indicated that many cardiovascular diseases follow chronobiological rhythms. But, there were few studies that investigated the chronobiologic rhythms in onset of massive PE. These studies found that massive PE has circadian and seasonal rhythms with peak of onset in the morning and in the winter. In addition, we could not find any study that investigate the weekly rhythms in onset of and the chronobiological rhythms of massive PE with regard to patients’ characteristics and risk factors.

The aim of present study was to investigate chronobiological rhythms in occurring massive PE in Iranian population and compare the results with those from other populations and to find any difference in chronobiological rhythms in subgroups of patients according to patients’ characteristics and risk factors.

Methods and Materials

This was a retrospective, cross-sectional, non-interventional study that assesses the chronobiological rhythms in onset of massive PE in Iranian population. The study was approved by the Research Ethics Committee of Madani Heart Hospital affiliated to Tabriz University of Medical Science, Iran. This Hospital is specialized Heart Center which serves as a major referral center for a large geographic area of the north west of Iran.

The study population included all patients’ records admitted with massive PE diagnosis, over a four-year period from March 2003 to March 2007. In this period 120 patients (49 women and 71 men) admitted in our Institute with massive PE diagnosis. The principal criterion in the diagnosis of acute massive PE was a massive systemic arterial hypotension (SBP ≤90 mmHg). Other signs and symptoms that helped in the diagnosis of massive PE included: dyspnea of sudden onset, syncope or near-syncope, tachypnea, right-sided heart failure, cyanosis, clinical signs of organ hypoperfusion and hypoxia. The diagnosis of massive PE in all patients was confirmed by using diagnostic methods (chest CT angiography or high probability lung Ventilation/perfusion scan) or postmortem examination. The time of onset of massive PE was documented for each patient by review patients’ medical records and research criterion for onset was the patients’ report of beginning signs and symptoms.

For assessing circadian distribution in onset of massive PE, the day was divided into twenty-four hours and four 6-hour intervals (24:00 to 5:59, 6:00 to 11:59, 12:00 to 17:59, and 18:00 to 23:59). The daily and monthly distributions were expressed as the number of massive PE cases per day and per month admissions. To assess the seasonal distribution, the year divided into 4 seasons: winter (December 21st to March 20th), spring (March 21st to June 20th), summer (June 21st to September 20th), autumn (September 21st to December 20th).

We analyzed possible differences in chronobiological rhythms in onset of massive PE with regard to the following patients’ characteristics and risk factors: sex (men, women), age (<60 years, ≥61 years), history of hypertension (hypertensive, normotensive), history of diabetes mellitus (diabetic, non-diabetic), smoking habit (smoker, non-smoker), history of previous surgery (in last six month), using oral contraceptives (for women), history of ischemic heart disease (IHD), history of chronic obstructive pulmonary disease (COPD), history of receiving streptokinase (SK) for prevent attack, and patients’ outcome (death or alive on hospital discharge).

All obtained data were analyzed by SPSS software version 13.0 (SPSS Inc., Chicago, IL). Chi-square test for goodness-of-fit was used to determine
whether massive PE uniformly occurred during days, weeks, months, and sessions. For comparing the distribution of massive PE in patients’ subgroups (binary variables), Chi-square test with continuing correction was used. A p value < 0.05 was considered statistically significant.

Results

One hundred and twenty patients’ medical records with definite diagnosis of massive PE were reviewed. 59.2% of patients were males, with the mean age of 63.63 ± 17.21 years ranging from 17 to 86 years. Table 1 shows the distribution of other patients’ characteristics and risk factors.

Circadian rhythm

The onset of massive PE showed a circadian variation with the morning peak between 9:00 and 10:00 (Fig. 1). Using 6-hour intervals, the frequency of massive PE are significantly higher in the morning period between 6:00 to 11:59 compared with other 6-hour intervals ($\chi^2 = 13.46$, df $= 3$, p $= 0.004$) (Fig. 1). Most frequent hours and day intervals in onset of massive PE reported for all patients’ subgroups in Table 1.

On further analysis no significant variation in 6-hour intervals could be found within subgroups of sex ($\chi^2 = 0.82$, df $= 3$, p $= 0.84$), age ($\chi^2 = 1.15$, df $= 3$, p $= 0.76$), history of hypertension ($\chi^2 = 5.27$, df $= 3$, p $= 0.15$), smoking habit ($\chi^2 = 3.74$, df $= 3$, p $= 0.29$), history of previous surgery ($\chi^2 = 0.98$, df $= 3$, p $= 0.80$), history of IHD ($\chi^2 = 2.12$, df $= 3$, p $= 0.54$), history of COPD ($\chi^2 = 1.06$, df $= 3$, p $= 0.78$), receiving SK ($\chi^2 = 4.70$, df $= 3$, p $= 0.19$), and patients’ outcome ($\chi^2 = 0.87$, df $= 3$, p $= 0.83$). But in history of

<table>
<thead>
<tr>
<th>Patients’ characteristics</th>
<th>Subgroups</th>
<th>N’</th>
<th>Hour**</th>
<th>Day intervals**</th>
<th>Day**</th>
<th>Month**</th>
<th>Season**</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
<td>Men</td>
<td>71</td>
<td>9</td>
<td>6:00 to 11:59</td>
<td>Sat</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>49</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td>Age</td>
<td>&lt; 60 years</td>
<td>43</td>
<td>9</td>
<td>6:00 to 11:59</td>
<td>Sat</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>≥ 61 years</td>
<td>77</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
<tr>
<td>History of HTN</td>
<td>Hypertensive</td>
<td>51</td>
<td>10</td>
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<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
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<tr>
<td></td>
<td>Normotensive</td>
<td>69</td>
<td>9</td>
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<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
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<tr>
<td>History of DM</td>
<td>Diabetic</td>
<td>17</td>
<td>17</td>
<td>12:00 to 17:59</td>
<td>Sun</td>
<td>Mar</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>Non-diabetic</td>
<td>103</td>
<td>10</td>
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<td>Sun</td>
<td>Feb</td>
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</tr>
<tr>
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<td>37</td>
<td>10</td>
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<td>Sun</td>
<td>Aug</td>
<td>Summer</td>
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<td></td>
<td>Non-smoker</td>
<td>83</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td>History of surgery</td>
<td>Previous surgery</td>
<td>18</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Mon</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>No previous surgery</td>
<td>102</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td>Using OCP***</td>
<td>Using OCP</td>
<td>13</td>
<td>3</td>
<td>24:00 to 5:59</td>
<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>No using OCP</td>
<td>36</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
<tr>
<td>History of IHD</td>
<td>Previous IHD</td>
<td>34</td>
<td>9</td>
<td>6:00 to 11:59</td>
<td>Mon</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
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<td>86</td>
<td>10</td>
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<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
<tr>
<td>History of COPD</td>
<td>Previous COPD</td>
<td>31</td>
<td>9</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>May</td>
<td>Spring</td>
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<tr>
<td></td>
<td>No previous COPD</td>
<td>89</td>
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<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Feb</td>
<td>Winter</td>
</tr>
<tr>
<td>Receiving SK</td>
<td>Receiving SK</td>
<td>59</td>
<td>9</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>No receiving SK</td>
<td>61</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
<tr>
<td>Patients’ outcome</td>
<td>Dead</td>
<td>40</td>
<td>10</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
<tr>
<td></td>
<td>Alive</td>
<td>80</td>
<td>9</td>
<td>6:00 to 11:59</td>
<td>Sun</td>
<td>Jan</td>
<td>Winter</td>
</tr>
</tbody>
</table>

* Number of each groups reported
** Most frequent times reported
*** Reported for female patients

HTN: Hypertension; DM: Diabetes mellitus; OCP: oral contraceptives; IHD: Ischemic heart disease; COPD: Chronic obstructive pulmonary disease; SK: streptokinase.
using OCP ($\chi^2 = 8.10, df = 3, p = 0.04$) and history of diabetes mellitus ($\chi^2 = 9.19, df = 3, p = 0.02$) significant variation in 6-hour intervals found. In other words, in women that have a history of using OCP and in patients with diabetes the pattern of onset of massive PE were different from other patient and have a trend to occur in the evening hours (12:00 to 17:59).

**Weekly rhythm**

Significant variation in onset of massive PE was found in different days of the week ($\chi^2 = 47.88, df = 6, p < 0.001$) and showed a peak on the beginning of weeks (Saturday, Sunday, and Monday) (Fig. 2). Most frequent days in onset of massive PE reported for all patients’ subgroups in Table 1.

On further investigation of subgroups no significant variation in onset of massive PE could be demonstrated in different days of the week within sex ($\chi^2 = 8.58, df = 6, p = 0.19$), age ($\chi^2 = 8.18, df = 6, p = 0.22$), history of hypertension ($\chi^2 = 5.92, df = 6, p = 0.43$), smoking habit ($\chi^2 = 7.10, df = 6, p = 0.31$), history of previous surgery ($\chi^2 = 6.65, df = 6, p = 0.35$), history of using OCP ($\chi^2 = 11.73, df = 6, p = 0.06$), history of IHD ($\chi^2 = 3.74, df = 6, p = 0.71$), history of COPD ($\chi^2 = 6.70, df = 6, p = 0.34$), receiving SK ($\chi^2 = 8.77, df = 6, p = 0.18$) and patients’ outcome ($\chi^2 = 7.11, df = 6, p = 0.31$). But patients with a history of diabetes mellitus ($\chi^2 = 13.91, df = 6, p = 0.03$) showed significant variation in onset of massive PE during the days of week and in spite of other patients, the onset of their disease trended to occur in the end of the weeks.

**Seasonal rhythm**

Regarding monthly distribution, the onset of massive PE was obviously most frequent in February, January, and April and least frequent in October.
Discussion

The chronobiological rhythms in onset of massive PE in our Institute in four year period, from March 2003 to March 2007 was examined. Our findings demonstrated prominent chronobiological rhythms in onset of this disease, with a significant increase in the number of events during the morning hours, during first three days of week, and during January and winter.

The effect of chronobiologic rhythms on onset of many cardiovascular events has been demonstrated in previous studies. For example, patterns have been found for hemorrhagic stroke, blood pressure, myocardial infarction, pulmonary edema, and aortic dissection. There have been a few attempts to investigate the chronobiologic rhythms in onset of pulmonary embolism. For example, Sharma et al found pulmonary embolism has a significant acrophase in the morning hours and in winter. This pattern was similar to that reported in other studies. Rhythmic occurrence of massive PE, however, has been reported in few studies. Colantonio et al reported circadian and seasonal rhythms of fatal PE with a predominant onset in the morning hours and the winter months. Gallerani et al reported a similar chronologic pattern in 48 patients dying suddenly from pulmonary thromboembolism. Our experience indicates similar circadian and seasonal rhythms. But, we could not find any studies that investigate the onset of massive PE with regard to weekly rhythms. This weekly rhythms previously reported for some cardiovascular disease, for example aortic dissection. Our finding show that the massive PE events increase during the beginning of the week (Saturday, Sunday, and Monday).

We found no chronobiologic rhythms differences in onset of massive PE events between male and female patients. One important finding of this study was that the chronobiologic rhythms in occurrence of events in diabetic patients were different from non-diabetic patients in hourly and weekly rhythms. There were 17 diabetic patients with definite diagnosis of massive PE during the study period. In contrary to other patients the events of massive PE were most frequent during evening and end of the week. In pervious study Kitzis et al found such differences for diabetic patients in onset of acute pulmonary edema but this finding
was not reported for onset of massive PE previously. However, because of low number of diabetic patients in this study this finding need further investigation.

Many mechanisms have been proposed for the increased cardiovascular risk in the morning, in particular, an increase in blood pressure, heart rate, sympathetic activity, basal vascular tone, vasoconstrictive hormones, prothrombotic tendency, platelet aggregability, plasma viscosity, and hematocrit\textsuperscript{25-27}.

Most available studies indicate a greater onset of massive PE during the winter months. These data are consistent with the seasonal pattern demostrated for other major cardiovascular events\textsuperscript{18-20}. Cold exposure determines increased blood pressure\textsuperscript{28}, with increased platelet count and volume, red blood cell count, blood viscosity\textsuperscript{29}, and clotting activity\textsuperscript{30}.

Regarding the study finding that the onset of massive PE has a frequency peak on first three days of the week we could not find proposed explanation for this finding. Perhaps the beginning of the week causing stress and this stress activated the sympathetic activity and enhance the release of embolus and cause PE. But this finding needs further investigation.

The findings of present study have diagnostic implications. Because this study confirms the hypothesis that massive PE has a predominant onset in the morning hours, in the beginning of week, and in the winter season, these findings raise the level of accurate and rapid diagnosis of this fatal disease and may prevent some death because of misdiagnosis.
References


UPPER LIP BITE TEST AS A PREDICTOR OF DIFFICULT MASK VENTILATION: A PROSPECTIVE STUDY


Forwarding comments

Failure to recognize a difficult airway before routine induction of anesthesia, can bring in its wage disastrous complications ranging from hypoxic brain damage to death. Several preoperative airway assessment tests exist that help in anticipating difficult airway. The upper lip bite test (ULBT) introduced by Khan et al almost 20 years after Mallampati classification, is perhaps the latest in predicting difficulty in endotracheal intubation.

ULBT test is performed according to the following criteria: class I = lower incisors can bite the upper lip above the vermilion line, class II = lower incisors can bite the upper lip below the vermilion line, class III = lower incisors cannot bite the upper lip. Based on its high Se, Sp and NPV obtained in the original study, we hypothesized that the ULBT could serve as a predictor of difficult mask ventilation (DMV).

DMV continues to be a major cause of morbidity and mortality with an increased incidence of almost 5%. Five preoperative risk factors (age older than 65 yr, body mass index ≥ 26 kg/m², presence of a beard, lack of teeth and history of snoring), have been considered to be independently associated with DMV. As DMV has been found to be significantly associated with difficult intubation, the ULBT with its inherently high level of accuracy in correctly predicting a high percentage of easy and difficult intubations in the original study by the author, appeared to be promising in predicting DMV, as the test assesses both buck teeth and mandibular subluxation simultaneously, factors that can be of vital importance in assessing DMV.
Abstract

Background: Oxygenation and ventilation by means of bag-mask and ambubag play a significant role in maintaining an optimal oxygen saturation of blood and hence the essence of life itself. Predicting difficulty in mask ventilation is again of paramount importance at the time of induction of anesthesia, and in emergency situations. In this study we aimed at evaluating factors that could help in predicting the difficulty of bag-mask ventilation.

Methods: In a prospective study, 200 patients were allocated into two groups, 100 each. First group with a ULBT class I, and the other group with ULBT class II and III. Factors such as height, weight, gender, past history of snoring, neck circumference, Mallampati class, sternomental and thyromental distances were then evaluated in each of the patients in the two groups in order to arrive at their impact on the incidence of difficult mask ventilation.

Data were analyzed using Chi-square, student t-test and Fisher’s exact tests depending upon the situation. A p<0.05 was considered to be statistically significant.

Results: The results revealed that negative predictive value (NPV) of ULBT class, history of snoring and neck circumference were 86%, 83%, 81%, respectively. A combination of these three predictors had an NPV of 95%.

Conclusion: ULBT class alone was of value in predicting difficulty in mask ventilation, but a combination of the three tests significantly improved the predictive value.

Key Words: Airway Management, Anesthesia Complications, Anesthesia Risk, Difficult Mask Ventilation, Upper Lip Bite Test.

Introduction

The human airway and its assessment has been a subject that has been studied at length and discussed in innumerable publications. Despite the methods forwarded so far in anticipating difficulty in laryngoscopy and intubation, there still are cases where anticipation of the ease of laryngoscopy becomes difficult. Under such circumstances maintaining mask ventilation becomes life saving. If oxygenation cannot be maintained via a bag-mask system, the patient’s life may be threatened.

Difficult mask ventilation (DMV) has received less attention, which of course does not diminish its importance. Studies in the past have elaborately discussed the possible incriminating factors for DMV. Mallampati class 3 or 4, body mass index (BMI) >25kg/m², old age, history of snoring and male gender have been declared independently as the possible causes of DMV\(^2\).

The aim of this study was to evaluate the diagnostic value of the upper lip bite test (ULBT) as a predictor of DMV and to also assess a combination of ULBT and other predictors in exploring the predictability of DMV before attempting induction of anesthesia.

Methods and Materials

After an institutional approval and obtaining written informed consent, 200 patients (82 males, 118 females) undergoing surgery and requiring endotracheal intubation were enrolled in this study. Exclusion criteria included compromised critical airway, emergent cases, noncompliable patients and those with anatomical anomalies in the airway, pregnant, edentulous, those having beard and patients less than 14 years and those in whom a good mask fit was not possible.

According to the pilot study, with negative predictive value of 85% for ULBT, \(\alpha = 0.05\) and \(d = 7\%\), the calculated sample size was at least 100 patients with ULBT class I. With low incidence of ULBT class III we decided to consider ULBT class II and III as a one group and a total of 100 patients were allocated into this group.

A questionnaire including demographic data [age, height, gender, weight, BMI, sex], past history of snoring, neck circumference, ULBT class, Mallampati classification, thyromental distance (TMD), and sternomental (SMD) for each patient was filled out by a 3rd year resident. The neck circumference was measured in cm by a measuring tape passing around the neck at the level of thyroid prominence.

ULBT was assessed and rated by the investigator as described by Khan et al\(^3\).

The Mallampati class was assessed as described by Samsoon and Young\(^4\). The observer noted the
pharyngeal structures in a seated patient protruding the tongue as far as possible.

The TMD was measured between the prominence of thyroid cartilage and the bony point of the chin with the head fully extended on the neck.

The SMD was measured as a straight distance from the upper border of the manubrium sterni to the mentum, with patient’s head fully extended.

After application of routine monitoring, midazolam 1 mg and fentanyl (1 μg/kg) were administered intravenously, then an induction dose of thiopental 4 mg/kg was given followed by atracurium 0.5 mg/kg given IV to facilitate endotracheal intubation.

Before attempting laryngoscopy, patient was ventilated by mask by an anesthesiologist blinded to the study. Mask ventilation was performed by means of an appropriate sized face mask applied to the face and a reservoir bag receiving a continuous flow of oxygen from the anesthesia machine. Mask ventilation was categorized Grade I as easy if the arterial oxygen saturation (SpO2) was >92% and chest expansion was visible. Grade II was categorized if additional measures such as an airway or O2 flush was to be needed to maintain ventilation or else the assistance of another person was required. Grade III was categorized if despite the use of all the above measures, the SpO2 failed to show a rise and endotracheal intubation thus attempted.

For statistical analysis, SPSS version 16 was used. Data were analyzed using Chi square, student T-test and Fisher’s exact test depending upon the situation. Multiple logistic regressions were employed to evaluate any confounding variable. The P values were determined in all situations, and they were considered statistically significant at P<0.05.

**Results**

A total of 200 patients in two groups were included in this study. 100 patients had ULBT class

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of patients according to difficulty of mask ventilation (MV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor</strong></td>
<td><strong>Easy MV</strong></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.8 ± 11.4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.4 ± 14</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>26.6 ± 4.9</td>
</tr>
<tr>
<td>Age (year)</td>
<td>35.6 ± 11.9</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>84(0.42)</td>
</tr>
<tr>
<td>Male</td>
<td>60(0.30)</td>
</tr>
<tr>
<td>Mallampati class</td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>90(0.45)</td>
</tr>
<tr>
<td>2.</td>
<td>52(0.26)</td>
</tr>
<tr>
<td>3.</td>
<td>2(0.01)</td>
</tr>
<tr>
<td>4.</td>
<td>0(0.00)</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>37.3 ± 4.5</td>
</tr>
<tr>
<td>TMD (cm)</td>
<td>6.8 ± 1.4</td>
</tr>
<tr>
<td>SMD (cm)</td>
<td>16.3 ± 2.6</td>
</tr>
<tr>
<td>History of snoring</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>94(0.47)</td>
</tr>
<tr>
<td>Yes</td>
<td>50(0.25)</td>
</tr>
<tr>
<td>ULBT</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>86(0.43)</td>
</tr>
<tr>
<td>2 &amp; 3</td>
<td>58(0.29)</td>
</tr>
</tbody>
</table>
Difficult mask ventilation was found to occur in 56 (28%) patients (7% in ULBT class I and 21% in class II & III). In none of the patients a cannot ventilate, cannot intubate scenario was encountered. Demographic characteristics (height, weight, BMI, age and sex) of patients were recorded at the beginning of the examination. Mallampati class, ULBT, TMD, SMD, history of snoring, neck circumference were also obtained and recorded during the study (Table 1).

Diagnostic value of ULBT, snoring and neck circumference as predictive criteria of DMV were calculated individually, then a combination of the tests were paired together and analyzed and finally a combination of all the three criteria was collectively assessed to ascertain its value in the prediction of DMV (Table 2).

In the multivariate analysis, the criteria of ULBT, snoring and neck circumference which correlated with DMV in the univariate analysis, were again found to be significantly associated with DMV (Table 3).

### Discussion

Difficult mask ventilation may occur before attempting intubation, that is after induction of anesthesia or it may occur after an unsuccessful attempt of intubation. Our study focuses on DMV in the first situation which has been grossly underestimated in the available literature.

Langeron et al³ in their study reported an incidence of 5% of this situation, and stressed that this happening was relatively common. In our present study as one group of patients was selected with a ULBT class of II and III, this in itself resulted in a high incidence of DMV in this particular group (28%) and as such a higher prevalence of DMV compared to that found in the general population was obtained.

A good mask fit and proper ventilation is of an indispensible and pivotal value prior to endotracheal intubation. Preoperative assessment helps in overcoming any difficulty in mask ventilation and its attendant complications. Although securing the airway with an endotracheal tube is the ultimate and safest objective of an anesthesiologist to conduct safe anesthesia, nevertheless mask ventilation provides an opportunity to cater for patient till other options are implemented and a secure airway guaranteed⁴.

Several studies have been conducted to assess airway preoperatively³,⁴,⁶, and assessing the ease of

### Table 2

<table>
<thead>
<tr>
<th>Criteria</th>
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</thead>
<tbody>
<tr>
<td>Sensitivity (Se)</td>
</tr>
<tr>
<td>Specificity (Sp)</td>
</tr>
<tr>
<td>Positive Predictive Value (PPV)</td>
</tr>
<tr>
<td>Negative Predictive Value (NPV)</td>
</tr>
<tr>
<td>ULBT(1)</td>
</tr>
<tr>
<td>Snoring(2)</td>
</tr>
<tr>
<td>Neck Circumference³</td>
</tr>
<tr>
<td>1+2</td>
</tr>
<tr>
<td>1+3</td>
</tr>
<tr>
<td>2+3</td>
</tr>
<tr>
<td>1+2+3</td>
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</table>

### Table 3

<table>
<thead>
<tr>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio (CI)</td>
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<tr>
<td>P value</td>
</tr>
<tr>
<td>ULBT</td>
</tr>
<tr>
<td>Snoring</td>
</tr>
<tr>
<td>Neck circumference</td>
</tr>
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</table>
mask ventilation\textsuperscript{1,7,8,9}. In these studies factors having an impact on mask ventilation such as SMD\textsuperscript{10}, TMD\textsuperscript{8}, Mallampati classification\textsuperscript{9}, mouth opening\textsuperscript{11}, mandible protrusion\textsuperscript{12}, age, gender, height, BMI, weight\textsuperscript{7}, dental morphology\textsuperscript{11}, neck extension\textsuperscript{13}, snoring\textsuperscript{8} and the presence of beard\textsuperscript{2}, were evaluated. These variables were considered both independently and in combination to predict the ease or else difficulty in mask ventilation. The ULBT classification forwarded by Khan et al (2003\textsuperscript{3}) to predict the airway configuration and ease in laryngoscopy and intubation has not been tested to predict difficulty in mask ventilation. On the hypothesis that as both mandibular movement and buck teeth which the ULBT fully incorporates could serve in anticipating difficulty in mask ventilation, the present study was designed and conducted. This study revealed that ULBT correctly and accurately depicted the ease in mask ventilation, as signified by its high sensitivity and odds ratio, both highly significant. Since no such study has been conducted so far, we cannot corroborate it with another similar study. Again we found that the ULBT class 2 and 3, history of snoring and a large neck circumference positively correlated with and could predict difficulty in mask ventilation. This is the only study that has been conducted so far and we could find that a higher ULBT class had a direct impact on difficulty in mask ventilation. In this study for SMD\textsuperscript{10}, TMD\textsuperscript{8}, the measurements advocated so far were utilized, but for measuring the neck circumference, ROC was utilized to determine the best cut off point, which as measured at the level of the thyroid cartilage was 37 cm. According to findings obtained (Table 1), it can be inferred that SMD and TMD in two groups did not have a notable difference as regards the ease or difficulty in mask ventilation (P>0.05). Although our goal was not to evaluate all the factors presumed to have an association or an impact on DMV, studies in the past have found gender, TMD and a Mallampati class to have an association with DMV\textsuperscript{8}. Our objective was to find an explicit association between ULBT class and DMV. Perhaps a reason for the disparity of our findings in this study about these variables could be attributed to the small sample size in this survey.

It has been stated that tracheal intubation may be achieved easily in some of the patients in whom DMV is encountered. Thus, the most prudent step would be to attempt tracheal intubation as the first intervention if mask ventilation is unmanageable with application of any additional measures such as an oral airway, O$_2$ flush or help of two providers. In case, these measure fail, the alternative and plausible approach would be to use the laryngeal mask airway (LMA). Airway management was based on American Society of Anesthesiologists Task Force on Management of the Difficult Airway\textsuperscript{14}. In our series of patients, we did not encounter a cannot ventilate-cannot intubate scenario, perhaps owing to small size of our patient population, its incidence is estimated to range between 0.01 and 2.0 per 10,000 patients\textsuperscript{15}.

Although an ideal test is the one that has a high sensitivity, specificity and positive and negative predictive values, presently no such test exists. In order to circumvent the problems associated with DMV, it should be predicted in advance and ruled out as far as possible before initiating induction of anesthesia, thus any test that has a high NPV would be of greater help. As depicted (Table 2) the presence of ULBT class I or the absence of ULBT class II and III carries a Se of 75% and a NPV of 86% imparts an optimism for the anesthesiologist that DMV would not be difficult, but as stressed earlier optimism cannot be guaranteed fully to be easy.

Again when the other variables (neck circumference and past history of snoring) are taken concurrently into consideration, the combination further enhances the Se and the NPV to 96% and 95% respectively, providing us a promising clue that the DMV could easily be ruled out, and mask ventilation in a high percentage of patients with a high dependability would be easy.

In conclusion, it is suggested that a combination of ULBT, past history of snoring and neck circumference be utilized in the prediction of DMV as these composite variables yielded the best results.
References

THE ‘BEST FIT’ ENDOTRACHEAL TUBE IN CHILDREN
- Comparison of Four Formulae -

TURKISTANI A*, ABDULLAH KM***, DELVI B**
AND AL-MAZROUA KA****

Abstract

Background: Uncuffed endotracheal tubes are still being recommended by most pediatric anesthetists at our Institutes. Different algorithms and formulae have been proposed to choose the best-fitting size of the tracheal tube. The most widely accepted is related to the age of the child [inner diameter [ID] in mm = (age in yr/4) + 4; the second is a body, length-related formula (ID in mm = 2 + height in cm/30); the third, a multivariate formula (ID in mm = 2.44 + age in yr × 0.1 + height in cm × 0.02 + weight in kg × 0.016)]; the fourth, the width of the 5th fingernail is used for ID prediction of the ETT (ID in mm = maximum width of the 5th fingernail).

The primary endpoint of this prospective study was to compare the size of the ‘best fit’ tracheal tube with the size predicted using each of the above mentioned formulae.

Patients and Methods: With Institutional Ethics Committee approval and parental consent, 27 boys, 23 girls, ASA I-III, 2-10 years, scheduled for different surgical procedures requiring general anesthesia and endotracheal intubation, were enrolled in the study. The size of ‘best fit’ endotracheal tubes in those children were compared. The internal diameter considered the ‘best fit’ by the attending pediatric anesthesiologist was compared to age-based, length-based, multivariate-based and 5th fingernail width-based formulae. For all tests, P < 0.05 was considered to be statistically significant.

Results: The mean (SD) IDs for the ‘best fit’, age-based, length-based, multivariate and 5th fingernail techniques were 5.31 (0.691), 5.54 (0.622), 5.82 (0.572), 5.71 (0.67) and 5.43 (0.821) mm, respectively.

Conclusions: The age-based and 5th fingernail width-based predictions of ETT size are more accurate than length-based and multivariate-based formulae in terms of mean value and case matching.

Key Words: pediatric, endotracheal tube, age, length, multivariate, 5th fingernail, formula
Introduction

Uncuffed endotracheal tubes are still being recommended for pediatric anesthesia in our Institutes. Smaller than ideal endotracheal tube size is not recommended because of increased incidence of tracheal tube replacement, less precise monitoring of respiratory mechanics and end-tidal CO₂, increased pollution of the operating room and increased cost related to increased consumption of volatile agents, in addition to increased airflow resistance.

The endotracheal tube (ETT) itself poses more resistance to airflow, and this resistance is inversely proportional to the fourth power of the radius and directly proportional to the length; i.e., narrower and longer tubes show greater flow resistance¹. This is of significant clinical importance for children during anesthesia or intensive care, and it suggests that the widest and shortest possible ETT should be used.

However, a tightly fitting endotracheal tube can easily result in decreased mucosal perfusion and subsequent edema, which can result in critical airway obstruction and associated syndromes, e.g. dyspnea, hypoxemia, and the potential need for invasive management. Even cartilage damage may occur, potentially resulting in permanent impairment and disability.

Anatomically, the larynx of a pediatric patient assumes a funnel shape with its narrowest part at the level of the cricoid ring, which cannot be seen during conventional laryngoscopy².

Different algorithms and formulae have been proposed to choose the best-fitting size of the tracheal tube.

The most widely accepted of which is age based formula (ABF) (inner diameter [ID] in mm = (age in yr/4) + 4³. This calculation overestimates the correct size in more than one in four cases⁴.

Pediatric emergency physicians have suggested a body length-related formula (ID in mm = 2 + height in cm/30)⁵. However, selection of the correct tube size in children might be more complex, leading others to propose a multivariate prediction model (ID in mm = 2.44 + age in yr × 0.1 + height in cm × 0.02 + weight in kg × 0.016)⁶.

Finally, the 5th fingernail width can be used for prediction of the ID of the ETT (ID in mm = maximum width of the 5th fingernail)⁷.

The primary endpoint of this prospective study was to compare the ‘best fit’ size of the tracheal tube with the size predicted using each of the above mentioned formulae.

Patients and Methods

After obtaining Ethics Committee approval and parental written informed consent, 50 patients (27 boys, 23 girls), ASA I-III, median (range) age 6.0 (2.0-10.0) years, mean (SD) height 121.14 (17.73) cm and mean (SD) weight 21.35 (8.96) kg, scheduled to undergo different surgical procedures requiring general anesthesia with oro-tracheal intubation and lasting more than 45 minutes, were prospectively included. Exclusion criteria included known or suspected airway anomalies, the need for exceptional tracheal tube sizes known from previous anesthetic treatment, concurrent or recent upper respiratory tract infection and requirement of postoperative mechanical ventilation.

Monitoring consisted of noninvasive measurement of blood pressure, heart rate via electrocardiogram, hemoglobin oxygen saturation, end-tidal CO₂ values, and inspiratory and expiratory oxygen concentrations.

General anesthesia was induced by inhalation of sevoflurane in O₂ or propofol (2 mg/kg) as appropriate and maintained by fentanyl (1 ug/kg) and sevoflurane in an O₂/N₂O gas mixture. Tracheal intubation was performed after complete muscle paralysis by cisatracurium 0.15 mg/kg. The correct position of the tracheal tube was confirmed by capnography and by auscultation for bilateral breath sounds.

The tracheal tube size was chosen and selected as ‘best fit’ by the attending pediatric anesthesiologist if air leakage was satisfactory at a maximum of 20 cmH₂O airway pressure⁸. The leak pressure was measured by carefully closing the pressure relief valve from the zero position until an audible air leak was obtained at the patient’s mouth and/or over the larynx. For the purpose of air leak measurement, the head and body positions were standardized; the patient was supine with the head roughly in a neutral position to limit any impact on the leak test⁹. The ETT would be changed to a bigger size when air leak is excessive. Alternatively,
when there was resistance to the passage of the ETT into the trachea or when air leak was not detected, a smaller tube was placed.

Standardized respirator settings were applied: pressure-controlled ventilation, peak inspiratory pressure of 10-15 cmH₂O to give tidal volume of 7-10 ml/kg, breathing frequency according to patient’s age and PetCO₂, fresh gas flow of 3 L/min.

At the end of the procedure, the tracheal tube was removed, and all patients were transferred to the recovery room for postoperative follow-up to assess post-extubation respiratory morbidities (croup, cough, sore throat, dyspnea, dysphonia or stridor).

For all patients, the size predicted by the above mentioned formulae was calculated preoperatively and recorded in a sheet that was not seen by the attending anesthesiologist. Because the calculated values might NOT be clinically applicable (0.5 multiples), we calculated the difference between the used and estimated sizes and considered the estimate to match the size actually used when the difference was between -0.5 and +0.5. We evaluated the proportions of matched cases using each method. Each value was approximated to the nearest 0.5 or 0.0 (e.g. 4.65 approximated to 4.5, 5.8 approximated to 6.0, and so on), and then the comparison of the means was repeated.

Data are presented as the mean ± standard deviation, numbers of cases (%) or median (range) as appropriate. All statistical tests were unpaired and two-tailed, and P < 0.05 was considered to be statistically significant. The Mann-Whitney U-test was used for nonparametric variables, and the Fisher exact test was used for nominal variables.

Power analysis was done assuming that the true difference between the ‘best fit’ ETT ID mean and hypothetical average mean of the predicted IDs of all used formulae is 0.27, our study has an 80% power with a significance level (alpha) of 0.05 (two-tailed).

**Results**

Non parametric correlation using spearman rank with no gaussian assumption showed that the ‘best fit’ ETT ID has a strong correlation with age (r = 0.872, P < 0.001) with 95% CI 0.880 to 0.927 and height (r = 0.804, P < 0.001) with 95% CI 0.673 to 0.886, and moderate correlation with weight (r = 0.675, P < 0.001) with 95% CI 0.482 to 0.806 (Figure 1). The p-values shown here describe the likelihood of no correlation (r = 0) and do not describe the strength of the association.

**Table 1**

<table>
<thead>
<tr>
<th>‘best fit’</th>
<th>N. of cases</th>
<th>Age (years)</th>
<th>Age-predicted size</th>
<th>Length-predicted size</th>
<th>Multivariate-predicted size</th>
<th>5th fingernail width-predicted size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>2.25 (2.0-3.0)</td>
<td>4.56 ± 0.269</td>
<td>4.65 ± 0.354</td>
<td>4.42 ± 0.071</td>
<td>4.0 ± 0.00</td>
</tr>
<tr>
<td>4.5</td>
<td>11</td>
<td>4.05 (2.5-7.0)</td>
<td>4.92 ± 0.205</td>
<td>5.30 ± 0.457**</td>
<td>5.09 ± 0.386**</td>
<td>4.82 ± 0.603</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>4.85 (3.0-7.0)</td>
<td>5.337 ± 0.566</td>
<td>5.75 ± 0.448*</td>
<td>5.49 ± 0.404</td>
<td>5.15 ± 0.337</td>
</tr>
<tr>
<td>5.5</td>
<td>13</td>
<td>6.65 (5.0-9.0)</td>
<td>5.66 ± 0.321</td>
<td>5.92 ± 0.263**</td>
<td>5.77 ± 0.273</td>
<td>5.38 ± 0.363</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>8.22 (6.0-10)</td>
<td>6.06 ± 0.391</td>
<td>6.22 ± 0.228</td>
<td>6.34 ± 0.365</td>
<td>6.22 ± 0.755</td>
</tr>
<tr>
<td>6.5</td>
<td>5</td>
<td>9.7 (9.0-10)</td>
<td>6.42 ± 0.112</td>
<td>6.57 ± 0.383</td>
<td>6.72 ± 0.29*</td>
<td>6.6 ± 0.418</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>6.13 (2.0-10)</td>
<td>5.54 ± 0.622</td>
<td>5.82 ± 0.572**</td>
<td>5.71 ± 0.67*</td>
<td>5.43 ± 0.821</td>
</tr>
</tbody>
</table>

Data are presented as number, mean ± SD, or mean (range). N. = number, * = p < 0.05, ** = p < 0.001
The mean (SD) IDs for the ‘best fit’, age-based, length-based, multivariate and 5th fingernail techniques were 5.31 (0.691), 5.54 (0.622), 5.82 (0.572), 5.71 (0.67) and 5.43 (0.821) mm, respectively. The differences were statistically significant for length-based and multivariate-based formulae (Table 1). The mean (SD) of the total fit used tube of 5.31 (0.691) (Table 1).

Table 2

<table>
<thead>
<tr>
<th>Match between ‘best fit’ and predicted size.</th>
<th>‘best fit’</th>
<th>best fit’</th>
<th>best fit’</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>predicted</td>
<td>&lt; size</td>
<td>&gt; size</td>
</tr>
<tr>
<td>Age-based</td>
<td>11 (22)</td>
<td>29 (58)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>Length-based</td>
<td>3 (6)</td>
<td>44 (88)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Multivariate-based</td>
<td>0 (0)</td>
<td>41 (82)</td>
<td>9 (18)</td>
</tr>
<tr>
<td>5th fingernail-based</td>
<td>24 (48)</td>
<td>15 (30)</td>
<td>11 (22)</td>
</tr>
</tbody>
</table>

Data are number (%)

Furthermore, after approximation of the predicted sizes for each formula as described above, no changes were observed. Number of matching cases between the size of ‘best fit’ and predicted size by each formula is summarized in Table 2. Number of matching cases between the size of ‘best fit’ and approximated predicted size by each formula is summarized in Table 3.

Table 3

<table>
<thead>
<tr>
<th>Matching between ‘best fit’ and approximated predicted size</th>
<th>‘best fit’</th>
<th>best fit’</th>
<th>best fit’</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>predicted</td>
<td>&lt; size</td>
<td>&gt; size</td>
</tr>
<tr>
<td>Age-based</td>
<td>43 (86)</td>
<td>7 (14)</td>
<td>00</td>
</tr>
<tr>
<td>Length-based</td>
<td>30 (60)</td>
<td>20 (40)</td>
<td>00</td>
</tr>
<tr>
<td>Multivariate-based</td>
<td>29 (58)</td>
<td>21 (42)</td>
<td>00</td>
</tr>
<tr>
<td>5th fingernail-based</td>
<td>46 (92)</td>
<td>3 (6)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Data are number (%)

Discussion

In 1971, Brown emphasized the proper selection of uncuffed ETT for use in the pediatric population in order to avoid related problems and complications10. Since the human body build and structure are different across populations, the predicted size of the ‘best fit’ ETT calculated for children of various countries does not remain consistent, even when using the same formula. Wang et al. demonstrated that body height had the best correlation to the size of an uncuffed oral ETT in Chinese children, in contrast to Caucasians5. Hofer et al. concluded that endotracheal tube size selection using the Broselow tape appeared to match the size of the tube used better than the ABF; the results in a European sample of children are comparable to the US data11. In Japan, Shima et al. concluded that endotracheal tube size was most correlated with body length, followed by body weight, tracheal size in X-ray photograph and age12. King et al. concluded that neither the 5th finger width nor the 5th finger diameter could accurately predict proper endotracheal tube size in most children. It was indicated that a more accurate estimation could be made using the ABF. That study did not examine length-based and multivariate-based formulae7.

In contrast to these findings, our results show that the ‘best fit’ ETT mean size is not significantly different from that predicted by age-based and 5th fingernail width formulas, but it is significantly different from that predicted by length-based and multivariate formulas. Davis et al. compared the ABF with the length-related formula. In agreement with our finding, it was concluded that the ABF was reliable and easily applied and accepted for routine anesthesia in their pediatric population9. Koichi et al. concluded from a retrospective analysis of 1301 charts from Japanese children undergoing pediatric surgery, that the ABF was applicable to Japanese children. However, it was recommended that three sizes should be available before endotracheal intubation13. In a recently published study on a weight-based formula (WBF) for tracheal tube size in children, it was found that the WBF was statistically inferior to the ABF in selecting the best tube size for children. However, when inaccurate the conventional ABF tended to underestimate while the WBF tended to overestimate the appropriate size of tracheal tube in pediatric anesthesia14.

In conclusion, the selection of the ETT as ‘best fit’ by observing the air leak test is subjective and may not be very accurate. Moreover, this is a descriptive study performed in a single institution and only a larger multicenter prospective study would be able to validate the results, especially with regard to the
different formulae used for predicting the adequate size of an uncuffed ETT. We believe that the age-based and 5th fingernail width-based formulae for predicting of ETT size are more accurate than length-based and multivariate-based formulae among our children.

References
SEDATION IN ICU: ARE WE ACHIEVING GOALS?

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Abstract

Objective: The purpose of this study was to examine whether sedation goals, utilizing a validated sedation assessment scale, the Riker Sedation-Agitation Scale (SAS), and a standardized sedation protocol, were achieved in Intensive Care Unit (ICU) patients.

Design: This is a nested prospective cohort study

Setting: The study was conducted in a tertiary care medical-surgical ICU.

Patients: All mechanically ventilated adult patients who were judged by their treating intensivists to require intravenous sedation for more than 24 hours, were included in the study.

Interventions: A goal-directed protocol using the SAS was initiated following an educational program to the medical and nursing staff.

Measurements and Main Results: The following data was collected: patients’ demographics, Acute Physiology and Chronic Health Evaluation (APACHE) II score, reason for admission, and outcome. For the first five ICU days, the bedside nurse documented ordered and average achieved SAS scores, every 4 hours. We compared the targeted versus achieved SAS scores using a paired Student’s t-test. One hundred and five (105) patients were included in the study with mean age (±SD) of 47 (±23) and APACHE II (±SD) of 21 (±9). Achieved sedation scores were consistently lower than the requested goals during daytime and nighttime shifts throughout the study period. This did not change even after 3 months of implementing the protocol.

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Financial support: None of the authors has any financial interests to disclose.


Abbreviations: Acute Physiology and Chronic Health Evaluation (APACHE) II, Do Not Resuscitate (DNR), Intensive Care Unit (ICU), Length of Stay (LOS), Sedation-Agitation Scale (SAS), Standard Deviation (SD), Visual Analogue Scale (VAS).
**Conclusion:** Achieved levels of SAS score were consistently lower than what was requested by physicians despite an educational program and the use of a standardized protocol. Differences between targeted and achieved SAS scores persisted throughout the whole study period even three months after protocol implementation. These data suggest the need for alternative, more sensitive and precise approaches, to titrate sedation to targeted levels.

**Key Words:** Sedation, Sedation-Agitation Scale, Intensive Care, Protocol.

**Introduction**

Targeted sedation is central to the care, and outcome of critically ill patients. Both under- and oversedation of critically ill patients are undesirable and are associated with complications. Inadequate sedation can result in anxiety, agitation and in recall

**Table 1**

Summary of the ICU Analgesia-Sedation Protocol

<table>
<thead>
<tr>
<th>Document Analgesia and Sedation Scoring every 4 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>DATE: TIME: This form is valid till 14:00 hours</td>
</tr>
</tbody>
</table>

**Target: Sedation Score**

| 1 | 2 | 3 | 4 |

**ANALGESIA**

- Morphine (Preferred in hemodynamically stable patients)
  - 1-2 mg IV q 5-10 min until pain is controlled (maximum dose _____ mg)
  - PRN doses _____ mg I.V. q _____ hourly
  - Infusion _____ mg/hour
- Fentanyl (Preferred in hemodynamically unstable patients)
  - 25-100 mcg IV q 5-10 minutes until pain is controlled (maximum dose _____ mcg)
  - PRN doses _____ mcg I.V. q _____ hourly
  - Infusion _____ mcg/hour

**SEDATION**

- If sedation is planned for ≤ 3 days
  - Propofol Infusion: _____ mg/hour (check triglyceride level after two days)
  - Dexmedetomidine Infusion: _____ mcg/kg/hour
- If sedation is planned for > 3 days
  - Midazolam PRN doses _____ mg IV q _____ hourly
  - Midazolam _____ mg IV q _____ hourly
  - Midazolam infusion _____ mg/hour

**IN PATIENTS WHO REACHED THE GOAL OF SEDATION AND ANALGESIA**

Taper infusion by 20% every 4 hours until infusion is discontinued

- Yes (most patients)
- No (only in selected patients, such as patients on neuromuscular blockers, recent severe head injury, high ventilation settings)
of stressful experience following ICU discharge. On the other hand, inappropriate and excessive sedation commonly occurs; and causes prolongation of mechanical ventilation and ICU and hospital length of stay (LOS), increased risk of pneumonia and sepsis, and increased mortality and costs. Therefore, optimizing sedation is a universal goal for critical care practitioners.

To avoid under- and oversedation, the use of sedation protocol and sedation scoring system, to regularly assess and document sedation level, have been recommended. The establishment of endpoints of sedation has been demonstrated to improve clinical practice of sedation.

The purpose of this study was to examine whether the ordered levels of sedation in the ICU, using a sedation scoring system (Riker Sedation-Agitation Scale: SAS) with a sedation protocol which incorporates nurse-driven dose titration directives, were achieved. Our hypothesis was that the use of a sedation-score-based protocol, would not achieve the sedation goal. This would have implications on clinical practice of sedation in the ICU.

Materials and Methods

Setting: This is a nested prospective cohort study from a prospective observational study comparing protocolized versus non-protocolized sedation practice. The study was conducted in a 21-bed, tertiary care medical-surgical ICU in an 800-bed teaching hospital in Riyadh, Saudi Arabia, between October 1, 2002 and March 31, 2003. The ICU, which admits more than a thousand patients per year, is run as a closed unit 24 hours a day, seven days a week by in-house, full-time critical care board-certified intensivists. The study was approved by the institutional review board (IRB) of the hospital.

Patients: The study included all mechanically ventilated patients who were managed with protocolized sedation and met the following criteria: adult (≥18 years of age), and ascertained by the treating intensivist to require intravenous sedation for more than 24 hours. Exclusion criteria included: (a) sedation not expected to be beyond 24 hours, (b) admission following cardiac arrest, (c) ICU readmission, (d) “Do-Not-Resuscitate” (DNR) status, (e) epidural analgesia, and (f) brain death.

Sedation Protocol: Prior to and during the study period, the medical and nursing staff attended an educational program on ICU sedation consisting of lectures and in-services.

A standardized goal-directed protocol was

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Dangerous agitation</td>
<td>Pulling at endotracheal tube (ETT), trying to remove catheters, climbing over bedrail, striking at staff, trashing side-to-side</td>
</tr>
<tr>
<td>6</td>
<td>Very Agitated</td>
<td>Does not calm despite frequent verbal reminding of limits, requires physical restraints, biting ETT</td>
</tr>
<tr>
<td>5</td>
<td>Agitated</td>
<td>Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions</td>
</tr>
<tr>
<td>4</td>
<td>Calm and Cooperative</td>
<td>Calm, awakens easily, follows commands</td>
</tr>
<tr>
<td>3</td>
<td>Sedated</td>
<td>Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands</td>
</tr>
<tr>
<td>2</td>
<td>Very sedated</td>
<td>Aroused to physical stimuli but does not communicate or follow commands, may move spontaneously</td>
</tr>
<tr>
<td>1</td>
<td>Unarousable</td>
<td>Minimal or no response to noxious stimuli, does or communicate or follow</td>
</tr>
</tbody>
</table>
established by a medical-nursing taskforce, based on published recommendations\textsuperscript{10} and consisted of a daily physician order form (Table 1). Validated scoring systems were used to assess the level of pain and sedation-agitation. Whenever possible, the level of pain reported by the patient was graded using a Visual Analogue Scale (VAS). Patients who could not communicate were assessed through observation of pain-related behaviors (movement, facial expression, and posturing) and physiological indicators (heart rate, blood pressure, and respiratory rate)\textsuperscript{10}. Sedation of agitated patients was started only after providing adequate analgesia and treating reversible physiological causes. A validated sedation assessment scale (SAS) was used to assess the level of sedation-agitation\textsuperscript{12,13} (Table 2). The treating physician decided the sedation goal ranging from one to four, on a daily basis, depending on the patient’s condition. The bedside nurse adjusted the dosage of analgesics and sedatives to reach the targeted level of sedation. To avoid oversedation, when sedation goals were reached, doses of analgesics and sedatives were reduced by 20% every 4 hours until discontinued. Doses were not tapered in patients with increased intracranial pressure, patients with high ventilatory settings, and patients receiving neuromuscular blocking agents. The use of short-acting drugs such as fentanyl, propofol, and dexmedetomidine was recommended for patients anticipated to require sedation for less than 3 days. Long-acting drugs such as benzodiazepines and morphine were otherwise used. Order form was valid only for 24 hours and had to be rewritten on a daily basis.

Data Collection: The following data were collected: demographics including age, and gender; Acute Physiology and Chronic Health Evaluation (APACHE) II\textsuperscript{16} scores; admission categories derived

| Table 3  
| Baseline characteristics |
|--------------------------|-------------------|
| Variable                 | 105               |
| Number, n                |                   |
| Age in years (mean ± SD) | 47 ± 23           |
| Male gender, n (%)       | 74 (71)           |
| APACHE II (mean ± SD)    | 21 ± 9            |
| Mechanical Ventilation, n (%) | 105 (100)   |

Admission Category

| Medical, n (%) | 52 (50) |
| Surgical, n (%) | 16 (15) |
| Trauma, n (%) | 37 (35) |

Chronic Underlying Illnesses

| Chronic respiratory disease, n (%) | 6(6) |
| Chronic renal disease, n (%) | 6 (6) |
| Chronic immunosuppression, n (%) | 7 (7) |
| Chronic cardiovascular disease, n (%) | 1 (1) |
| Chronic liver disease, n (%) | 7 (7) |

Mortality

| ICU, n (%) | 16 (16) |
| Hospital, n (%) | 24 (23) |

SD: Standard Deviation
APACHE: Acute Physiology and Chronic Health Evaluation
ICU: Intensive Care Unit
from the APACHE II system divided into the following groups: medical, surgical, and trauma\(^16\); severe chronic illnesses classified using APACHE II definitions\(^16\) (chronic respiratory disease, chronic cardiovascular disease, chronic renal disease, chronic liver disease, and immune suppression); and ICU and hospital outcome. The average SAS score achieved for each 12-hour shift for the first 5 days (or for the ICU stay if less than 5 days) was calculated and compared to the targeted score. Differences between achieved and targeted scores were compared for the first and second three months intervals to discern whether sedation goals were better achieved after a period of protocol implementation.

**Statistical Analysis:** Minitab for windows (Minitab Inc., Release 12.1, State College, PA, U.S.A.) was used for statistical analysis. Descriptive statistics were used to describe patients’ baseline characteristics. Continuous variables were described as mean and standard deviation (±SD) and compared using a paired Student’s t-test. Categorical variables were expressed as absolute and relative frequencies and compared using a Chi-Square test. A P value of ≤ 0.05 was considered significant.

### Results:

**Baseline Characteristics:** One hundred and five (105) patients were included in the study. The mean (±SD) age of patients was 47 (±23) years. There were 74 (71%) male patients. The mean (±SD) APACHE II score was 21 (± 9). As per study inclusion criteria, all 105 (100%) patients received mechanical ventilation. The admission categories were as follows: medical

### Table 4

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Ordered versus achieved SAS scores (±SD) during the 1st and 2nd three months.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First 3 months</td>
</tr>
<tr>
<td></td>
<td>Ordered SAS</td>
</tr>
<tr>
<td>D1</td>
<td>2.85 ±1.13</td>
</tr>
<tr>
<td>N1</td>
<td>2.68 ±1.21</td>
</tr>
<tr>
<td>D2</td>
<td>2.69 ±1.33</td>
</tr>
<tr>
<td>N2</td>
<td>2.77 ±1.36</td>
</tr>
<tr>
<td>D3</td>
<td>2.90 ±1.29</td>
</tr>
<tr>
<td>N3</td>
<td>2.89 ±1.33</td>
</tr>
<tr>
<td>D4</td>
<td>2.88 ±1.32</td>
</tr>
<tr>
<td>N4</td>
<td>2.98 ±1.31</td>
</tr>
<tr>
<td>D5</td>
<td>3.20 ±1.19</td>
</tr>
<tr>
<td>N5</td>
<td>3.16 ±1.23</td>
</tr>
</tbody>
</table>

SAS: Sedation - Agitation - Scale
D: Day (7:00 am - 6:59 pm)
N: Night (7:00 pm - 6:59 am)
a period of protocol implementation. However, the achieved level of sedation remained significantly lower in the second three months interval as compared to the first three months interval.

Despite the implementation of guidelines and recommendations for continuous administration of analgesics and sedatives, critically ill patients are often more sedated than requested. Our study suggests that oversedation is not finally avoided by implementing these guidelines. We suggest that other factors may be responsible for oversedation including the lack of validated and objective methods for assessment of sedation and the difficulty in discriminating between degrees of sedation using only subjective clinical assessments. Oversedation may also be reduced by the use of ultra-short-acting analgesics and sedatives that can be tapered and titrated with immediate effects.

Sedation is an essential component of the management of patients who are critically ill and require mechanical ventilation. The goal for sedation is to provide environmental and nonpharmacologic interventions, as well as pharmacologic therapies to achieve and maintain an optimal level of comfort and safety for the critically ill patient. Deep sedation is necessary in only a selected group of ICU patients, such as those with elevated intracranial pressure, neuromuscular blockade, or high ventilatory settings.

**Fig. 1**

*Ordered versus achieved SAS scores*

SAS: Sedation-Agitation-Scale
D: day (07:00 a.m. to 06:59 p.m.)
N: night (07:00 p.m. to 06:59 a.m.)

52 (50%), surgical 16 (15%), and trauma 37 (35%). Severe chronic illnesses were distributed as follows: respiratory 6 (6%), cardiovascular 1 (1%), renal 6 (6%), hepatic 7 (7%), and immune suppression 7 (7%). The ICU and hospital mortality were 16 (16%) and 24 (23%), respectively (Table 3).

**Targeted versus achieved SAS scores:** Achieved SAS scores were slightly but significantly and consistently lower than the targeted scores during both daytime (07:00 am to 06:59 pm) and nighttime (07:00 pm to 06:59 am) shifts throughout the study period (Fig.1). Differences between achieved and targeted scores remained significant in the second three months interval as compared to the first three months interval (Tables 4).

**Discussion**

This prospective study found that despite the use of a scoring system and a sedation protocol, achieved levels of sedation were lower than those targeted by the treating physician.

Our study is the first to demonstrate a significant difference between the ordered and the achieved level of sedation in critically ill patients. The discrepancy between the desired and achieved level of sedation persisted throughout the whole study period. One may expect sedation goals to be better achieved after
or in patients requiring immobility due to unstable spinal fracture, open surgical wound, or invasive medical devices. Both undersedation and oversedation are undesirable and should be avoided in intensive care patients. Undersedation can result in anxiety, agitation, self-removal of medical devices, and in recall of stressful experiences in the post-ICU phase and posttraumatic stress disorder. Oversedation can lead to hemodynamic compromise; prolonged ventilation and ICU and hospital length of stay (LOS); increased risk of pneumonia and sepsis; and increased mortality and costs. Optimal sedation, while a universal goal for all critical care practitioners, remains a difficult task to accomplish. In 2002, the American Society of Health-System Pharmacists (ASHP) and the Society of Critical Care Medicine (SCCM) published “Clinical Practice Guidelines for the Sustained Use of Analgesics and Sedatives in the Critically Ill Adult”. These guidelines are intended to standardize patient care and provide specific recommendations including: a) establishing and regularly redefining a patient-specific sedation goal or endpoint; b) documenting regular assessment and response to therapy; c) using a validated sedation assessment scale such as the Ramsay sedation scale (RSS), Riker Sedation-Agitation Scale (SAS), Motor Activity Assessment Scale (MAAS), Richmond Sedation-Agitation Scale (RASS), and d) using a sedation protocol.

Reported data suggest that ICU sedation protocols used to prevent oversedation can significantly improve outcomes. In a previous study, we have demonstrated that implementing a sedation protocol along with an educational program was effective in improving sedation practices and patients’ outcomes in the ICU. Moreover, the educational and feedback program rather than the direct effect of the protocol itself appeared to be responsible for most of the observed effects. We concluded that such an educational program is critical for the success of ICU sedation protocol.

This study has a number of strengths including the prospective nature of data collection, the consecutive placement of all patients on a sedation protocol and, to the best of our knowledge, it is the first to examine the difference between the targeted and the achieved levels of sedation.

Our study has also several limitations. First, it was conducted in a single center with heterogeneous group of patients. Second, the lack of objective methods for assessment of sedation and the use of subjective clinical assessments may have made the measurement of achieved levels not as accurate as actual; however, this difference could have been in either direction. Third, more than nurse assessed the achieved level of sedation during the course of the study and there may have been some disparity in discriminating the levels of sedation among the nurses.

Conclusion

Achieved levels of sedation were consistently lower than what was requested by physicians despite the conduction of an educational program and the implementation of a standardized protocol and a validated scoring system for sedation of critically ill patients. More reliable and objective measures of sedation may help to overcome this difficulty and improve clinical practice of sedation. Further studies are required to confirm these findings and to explore methods that would more reliably allow the targeted level of sedation to be reached.
References


15. ARABI Y, ALSHIMEMRI A, TAHER S: Weekend and weeknight admissions have the same outcome of weekday admissions to an intensive care unit with onsite intensivist coverage. *Crit Care Med*; 2006, 34:605-611.


Abstract

60 patients, ASA I-III, underwent one-lung ventilation for open or video-assisted thoracic surgery randomized either with intravenous anesthesia with propofol or with inhalational anesthesia with 1 MAC sevoflurane. Propofol was titrated during one-lung ventilation to achieve a mean arterial pressure of 75-80 mmHg. Blood gas analyses, hemodynamic and respiratory parameters were measured during two-lung ventilation at the beginning of the surgical procedure and 10 min, 20 min and 30 min after start of one-lung ventilation. At all time points, hemodynamic and respiratory parameters were comparable in both groups. Oxygenation did not differ between groups at comparable mean arterial blood pressures.

Introduction

Inhibited hypoxic pulmonary vasoconstriction (HPV) during one-lung ventilation (OLV) deteriorates oxygenation by increasing the intrapulmonary shunt. In vitro volatile anesthetics inhibit HPV, whereas intravenous agents, like propofol, do not affect HPV. This may lead to favour propofol for thoracic anesthesia. On the other hand fast on-and offset and bronchodilatatory effects may encourage the use of volatile agents like sevoflurane during OLV.

In a prospective randomized study we compared the effects of sevoflurane and propofol on oxygenation during OLV for thoracic surgery at comparable mean arterial pressures.
Methods and Materials

The study was performed at the University Hospital in Jena, Germany. Following IRB-approval and with written patient informed consent, 60 patients ASA I-III scheduled for thoracic surgery were randomized to receive either total intravenous anesthesia with propofol, or inhalational anesthesia with sevoflurane.

Premedication was done orally with 25-50 mg clorazepate dipotassium in the evening and 7.5-15 mg midazolam 1h before surgery. Anesthesia was induced with propofol (2 mg/kg) and remifentanil (0.5-1.0 µg/kg). Rocuroniumbromide (0.9 mg/kg) or cisatracurium (0.15 mg/kg) was used to facilitate tracheal intubation with a double-lumen endotracheal tube (Broncho-Cath®, Mallinckrodt, Athlone, Ireland). Tube positioning was controlled via bronchoscopy before and after patients were placed in the lateral position3. A radial arterial cannula was inserted in every patient. Anesthesia was maintained by continuous infusion of remifentanil (400-1800 µg/h) and 1.0 MAC sevoflurane in oxygen or propofol, which was titrated within a range of 3-6 mg kg⁻¹ h⁻¹ to achieve a mean arterial pressure of 75-80 mmHg. If an epidural catheter for postoperative pain treatment was placed before induction of anesthesia, no epidural medication was given until the end of the study period.

After thoracotomy or positioning of the trocars for thoracoscopy OLV was started. Lung collapse was verified by view and by continuous capnometry of the upper lung. Patients were ventilated in a pressure-controlled mode with a PEEP of 5 cm H₂O with a FiO₂ of 0.9 (ADU plus ventilator, Datex, Helsinki, Finland). Respiratory frequency was increased up to 20 per min and the peak inspiratory pressure was raised stepwise up to a maximum of 30 cm H₂O to maintain endtidal CO₂ at approximately 32 mmHg during OLV.

10 minutes, 20 minutes and 30 minutes after beginning of OLV, arterial blood gases (ABL 625, Radiometer Copenhagen, Danmark), heart rate, mean arterial pressure, SpO₂ and ventilatory parameters were measured (AS 3, Datex, Helsinki, Finland). During the study period no surgical occlusion of blood flow to the non-ventilated lung took place.

Patients received 15-20 ml/kg of body-warm balanced electrolyte solutions during the study period. If the mean arterial pressure dropped below 60 mmHg norepinephrine was given intravenously.

If at any time patients’ SpO₂ decreased below 91%, OLV would be interrupted and the collapsed lung would be ventilated for one minute. Then the study period would start afresh 10 minutes after restart of

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic Patient Data. Data are presented as numbers or mean and standard deviation when appropriate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male: female)</td>
<td>19:9</td>
<td>16:10</td>
</tr>
<tr>
<td>Bodyweight</td>
<td>75 ± 14</td>
<td>78 ± 14</td>
</tr>
<tr>
<td>Age</td>
<td>61 ± 14</td>
<td>57 ± 14</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Operated lung (right/left)</td>
<td>17/11</td>
<td>16/10</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Video-assisted thoracic surgery</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Metastasectomy</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Cardiovascular disease included hypertension, coronary artery disease, and valvular heart disease
Pulmonary disease included obstructive or restrictive lung disease or a combination of both
OLV. If SpO₂ would decrease two times below 91%, CPAP-should be used continuously and the study would be discontinued in this patient.

Data are presented as mean and standard deviation. Analysis of variance, using a repeated-measures term, was performed for comparison of hemodynamic and respiratory variables between groups and over time. A p<0.05 was considered significant.

Results
Six of 60 patients had to be excluded from the analysis: following the study protocol one patient in the propofol group was excluded because SpO₂ dropped without CPAP two times below 91%, in a second patient in the sevoflurane group CPAP of the non-ventilated lung had to be used on demand of the surgeon, in four patients thoracoscopy was finished before the third time point for measurements was reached. 26 of the included 54 patients were treated with propofol (mean dosage 4.54 mg kg⁻¹ h⁻¹).

Both study groups were comparable with regard to demographic characteristics, concomitant diseases and type of surgery (Table 1).

Also the demand for norepinephrine during OLV in both groups differed not significantly (5 patients in the propofol group versus 7 patients treated with sevoflurane).

Heart rate and mean arterial pressure differed neither between the groups nor time dependend during the study period (Table 2).

During the study period respiratory parameters, PaO₂, PaCO₂, O₂Hb and SpO₂ were comparable between groups at the same time, but differed over time (Table 3, 4).

Discussion
The major finding of this study is that oxygenation during a 30 min period of OLV did not differ between 1 MAC sevoflurane and intravenous anesthesia with propofol in a study protocol which demands comparable mean arterial pressure in both study groups.

Whereas experiments conducted in isolated lung models usually demonstrate direct inhibitory effects of sevoflurane on HPV, in vivo the direct effect on HPV interacts with indirect effects of inhalational anesthetics on the hemodynamic status producing different results: Ishibe et al. demonstrated in vitro that sevoflurane impairs HPV in isolated rabbit lungs^1. In vivo, however, Lesitsky and Kerbau1 found no attenuation of HPV in dogs and piglets^4,5.

Clinical trials may be further influenced by the pulmonary pathology and hemodynamic effects of the operative procedure: Abe et al found a lower oxygenation during sevoflurane anesthesia as during propofol anesthesia^6. In contrast, Beck et al. reported in a clinical study an unchanged shunt fraction and oxygenation during OLV with sevoflurane compared with intravenous anesthesia with propofol^7. In 2007 Pruszkowski et al. as well could not demonstrate a difference between sevoflurane and propofol in their study in 65 patients^8. They used epidural anesthesia during the study period of 40 min OLV in all patients. The application of Sevoflurane and propofol was adjusted to maintain bispectral index monitor (BIS) values between 40 and 60.

The comparison between an inhalational agent and an intravenous anesthetic agent is always difficult. Since in the clinical setting cardiovascular stability is often judged by MAP, we chose to adjust propofol levels in accordance with this parameter. Interestingly the concept of Pruszkowski and coworkers to compare sevoflurane and propofol in a BIS-controlled manner resulted in comparable mean arterial pressures between the two treatment groups^8. The overall MAP was slightly higher than in our study, which is easily explainable by the lower endtidal sevoflurane concentration of 1.3 ± 0.3% (i.e. ~0.5-0.7 MAC) in the study of Pruszkowski.

In conclusion in our study oxygenation during OLV differed not with propofol or sevoflurane at comparable mean arterial pressures.
Table 2
Hemodynamic parameters and number of patients treated with vasoactive agents.
Data are presented as mean and standard deviation

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Sevoflurane</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (bpm)</td>
<td>MAP (mmHg)</td>
</tr>
<tr>
<td>TLV</td>
<td>75 ±18</td>
<td>81 ±14</td>
</tr>
<tr>
<td>10 min OLV</td>
<td>75 ±16</td>
<td>89 ±14</td>
</tr>
<tr>
<td>20 min OLV</td>
<td>75 ±16</td>
<td>78 ±13</td>
</tr>
<tr>
<td>30 min OLV</td>
<td>75 ±15</td>
<td>80 ±12</td>
</tr>
</tbody>
</table>

No significant differences between TLV versus corresponding time within the treatment group or between sevoflurane and propofol.

Table 3
Respiratory parameters. Data are presented as mean and standard deviation

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Sevoflurane</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pmax</td>
<td>PEEP</td>
</tr>
<tr>
<td>TLV</td>
<td>24 ±4 *</td>
<td>5 ±0</td>
</tr>
<tr>
<td>10 min OLV</td>
<td>28 ±4</td>
<td>5 ±0</td>
</tr>
<tr>
<td>20 min OLV</td>
<td>27 ±4</td>
<td>5 ±0</td>
</tr>
<tr>
<td>30 min OLV</td>
<td>28 ±3</td>
<td>5 ±0</td>
</tr>
</tbody>
</table>

*p<0.01 for TLV versus corresponding time within the treatment group, no significant difference between sevoflurane and propofol.

Table 4
Oxygenation, oxygen saturation and PaCO2. Data are presented as mean and standard deviation.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Sevoflurane</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PaO2</td>
<td>SpO2</td>
</tr>
<tr>
<td>TLV</td>
<td>400 ±98 *</td>
<td>99 ±1 *</td>
</tr>
<tr>
<td>10 min OLV</td>
<td>211 ±96</td>
<td>98 ±2</td>
</tr>
<tr>
<td>20 min OLV</td>
<td>169 ±77</td>
<td>98 ±2</td>
</tr>
<tr>
<td>30 min OLV</td>
<td>166 ±83</td>
<td>97 ±2</td>
</tr>
</tbody>
</table>

*p<0.01 for TLV versus corresponding time within the treatment group, no significant difference between sevoflurane and propofol.

**p<0.05 for TLV versus corresponding time within the treatment group, no significant difference between sevoflurane and propofol.

References
Abstract

**Purpose:** Propofol is a popular IV anesthetic induction drug that causes pain when given IV, the incidence of which is between 28%-90%. We plan to determine the optimal dose of ketamine in the prevention of propofol injection pain and compare it with lidocaine, the commonly proposed pre-treatment.

**Methods:** In a double-blind randomized study 500 Patients (ASA I, II) scheduled for elective strabismus surgery under general anesthesia were randomly allocated into five groups. After obtaining the informed consent., patients received normal saline (Group NS), lidocaine 1mg.kg⁻¹ (Group L), and different doses of ketamine 50-75-100 μg.kg⁻¹ (Group K50-K75-K100 respectively), immediately before the injection of 2.5 mg.kg⁻¹ propofol. Each patient’s pain scores were measured at five seconds intervals by a blinded anesthesiologist. Statistical analysis were made by SPSS vs 11.5.

**Results:** The incidence and intensity of pain in all study groups were significantly lower than placebo group(Group NS) (P<0.005).Patients in the K100 Group had significantly lower incidence of pain and lower pain scores compared with the K50 and L Groups (P<0.0001). There were no significant differences in hemodynamic parameters between groups.

**Conclusion:** Administration of ketamine 100 μg.kg⁻¹ immediately before propofol injection is a safe and effective method in preventing propofol injection pain.

**Key words:** ketamine, propofol, lidocaine, pain on injection
Introduction

Propofol is one of the most popular IV anesthetic induction drugs that causes pain when given IV. Several methods have been used to reduce this pain: adding lidocaine, warming or cooling the solution, dilution of propofol, injection through large bore veins, changing the speed of injection, using tourniquet and previous injection of lidocaine, benzodiazepines, ondansetron, metoclopramide, opioids, thiopental, flurbiprofen, ephedrine and ketamine. Lidocaine pre-treatment has been commonly proposed to decrease propofol induced pain, but its failure rate is between 13-32%.

Ketamine (a phencyclidine derivative) has potent analgesic effects and local anesthetic properties. It seems likely that the reduction in propofol injection pain was the result of a peripheral action which attenuated the afferent pain pathways. Ketamine as a NMDA receptor antagonist may activate these receptors either in the vascular endothelium or in the central nervous system. Although unpleasant dreams and emergence reactions seems to be associated with, it has some unique advantages notably, less cardiorespiratory depression than other anesthetics, which makes it a good choice in specific conditions. Few studies have evaluated the advantages of ketamine to reduce propofol-induced pain suggesting the effectiveness of ketamine in adults and children. Although lack of efficacy of the ketamine-propofol admixture in pediatrics was reported.

The purpose of this study is to determine the safe and optimal dose of IV ketamine and comparing it with IV lidocaine, as a pre-treatment for propofol-induced pain on injection during induction of general anesthesia.

Materials and Methods

Ethics Committee approval was obtained and all patients signed informed consent before enrollment in the study.

In a prospective, randomized, placebo-controlled, double-blinded study, 500 ASA I-II patients of 18-40 years old scheduled for elective strabismus surgery, were enrolled. Patients taking sedatives or analgesics in the past 24 hours before surgery and those with history of allergic reactions to anesthetic drugs, neurologic or cardiovascular disease and pregnant patients, were excluded from the study.

In all patients, a 20-gauge teflon catheter was inserted into a vein of the dorsum or wrist of the hand at approximately 60 minutes before the induction of anesthesia and 5cc.kg⁻¹ ringer lactate solution was infused.

Patients were randomly allocated into one of 5 treatment groups (100 each):

- Group NS received 5 ml 0.9% NS,
- Group L received 1mg.kg⁻¹ lidocaine,
- Groups K50, K75, K100 received 50μg.kg⁻¹, 75μg.kg⁻¹ and 100μg.kg⁻¹ ketamine respectively.

Study drugs were diluted with NS 0.9% up to 5cc and were prepared by an investigator not involved in drug injection or assessment of patients' responses.

All study drugs were slowly administered before propofol injection in 15 seconds. Immediately propofol (1%) 2.5mg.kg⁻¹ was injected slowly over 30 seconds. A blinded anesthesiologist before the administration of propofol asked the patient to rate any sensation of pain every 5 seconds during propofol injection graded as 0-3 VRS (Verbal Rating Scale) and recorded the highest score of pain. The grading criteria of VRS were as follows: 0 = no pain, 1 = mild pain or soreness, 2 = moderate pain and 3 = severe pain associated with grimacing, withdrawal, movement or both.

After the propofol injection and patients' loss of consciousness, atracurium 0.5mg.kg⁻¹, fentanyl 1.5μg.kg⁻¹, midazolam 0.02 mg.kg⁻¹ were administered and 3 minutes after atracurium injection the trachea was intubated and anesthesia was maintained with propofol infusion of 100μg.kg⁻¹.min⁻¹. Non-invasive blood pressure monitoring (MAP), HR monitoring by ECG and O₂ saturation with pulse oximetry were used in all patients. Patients were assessed regarding emergence reactions like delusion and agitation in the recovery room by an anesthesiologist blinded to patients' group.

Data were analysed by SPSS (v11) and were expressed as mean ± SD. Statistical comparison between groups were made by Chi² and One-way analysis of variance. For ordinal data of pain score, medians were compared by Man-Whitney test. A P<0.05 was considered significant in all tests.
Discussion

The incidence of propofol caused pain on injection has been reported to be between 28-91% in adults (88% in present study). Even small dose of propofol administered for sedation may induce pain varied between 33-50%.

Although the mechanism of this pain remains obscure, the endothelium irritation, osmolality changes, non pharmacologic pH and activation of pain cascade mediators like kinin have been suggested to be involved.

Different methods have been used to reduce this pain incidence and intensity, the most popular is the use of lidocaine either by mixing or pre-treatment. In this study the incidence of pain in lidocaine group was reported to be 65% which is somewhat higher than previous studies. Moreover ketamine doses of 100 μg.kg⁻¹ were more effective than IV.

Results

Patients demographic characteristics including age, gender and weight in each group are presented in Table 1. There were no significant differences among groups.

The incidence and intensity of pain in all study groups were significantly lower than placebo group (Group NS) (P<0.005) (Table 2). Patients in K100 Group had significantly lower pain incidence and median pain score compared with K50 and L groups (P<0.0001) (Table 2).

None of patients in K100 and K75 groups had severe pain or score 3 VRS. There were no significant differences in hemodynamic parameters between groups and no adverse events such as arrhythmias and allergic reactions during induction or intubation were seen. None of the patients had post anesthesia emergence reactions during recovery.

Table 1
Patients’ characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>NS (N=100)</th>
<th>L (N=100)</th>
<th>K50 (N=100)</th>
<th>K75 (N=100)</th>
<th>K100 (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>28.9±7.4</td>
<td>29.7±6.8</td>
<td>29.4±7.8</td>
<td>29.7±6.8</td>
<td>30.7±4.6</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>43/55</td>
<td>49/51</td>
<td>52/48</td>
<td>44/56</td>
<td>51/49</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>53±8.9</td>
<td>50±6.9</td>
<td>49.4±11</td>
<td>53.7±9</td>
<td>55.0±7</td>
</tr>
</tbody>
</table>

NS=Normal saline, L=Lidocaine, K100=Ketamine 100 μg.kg⁻¹, K50=Ketamine 75 μg.kg⁻¹ and K100=Ketamine 100 μg.kg⁻¹. Data are presented as mean±sd and number of patients.

Table 2
Incidence and intensity of pain on injection of Propofol in different study groups

<table>
<thead>
<tr>
<th>Intensity of pain</th>
<th>NS</th>
<th>L</th>
<th>K50</th>
<th>K75</th>
<th>K100</th>
</tr>
</thead>
<tbody>
<tr>
<td>None (Score 0)</td>
<td>12</td>
<td>35</td>
<td>40</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>Mild (Score 1)</td>
<td>34</td>
<td>39</td>
<td>35</td>
<td>39</td>
<td>42</td>
</tr>
<tr>
<td>Moderate (Score 2)</td>
<td>40</td>
<td>19</td>
<td>21</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Severe (Score 3)</td>
<td>14</td>
<td>7</td>
<td>4</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Any pain (%)</td>
<td>88%</td>
<td>65%</td>
<td>60%</td>
<td>55%</td>
<td>45%</td>
</tr>
<tr>
<td>Median pain score</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

NS=NaCl and Saline, L=Lidocaine, K100=Ketamine 100 μg.kg⁻¹, K50=Ketamine 75 μg.kg⁻¹ and K100=Ketamine 100 μg.kg⁻¹. Data are presented as mean±sd and number of patients.)
lidocaine 1mg.kg\(^{-1}\) (the commonly popular pre-treatment).

In the present study we observed that small dose ketamine (50-75-100 \(\mu g.kg^{-1}\)) administered just before propofol injection, reduced both the incidence and intensity of propofol injection pain without significant adverse hemodynamic effects, which strongly suggests this analgesic action is brought locally, not through the central nervous system because the dose used by us is much lower than the dose one would choose for a central analgesic effect. In addition, sympathetic activation caused by ketamine may attenuate the hypotension induced at induction with propofol, in comparison to lidocaine\(^{10}\).

In conclusion, our findings suggest that a dose of 100 \(\mu g.kg^{-1}\) ketamine administered just before propofol can reduce the incidence and intensity of propofol injection pain without significant adverse effects.

**Acknowledgements**

We thank the operating room staff of Farabi Hospital, Mr Akhavan and Miss Shahbazi from the Clinical Research Centre of Besat Hospital for their help.

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ACUTE POSTOPERATIVE PAIN MANAGEMENT
BY A SURGICAL TEAM IN A TERTIARY
CARE HOSPITAL: PATIENTS SATISFACTION

Masood Jawaid*, Shah Muhammad**, Faraz Shafiq***
and Khalid Ahsan Malik****

Abstract

Objective: To assess the acute postoperative pain management by a surgical team and patient satisfaction in a tertiary care teaching hospital.

Patients and Methods: 105 patients, ASA I & II, both sexes, mean age of 35.1 ± 14.6 years, scheduled for general surgery under routine practice conditions, were included in the study. All patients were assessed 12 and 24 hours postoperatively by two numerical visual analogue scale (VAS 0-10), related to rest and dynamic pain. Patients were also requested to indicate their satisfaction level with the help of VAS. Data was analyzed by SPSS version 10. Student t test was applied to find significant differences between the groups.

Results: At 12 hours postoperatively mean rest and dynamic pain scores were 3.85 ± 2.45 and 5.32 ± 2.61 respectively. At 24 hours postoperatively mean rest and dynamic pain scores were 2.84 ± 1.86 and 4.65 ± 2.47 respectively. Overall, female patients experienced more pain but there was no statistically significant difference apart from rest pain at 24 hours. Forty-seven (44.8%) patients were very satisfied, 42 (40%) moderately satisfied and 16 (15.2%) patients were mildly satisfied with the pain management.

Conclusion: Overall management of acute postoperative pain by surgical team in a tertiary care hospital was satisfactory. Most of patients were moderately to very satisfied by the care provided.

Key words: Postoperative Pain, Acute, Patient Satisfaction, Surgical Team, Audit
Introduction

Good quality care is considered to be the right of all patients and the responsibility of all staff within a hospital. One of the essential components of surgical patient care is effective postoperative pain control. Inadequate pain control, apart from being callous, may result in increased morbidity and mortality. Important goals for postoperative pain management are to minimize discomfort, facilitate the recovery process and avoid complications. Recognizing some of these concerns, a special congressional mandate declared 2000-2010 to be the Decade of Pain Control and Research, to generate increased understanding and awareness of pain.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) implemented pain management standards in 2001 that recognized patients’ rights to appropriate assessment and management of pain. In the JCAHO guidelines, examples of implementation include the addition of pain as the “fifth” vital sign to be noted in the context of initial assessment; the use of pain intensity ratings; and posting of a statement on pain management in all patient care areas. In 2005, JCAHO National Patient Safety Goals promoted specific improvements in the use of medications and infusion pumps, among others. However, despite numerous regulatory initiatives and evolving advanced methods, postoperative pain remains a major challenge for many hospitals. Detailed information about patient’s assessments of pain and whether standards of pain management are being met are important factors to consider when identifying potential areas for improvement. Pain intensity is thought to be one of the primary factors that determine the impact of pain on a person’s overall function and sense of well-being.

For better management of postoperative patients, Acute Pain Service (APS) has been introduced in many countries. This provides high quality of pain management service which results in significant improvement in pain management in surgical patients along with the reduction in side effects associated with the different modalities.

The first anesthesia based APS was introduced in Pakistan at Aga Khan University Hospital Karachi in 2001 but only few other hospitals have properly functioning APS service. As there was no APS in our Institute, acute postoperative pain management became the responsibility of the surgical team. This study was planned to observe the results of routine management of postoperative pain by surgical team and to assess patient satisfaction.

Patients and Methods

The study was conducted in Surgical Unit II of Civil Hospital, Karachi in the period from October to December 2007 under routine practice conditions. After obtaining patients’ informed consent, 105 patients (65 males, 40 females), ASA I and II, mean age of 35.1 ± 14.6 years, scheduled for general surgery under routine practice conditions, were included in the study. All patients were provided with routine analgesic medication with intravenous or intramuscular route. The Numerical Visual Analogue Scale (VAS) was used to measure pain intensity. Participants were instructed to select the number that best reflected the intensity of pain, (1 no pain and 10 the worst possible pain imaginable). This scale was selected because it is more commonly used in clinical practice and has been found to be a reliable and valid measure of pain intensity.

All patients were assessed at 12 hours and 24 hours postoperatively by two numerical visual analogue scales (resting and dynamic pain). Resting pain was defined as pain at the surgery site experienced by patient when they are not moving, while dynamic pain was pain experienced on movements like walking, coughing, deep breathing. Total analgesics used were also recorded. The patients were also asked to indicate their satisfaction level with pain management with the help of Numerical Visual Analogue Scale (1-10). All the data was collected in a specially designed proforma and analyzed by SPSS version 10. Student t test was applied to find significant between different groups.

Results

Surgical procedures of all patients is shown in Table I.

At 12 hours postoperatively mean rest and dynamic pain scores, were 3.85 ± 2.45 and 5.32 ± 2.61 respectively. At 24 hours postoperatively mean rest and dynamic pain scores were 2.84 ± 1.86 and 4.65 ± 2.47
respectively. All pain scores with standard deviation are shown in Table II.

### Table II

<table>
<thead>
<tr>
<th>Pain</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperatively 12 hr Rest Pain</td>
<td>3.85 ± 2.45</td>
</tr>
<tr>
<td>Dynamic Pain</td>
<td>5.32 ± 2.61</td>
</tr>
<tr>
<td>Postoperatively 24 hr Rest Pain</td>
<td>2.84 ± 1.86</td>
</tr>
<tr>
<td>Dynamic Pain</td>
<td>4.65 ± 2.47</td>
</tr>
</tbody>
</table>

Total analgesics required during first 24 hours postoperative period are shown in Table III.

Pain scores difference between male and females is shown in Table IV.

### Table III

<table>
<thead>
<tr>
<th>Drug (IM/IV)</th>
<th>Mean (mg)</th>
<th>Standard Deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac Sodium (n = 105)</td>
<td>147.89</td>
<td>31.35</td>
<td>75-225</td>
</tr>
<tr>
<td>Nalbuphine (n = 51)</td>
<td>13.96</td>
<td>7.45</td>
<td>3-30</td>
</tr>
<tr>
<td>Tramol (n = 24)</td>
<td>200</td>
<td>51.5</td>
<td>100-400</td>
</tr>
</tbody>
</table>

IM: Intramuscular; IV: Intravenous; mg: milligram

Overall female patients experienced more pain but there is no statistically significant difference apart from pain at rest at 24 hours.

Forty-seven (44.8%) patients were very satisfied, 42 (40%) moderately satisfied and 16 (15.2%) patients were mildly satisfied with pain management (Table V).

### Table IV

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperatively 12 hr Rest Pain</td>
<td>Male</td>
<td>3.58</td>
<td>2.42</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4.28</td>
<td>2.48</td>
</tr>
<tr>
<td>Postoperatively 12 hr Dynamic Pain</td>
<td>Male</td>
<td>5.02</td>
<td>2.69</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>5.83</td>
<td>2.44</td>
</tr>
<tr>
<td>Postoperatively 24 hr Rest Pain</td>
<td>Male</td>
<td>2.51</td>
<td>1.58</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>3.38</td>
<td>2.16</td>
</tr>
<tr>
<td>Postoperatively 24 hr Dynamic Pain</td>
<td>Male</td>
<td>4.40</td>
<td>2.45</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>5.05</td>
<td>2.47</td>
</tr>
<tr>
<td>Patient Satisfaction</td>
<td>Male</td>
<td>6.57</td>
<td>2.82</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>6.20</td>
<td>2.67</td>
</tr>
</tbody>
</table>

* Significant p < 0.05

### Table V

<table>
<thead>
<tr>
<th>VAS*</th>
<th>Level of Satisfaction</th>
<th>n = 105</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>Mildly satisfied</td>
<td>16</td>
<td>15.2</td>
</tr>
<tr>
<td>4-7</td>
<td>Moderately satisfied</td>
<td>42</td>
<td>40.0</td>
</tr>
<tr>
<td>8-10</td>
<td>Very satisfied</td>
<td>47</td>
<td>44.8</td>
</tr>
</tbody>
</table>

* VAS: Visual Analogue Score

### Discussion

It is essential that regular assessments of postoperative pain are performed in the postoperative period. In Sweden, documentation of pain care by nurses was made compulsory by law in 1986.

Clinical guidelines and quality programs are considered as essential tools to enhance postoperative pain management.

Unfortunately in Pakistan, we do not have any national post operative pain management guidelines. Still worse is that we lack any institutional guideline about this important aspect of patient care. Despite all these facts, our study showed good quality of acute pain management by the surgical team. This should be seen with the understanding that we are using the conventional methods of pain management despite
global availability of modern techniques like Patient Controlled Analgesia, epidural or regional blocks. Being a government sector hospital, these modalities were routinely not used in our Department because of cost. Possible reasons of reporting less pain by our patients is the desire to be ‘a good patient’ as was observed by Lin et al, from Taiwan, or patients anticipated postoperative pain and wanted to be considered cooperative.

Our results highlight the differences (although statistically insignificant) between the gender in the reporting of pain, with females reporting higher level of pain. These findings are consistent with findings from other studies. Whether the higher reported pain is due to the higher sensitivity in somatic responses to painful stimuli, or because it is more socially acceptable for females to express pain is yet to be determined.

Postoperative pain relief must reflect the needs of each patient since the final determinant of the adequacy of pain relief will be the patient’s own estimation. A Swedish study showed that less than 10% of patient records contained notes on systematic assessment with a pain assessment instrument. Several authors have reported that the treatment of postoperative pain is inadequate for many patients, some of whom still suffer moderate to severe pain. Equally shocking is that 38% of patients at a university hospital were readmitted following same-day surgery due to pain. Klopfenstein et al considered the reasons for poor postoperative pain management as insufficient education, training of staff and patients and lack of communication between them. There were also divergent attitudes, absence of systematic recordings, pain assessment done only at rest, and lack of public awareness.

Patient satisfaction is rapidly evolving as an important consideration in the field of postoperative pain management. Organizations such as JCAHO and The National Committee for Quality Assurance (NCQA) have introduced standards that list patient satisfaction as one of several performance yardsticks.

Most of our patients were moderately to very satisfied with our pain management. Chung, et al showed that 21% of postoperative patients were extremely satisfied and 66% were satisfied with the degree of pain relief obtained. Twenty-eight (11.2%) were fairly satisfied, 4 (1.6%) were dissatisfied and 1 (0.4%) was extremely dissatisfied. All subjects received the prescribed dosage of analgesics, with the exception of 12 subjects who required an increase in their original prescribed dosage. Involvement of patients in their pain management might increase the awareness of pain but their satisfaction about postoperative pain control was significantly improved. Preoperative information and general condition affect the satisfaction with pain management as reported by Niemi-Murola, et al. In their study 80% of patients were satisfied with pain management, and their satisfaction correlated significantly with received preoperative information and preoperative well-being.

There are different challenges in the assessment of patient satisfaction: the lack of correlation between satisfaction and pain ratings; patients often report high levels of satisfaction despite moderate to severe pain experience. Idvall found that postoperative patients were very satisfied with the pain relief even if they reported severe pain in the previous 24 hours. This has been seen in other studies as well indicating that the level of pain does not correlate with the satisfaction of patients. This may be due to patient’s expectations that pain will be experienced after surgery. Prior experience with postoperative pain may also play a role in patient satisfaction, with previous experience often serving as a yardstick. Patient satisfaction cannot therefore be used as the sole indicator of an effective pain service in hospitals.

**Limitations of the Study**

One limitation is the fact after different surgical procedures, patients experienced different levels of pain, which was not taken into account in this study. Another limitation is that the intraoperative analgesia requirement and the type of narcotic used may alter the postoperative pain. For future studies along those lines, therefore, we recommend that the monitoring of hemodynamic variables and side effects associated with the conventional pain management therapy be considered, as their incidence of pain may be higher in the absence of properly functioning APS.
Conclusion

Despite the fact that Acute Pain Service (APS) is not available in our Institute, postoperative pain management by surgical team is satisfactory. Most of the patients were moderately to very satisfied by the care provided. Routine measurement of postoperative pain consistent with JCAHO requirements may result in much better patient care. This has the potential for improved pain management outcomes.
References

EFFECT OF MICROCURRENT SKIN PATCH ON THE EPIDURAL FENTANYL REQUIREMENTS FOR POST OPERATIVE PAIN RELIEF OF TOTAL HIP ARTHROPLASTY

TAREK M SARHAN*, AND MAHER A DOGHM* 

Abstract

Introduction: Major orthopedic surgery that cause considerable pain like total hip arthroplasty, requires good post operative pain management. Microcurrent therapy (MCT) is a new therapy whereby electric current is provided in literally millionth of an ampere. MCT comes as two self adherent active electrode patches linked by a cable. Efficacy of MCT in the management of musculoskeletal pain and enhancement of wound healing has been reported.

Aim of the work: To study the effect of microcurrent therapy (MCT) on the epidural fentanyl requirements and degree of wound healing after total hip arthroplasty.

Materials and Methods: Twenty eight patients undergoing total hip replacement (THR) were randomly allocated into two groups.

Group I: had micro current skin patches (two adhesive electrode) attached above the site of operation in addition to the lumbar epidural catheter. Post operative epidural fentanyl infusion with a syringe pump given at a rate ranged between 25 and 75 microgram per hour to keep visual analogue pain score (VAS) less than 3/10. Group II had only continuous epidural infusion with fentanyl at the same range to keep VAS less than 3/10 without MCT.

Results: There was statistically significant lower mean epidural fentanyl requirement in Group I (23.24 microgram) when compared to Group II (58.36 microgram).

There was 23% incidence of dermatitis in Group I due to application of micro-current skin patch which resolved by treatment.

There was statistically significant higher frequency of grade 1 of wound healing in the microcurrent group (41.3 %) when compared to Group II (7.2%). Grade 2 and 3 were more frequent in Group II.

Conclusion: The microcurrent skin therapy lead to reduction in the requirements of the post operative epidural fentanyl with improvement of degrees of wound healing but with considerable incidence of skin dermatitis after total hip arthroplasty.

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Introduction

Major orthopedic surgery that cause considerable pain like total hip arthroplasty requires good post operative pain management. Several techniques have been used for that purpose such as: intermittent injection of systemic opioids, epidural opioids and or local analgesia drugs, non steroidal anti-inflammatory drugs (NSAIDs), patients controlled analgesia (PCA) with opioids with different reports of efficacy and adverse effects1,2,3,4,5.

Non pharmacological treatments and alternative approaches are less widely accepted, they span over physical therapy, cryotherapy, continuous passive motion, transcutaneous electric nerve stimulation (TENS) and patient education, an individualized approach of one or more of the above mentioned approaches6,7,8,9,10.

Microcurrent therapy (MCT) is a totally new physical treatment method for electrotherapy11. It is a therapy used whereby electric current is provided in literally millionth of an ampere. It works on a cellular level to help stimulate the healing process. It is based upon the theory that the body’s electrical balance is disrupted when one is injured, so that the natural electrical current of the body changes course. Microcurrent stimulation restores this balance12.

In fact, microcurrent therapy can relieve pain, stimulate wound healing, help stimulate the regeneration of injured tissue, provide relief to myofascial trigger points, increase protein synthesis, and stimulate lymphatic flow. Microcurrent stimulation is produced in therapy at literally one millionth of an ampere, because this is believed to be the body’s own natural current strength. This therefore restores the body’s own natural current11.

When microcurrent stimulation is provided, it cannot be felt, because the sensory receptors are not stimulated. Other electrotherapy pain relief methods, such as TENS, are provided at higher occurrence in milliamps, thereby causing muscle contraction12.

With microcurrent therapy, ATP production increases by 500%. ATP is the primary molecule our bodies use to produce energy and is found in every cell of the body. In fact, it has been found that ATP production increased fivefold after microcurrent therapy was administered. As stated previously, protein synthesis also increased, and so did amino acid transport11.

When microcurrent therapy is used to help heal injured tissue, it restores the natural current flow to the tissue. This in turn allows the cells to regain their own natural energy flow. When injury occurs, the area that has been injured has a higher electrical resistance than the surrounding tissue does. This in turn decreases and perhaps even stops electrical flow through the injured area, which impedes the healing process and promotes inflammation. When microcurrent therapy is used, this resistance is reduced, which allows electricity to flow through and therefore restore normal function. This, in turn, helps stimulate natural healing12.

In addition, microcurrent therapy can be used at specific frequencies for a variety of tissues and conditions. This can often soften tissue and decrease pain, which provides long-lasting pain relief that may even be permanent. This has some promising benefits that may be applicable to current chronic pain conditions as well13.

MCT comes as a two self adherent active electrode patches linked by a cable, self generate the necessary current of approximately 10 micro amber required for stable galvanism.. The treatment however lasts 100 times longer than usual. Crucial for galvanic treatment is the quantity of charge carries Q (ions), which are being moved in the body tissues in the electrical field between the therapeutic electrodes as a measure of the degree of stimulation of electric active body structures (Gillert), in accordance with the equation for the physiologic galvanization effect:

\[ Q(\text{carrier}) = I(\text{current}) \times t(\text{time}). \]

An equal quantity of ions are moved during the course of 24 to 48 hours treatment with the microcurrent skin patch as with the more usual electrotherapy involving approximately an I (current) of 1 m A for a t (time) of 15 to 20 minutes13.

Recent reports on the efficacy of micro current therapy (MCT) in the management of musculoskeletal pain may offer a new non pharmacological approach for post operative pain relief of major orthopedic surgery.
Aim of the work

To study the effect of microcurrent therapy (MCT) on the requirements of epidural fentanyl for postoperative pain relief of total hip arthroplasty.

Patients and Methods

This study was a prospective randomized study included 28 patients who underwent total hip replacement (THR). After approval by local Ethical Committee, informed written consent were taken from all patients included in the study, they were randomly allocated into 2 groups of 14 patients each.

Group I: had microcurrent skin patches (Fig. 1) (two adhesive electrode) attached above the site of operation just away from the wound, in addition to the epidural catheter that was inserted at L4-L5 lumbar interspace. Postoperative fentanyl infusion was given at a rate ranged between 25 and 75 microgram per hour, using a syringe pump to keep visual analogue pain score (VAS) less than 3/10.

Group II: had only continuous epidural infusion with fentanyl at the same rate and range to keep VAS less than 3/10 without MCT.

Measurements

1 - Visual Analogue Scale (VAS) before starting postoperative pain treatment and every one hour for the first 36 hours.
2 - The mean dose of epidural fentanyl in both groups after 36 hours of postoperative period.
3 - Side effects and complications.

4 Degree of wound healing measured at the end of follow up period and categorized into grade 1, 2 and 3 (grade 1: dry suture line, no redness around suture line, normal skin texture around suture line, grade 2: wet suture line, no or minimal redness, normal skin, grade 3: wet or draining suture line, redness and surrounding skin changes of edema or bullae).

Results

There was no statistically significant differences on the Visual Analogue Scale (VAS) on both groups at all time of measurements.

There was statistically significant lower mean epidural fentanyl dose in Group I (microcurrent skin therapy group) (23.24 microgram) when compared to Group II (58.36 microgram) (Fig. 2).

There was 23% incidence of dermatitis in Group I due to application of microcurrent skin patch which resolved by treatment.

There was statistically significant higher frequency of grade 1 of wound healing in the microcurrent Group (41.3%) when compared to Group II (7.2%). Grade 2 and 3 were more frequent in Group II (Table 1).

<table>
<thead>
<tr>
<th>Grade</th>
<th>MCT</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>41.3%</td>
<td>7.2%</td>
</tr>
<tr>
<td>2</td>
<td>47.7%</td>
<td>58.8%</td>
</tr>
<tr>
<td>3</td>
<td>12%</td>
<td>34%</td>
</tr>
</tbody>
</table>
Discussion

Orthopedic procedures such as total hip arthroplasty (THA) is an ongoing challenge regarding post operative pain control, as current pain management techniques often result in undermedication and/or complications. The standard approach depends on systemic opioids given in bolus IV or IM or in patient controlled analgesia (PCA), epidural analgesia with narcotics with or without local analgesia and NSAIDs.

Non pharmacological methods are less widely accepted in the management of severe pain induced by this group of operations, they include physical therapy, cryotherapy, continuous passive motion (CPM), transcutaneous electric nerve stimulation (TENS) and patient education. Reports on the efficacy of cryotherapy and TENS are generally disappointing, while the use of CPM to control pain is controversial.

Several reports support a favourable effect of MCT as related to pain control and tissue healing, through the modification and recruitment of cell membrane ATP (adenosine triphosphate), but this was mostly reported in chronic painful conditions.

Microcurrent stimulation to the body causes radically increased production of adenosine triphosphate (ATP) levels. This allows the body to perform whatever healing process it has undertaken in an accelerated fashion. It may even allow one to get over the proverbial “hump” that was unachievable, due to insufficient ATP concentrations to perform the changes needed.

The result of the present study showed efficacy of MCT patches in reduction of the epidural fentanyl requirements after THR, demonstrating its efficacy in contribution of post operative pain relief. The present study shows that reduction of analgesic dose post operatively goes with that of El-Husseini et al during their study of the effect of microcurrent skin patches (MCT) for post operative pain relief in total knee arthroplasty which demonstrated reduction in the post operative tramadol dose with MCT patches.

Result of our study showed marked acceleration of wound healing with the microcurrent therapy which goes also with that of El-Husseini et al.

Microcurrent therapy, which is used from one to 600 uA clinically, is the modality of choice for increased tissue healing. Research and clinical trials have shown that the microcurrent stimulation, there is a 40-50% reduction in healing time of ulcers and sprain/strains ; fracture heal faster and stronger; that bad scarring remodel to become a healthier, stronger scar. Other ATP related microcurrent stimulatory effects include decrease inflammation, edema and swelling.

Conclusion

The microcurrent skin therapy lead to reduction in the requirements of the post operative epidural fentanyl with improvement of degrees of wound healing but with considerable incidence of skin dermatitis.
EFFECT OF MICROCURRENT SKIN PATCH ON THE EPIDURAL FENTANYL REQUIREMENTS FOR POST OPERATIVE PAIN RELIEF OF TOTAL HIP ARTHROPLASTY

References

SUCCINYLCHOLINE-INDUCED MYALGIA IN OBSTETRIC PATIENTS SCHEDULED FOR CAESAREAN SECTION

- Diclofenac vs Placebo Patches -

MOJGAN RAHIMI*, JALIL MAKAREM** AND AFSHIN GOSHTASBI GOHARRIZI**

Abstract

Background: Succinylcholine-induced myalgia is a minor but frequent complication. Its incidence and severity is different according to the studied population. The aim of this study was evaluation of the diclofenac patch effect on postoperative succinylcholine-related myalgia in cesarean section.

Methods: The study was a prospective randomized double blind, placebo-controlled trial. One hundred twenty six participants undergoing elective cesarean section (previous cesarean section) were randomized in two equal groups (63 participants in each): the diclofenac patch (containing 180 mg of diclofenac epolamine salt) and the placebo. Surgery was performed following rapid sequence induction of general anesthesia. All patients were paralyzed for intubation by succinylcholine (1.5 mg/kg). Data on baseline characteristics, fasciculation, postoperative myalgia (at 12, 24 and 48 hours after operation), the need to analgesic agents, and adverse effects of diclofenac patch were collected.

Results: The basic characteristics were comparable between the two groups. The severity of fasciculation did not significantly vary between two groups. In diclofenac group, the incidences of myalgia at 12, 24 and 48 hours after operation were 23.8%, 19.1%, and 12.7% respectively versus incidences of 52.4%, 47.6%, and 44.4% respectively in placebo group. The incidence and severity of myalgia were significantly lower in patients receiving diclofenac through three evaluation periods (all p values less than 0.01). No participants left the study because of the complications.

Conclusion: Diclofenac patch is effective and safe in the prevention of postoperative succinylcholine induced myalgia after cesarean section.

Keywords: Succinylcholine, postoperative complications, myalgia, diclofenac
**Introduction**

Succinylcholine remains the drug of choice during rapid sequence induction of anesthesia in many countries. Fasciculation and myalgia are minor but frequent adverse effects of succinylcholine administration. Myalgia, which can be accompanied by muscle stiffness, can last for several days and at least in some patients, can induce significant discomfort. In females, postoperative myalgia (POM) is more frequent than males and early ambulation is associated with higher incidence and severity of succinylcholine-induced POM.

In our country, Iran, the use of general anesthesia still prevails for cesarean section because of patient’s request, succinylcholine is used almost always as a muscle relaxant in this condition. Therefore, POM is a frequent problem. The incidence of myalgia at the first 24 hours after operation has been reported from 10 to 83%. In a recently published study, POM was important to eighty-nine percent of patients, and they requested to be avoided.

The topical application of non-steroidal anti-inflammatory drugs (NSAIDs) were effective in decreasing both acute and chronic pain, but the evidence supporting the use of transdermal NSAIDs to alleviate succinylcholine-induced myalgia is limited.

The aim of this study was to determine if the application of diclofenac patch at the beginning of the cesarean section could prevent succinylcholine-induced POM.

**Methods and Materials**

The study was performed from May to December 2008 in a referral educational hospital. The protocol was approved by our University Ethics Committee. Informed consent was obtained from all participants before enrollment in the study. We conducted this study to evaluate the hypothesis that diclofenac patch can prevent or reduce postoperative myalgia (POM).

Participants were ASA I or II, scheduled for repeated cesarean section (elective surgery) and had refused regional anesthesia. They were included in this prospective, randomized, double blinded, placebo controlled study. The history of asthma, smoking, known hypersensitivity to NSAIDs, coagulopathy, anticipated difficult airway, evidence of preeclampsia, history of gastrointestinal bleeding, significant liver or renal disease, history of psychological disorders, steroid consumption, and recent upper respiratory tract infection or irritation, were the exclusion criteria.

One hundred twenty six participants were randomly allocated in two equal groups of 63: diclofenac patch group or placebo patch group (Fig. 1).

---

**Fig. 1 Trial profile of the 168 participants**

- Assessed for eligibility: n = 168
  - Enrollment: n = 63
    - Randomization: n = 63
      - Allocation: n = 63
        - No loss to follow up
        - No discontinuation of intervention
          - Analysis of data: n = 63
    - Follow-up: n = 63
      - No loss to follow up
      - No discontinuation of intervention
        - Analysis of data: n = 63
  - Excluded (n= 42)
    - Not according to inclusion criteria (n= 31)
    - Refused to participate (n= 11)
Randomization was done by computerized random numbers. The anesthesiologist and the participants were not aware of the allocation.

Following pre-oxygenation, rapid sequence induction of general anesthesia consisted of thiopental sodium (5 mg/kg) and succinylcholine (1.5 mg/kg). Maintenance of anesthesia was preserved with isoflurane 0.6% in combination with nitrous oxide 50% in oxygen. Atracurium (0.2 mg/kg) was administered as maintenance of muscle relaxant. Fentanyl (2 µg/kg, i.v.), midazolam (0.03 µg/kg, i.v.), meperidine (1mg/kg, i.v.) were administered after clamping of the umbilical cord. Neuromuscular blockade was reversed by neostigmine (40 µg/kg) and atropine (20 µg/kg) intravenously at the end of the procedure.

Postoperative care was standardized for all patients. For post operative analgesia patients received vaginal suppository of diclofenac sodium (50 mg every 8 hours). Pain related to surgical intervention was treated with meperidine (1 mg/kg i.v.), if not controlled by diclofenac suppository meperidine is considered a rescue analgesia). Intramuscular injection was not performed during the preoperative or postoperative period.

Diclofenac epolamine patch (Flector® Tissuegel, IBSA, Switzerland) consists of 1.3% diclofenac epolamine (Equivalent to 1%diclofenac free acid or 180 mg of diclofenac epolamine) in a hydrophilic adhesive applied to a non woven polyester felt backing. Surface area of diclofenac patch was 140 cm² (the patch was 14 cm long and 10 cm wide). The placebo patch (supplied by Daru pakhsh, Tehran, Iran) was indistinguishable from the diclofenac patch. Diclofenac or placebo patch were applied to the posterior skin of the neck 30 minutes before the induction of anesthesia. Patches were removed 12 hours later.

The incidence and severity of postoperative fasciculation and myalgia were the main outcomes of the study. Fasciculation was recorded based on a four-point rating scale: a) no fasciculation, b) mild: fine fasciculation of the eyes, face, neck, or fingers but without limb movement c) moderate: fasciculation involving limbs and trunk, d) severe: fasciculation requiring a forceful retention9. Muscle pain not related to the surgical intervention was graded according to Kararmaz et al10: absence of muscle pain = no myalgia (0 points); minor stiffness limited to one area of the body = mild(1 point); muscle pain or stiffness noticed spontaneously by the patient, which may require analgesic therapy = moderate(2 points); and generalized, severe, or incapacitating discomfort = severe(3 points).

Myalgia data were gathered by a trained nurse who was blinded to the patches; 12, 24, and 48 hours after operation. Adverse effects on the digestive system and skin, if any, were noted, by the nurse. Excessive postoperative bleeding was supposed to be related to impairment of platelet function.

In our pilot study (on 10 participants), the incidence of POM was 60%. Our goal was to achieve a minimum of 50% decrease in the frequency of myalgia. With a power of 90% and a significance level of 0.05, we calculated that 63 participants were required in each group.

Participants’ characteristics such as age, weight and duration of anesthesia were compared by using student’s T-test. Chi square test was used to identify differences in the incidence of myalgia and the need to rescue analgesia. Difference in the severity of myalgia was compared by using Mann Whitney U-test. SPSS software version 16 (SPSS, Inc., Chicago, ILL) was used for statistical analysis. P values < 0.05 was considered as statistically significant.

Results

In the 126 participants studied, no loss to follow up occurred. Basic characteristics were comparable between two groups. Scale of fasciculation was similar in both groups (Table 1).

<table>
<thead>
<tr>
<th>Variable*</th>
<th>diclofenac (n=63)</th>
<th>placebo (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>27.5 ±6.4</td>
<td>26.8 ±7.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.7 ±5.3</td>
<td>69.6 ±4.1</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>49.2 ±4.7</td>
<td>51.3 ±6.1</td>
</tr>
<tr>
<td>Severity of fasciculation (no/mild/moderate/severe)</td>
<td>2/43/16/2</td>
<td>3/45/14/1</td>
</tr>
</tbody>
</table>

*values are mean ± standard deviation (SD) or number. All p values were >0.05.
In this study, preoperative application of diclofenac patch significantly palliated the incidence and severity of succinylcholine induced post cesarean section myalgia. Based on our search, transdermal application of NSAIDs for the prevention of POM had not been reported previously. However, there have been several reports to reduce POM with different medical interventions, but a few studies evaluated the effects of systemic NSAIDs. Naguib et al. compared lysine acetyl salicylate with the muscle relaxant atracurium 3 minutes before paralysis. Both groups were found to have a lower incidence and intensity of POM than control group, with no significant difference between treatment groups. Kahraman et al. showed that intramuscularly administered diclofenac was effective on prevention of succinylcholine-induced myalgia.

In this study we administered diclofenac hydroxyl ethyl pyrrolidine (DHEP), also known as diclofenac epolamine, that is a patented salt of diclofenac. This

### Table 2
Comparison of myalgia in the two groups

<table>
<thead>
<tr>
<th></th>
<th>diclofenac (n = 63)</th>
<th>Placebo (n = 63)</th>
<th>P value (for incidence)</th>
<th>P value (for severity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 hours postop.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>48 (76.2)</td>
<td>30 (47.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>10 (15.9)</td>
<td>9 (14.3)</td>
<td>0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (6.3)</td>
<td>19 (30.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>1 (1.6)</td>
<td>5 (7.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hours postop.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51 (80.9)</td>
<td>33 (52.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>10 (15.9)</td>
<td>16 (25.4)</td>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (3.2)</td>
<td>13 (20.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>1 (1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>48 hours postop.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>55 (87.3)</td>
<td>35 (55.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>8 (12.7)</td>
<td>21 (33.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>7 (11.1)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are number (percent).

### Table 3
The complications of patches in two groups.

<table>
<thead>
<tr>
<th></th>
<th>diclofenac (n = 63)</th>
<th>Placebo (n = 63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin (Pruritus, dermatitis) †</td>
<td>2 (3.2)</td>
<td>3 (4.8)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders (dyspepsia, nausea) †</td>
<td>3 (4.8)</td>
<td>1 (1.6)</td>
</tr>
</tbody>
</table>

Values are number (percent).
† p values > 0.05.

**Discussion**

In this study, preoperative application of diclofenac patch significantly palliated the incidence and severity of succinylcholine induced post cesarean section myalgia.

Based on our search, transdermal application of NSAIDs for the prevention of POM had not been reported previously. However, there have been several reports to reduce POM with different medical interventions, but a few studies evaluated the effects of systemic NSAIDs. Naguib et al. compared lysine acetyl salicylate with the muscle relaxant atracurium 3 minutes before paralysis. Both groups were found to have a lower incidence and intensity of POM than control group, with no significant difference between treatment groups. Kahraman et al. showed that intramuscularly administered diclofenac was effective on prevention of succinylcholine-induced myalgia.

In this study we administered diclofenac hydroxyl ethyl pyrrolidine (DHEP), also known as diclofenac epolamine, that is a patented salt of diclofenac. This
salt of diclofenac exerts very peculiar characteristics differentiating it from other diclofenac salts as well as from other available NSAIDs. The main peculiar characteristic of this salt of diclofenac is its very high solubility in both lipidic and hydrophilic tissues which is not seen, in other NSAIDs\textsuperscript{13}. These properties cause effective absorption in regional tissues with low but sustained circulating levels\textsuperscript{14}.

However, there are debates about inflammatory origin of succinylcholine induced myalgia\textsuperscript{15,16}, and several authors considered anti inflammatory mechanism for NSAIDs in lessening POM\textsuperscript{11,12,17}. There may be parallels between the calcium influx seen after succinylcholine and that observed in experimentally induced muscle damage. Lipo-oxygenase products are mediators of calcium induced intracellular enzyme efflux from skeletal muscle, whereas cyclo-oxygenase products may mediate myalgia. Prostaglandins produce further tissue damage, resulting in more pain and damage. The use of NSAIDs may interrupt this prostaglandin-mediated destructive cycle and this may provide a rationale for their use in preventing POM\textsuperscript{15}.

The analgesic actions of NSAIDs; Can be dissociated from anti-inflammatory effects and this may reflect additional spinal and supraspinal actions of NSAIDs to inhibit various aspects of central pain processing\textsuperscript{18}. Low stable concentration of diclofenac with transdermal administration on this study may exert an effective analgesic action. On the other hand, high local concentration of diclofenac on the head and neck region may be effective on alleviating the postoperative neck and/or shoulder myalgia.

Fasciculation was not different between two groups in the study as the same as mentioned by others\textsuperscript{5}. Diclofenac i.m. did not have any effects on severity of suxamethonium induced fasciculation, too (12). However, the relationship between fasciculation and POM has not been well defined\textsuperscript{2,5} In this study, no significant complications had occurred by application of diclofenac patch, as previously reported by Rahimi et al\textsuperscript{19}.

Measurement of serum levels of inflammatory and anti-inflammatory cytokines can help to clarify the pathophysiologic mechanisms of succinylcholine induced myalgia and the effects of transdermal NSAIDs, especially diclofenac patch.

It can be concluded that application of preoperative diclofenac patch is effective and safe in the prevention of POM in cesarean section.

**Acknowledgements**

Authors themselves have provided all financial support for this study. We give warm thanks to Shohre Alavi for her text editing.
References
INTRAOPERATIVE MINIMAL ACUTE NORMOVOLEMIC HEMODILUTION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS SURGERY

Alireza Mahoori1*, Farhad Heshmati2*, Heydar Noroozinia2*; Hamid Mehdizadeh3#, Shahrad Salehi3# and Mojtaba Rohani4*

Abstract

Background & Objective: Efficacy of minimal acute normovolemic hemodilution (ANH) in avoiding homologous blood transfusion during cardiovascular surgery remains controversial. Postoperative bleeding and transfusion remain a source of morbidity and cost after open heart operations. Our objective was to evaluate the impact of minimal ANH on blood transfusion requirements during open cardiovascular surgery using cardiopulmonary bypass (CPB).

Methods: This study was a randomized controlled trial. One hundred one patients scheduled for elective coronary artery bypass graft (CABG) under cardiopulmonary bypass in October 2007 through March 2008 in Imam Khomeini hospital were randomly assigned to a control group (standard care, no = 47) or an ANH or study group (no = 54). We used minimal ANH (representing 10% of patients’ blood volume). Mean 490 ± 50 mL of fresh autologous blood was removed after induction of anesthesia and reinfused at the end of CPB. The blood transfusion guidelines were uniformly applied to all patients.

Results: Significant decrease in the number of red blood cell units transfused per patient per group (1.39 ± 1.0 and 2.55 ± 1.9; p < 0.0001) in the ANH group versus the control group was observed. Conversely, chest tube output, postoperative hematocrits, and platelet count did not differ between two groups. Percentage of patients in whom allogeneic red blood cells were transfused was 44% in study group versus 76% in control group; (p < 0.01). No patient was transfused with platelet concentrates or fresh frozen plasma.

Conclusions: Minimal ANH is safe and cost effective and its routine use in eligible patients is therefore justified. Intraoperative autologous blood donation in CABG surgery decreased perioperative allogeneic blood requirement. However, the removal and reinfusion of about one unit autologous blood had no effect on postoperative bleeding or platelet count.

Key words: Transfusion, Autologous, Hemodilution, Coronary Artery Bypass Graft.
Introduction

Autologous blood transfusion was employed as early as 1818, and preoperative blood donation was used in the 1930s. In recent years, the potential benefits of avoiding homologous blood transfusion and optimizing oxygen delivery in vital organs have led to a renewed interest for autologous blood transfusion and acute normovolemic hemodilution (ANH) in major surgery.

Primary reasons for autologous blood transfusion employment are, avoidance of complications related to allogeneic blood transfusion, and conservation of blood resources. The introduction of complex operative procedures such as: cardiac surgery and organ transplantation, has led to search and attention for alternatives to allogeneic transfusion.

Coronary artery bypass graft surgery (CABG) is one of the most frequently performed major operations and is highly effective in improving life expectancy and quality of life in patients with coronary artery disease. Although the number of surgical procedures will continue to decline along with the advances in interventional cardiology, the proportion of higher-risk patients requiring complex surgical procedures will likely continue to increase in the near future.

In these types of surgeries, as with other autologous transfusion techniques, ANH can be used to reduce the need for allogeneic blood transfusion. There are additional benefits of ANH that are not common to other autologous transfusion modalities. When the blood is kept in the same operating room, the chances of clerical error are eliminated. On the other hand, because blood collected by ANH is stored at room temperature and is usually returned to the patient within eight hours of collection, there is little deterioration of platelets or coagulation factors.

Recently, various studies have demonstrated cardio-protective effects of acute normovolemic hemodilution in cardiac surgeries under cardiopulmonary bypass (CPB), and in addition to conventional myocardial preservation techniques, preoperative ANH achieved further cardiac protection in patients undergoing on-pump myocardial revascularization and severe aortic stenosis.

In some studies that ANH was employed during CABG, net blood loss, amount of reinfused shed blood, postoperative blood requirements, the percentage of patients who received allogeneic blood and the number of blood units transfused per patients, were less in the ANH group. Despite the fact that some believe that preoperative or intraoperative collection of platelet-rich plasma during cardiopulmonary bypass surgery may improve hemostasis and decrease allogeneic exposures, others however have found no benefit, and various studies have questioned the efficacy of intraoperative acute normovolemic hemodilution (ANH) in reducing bleeding and the need for allogeneic transfusions in cardiac surgery and its capacity to reduce perioperative allogeneic transfusion remains controversial.

The effect of "minimal" ANH on postoperative blood requirements have not been studied, the aim of the present study was to evaluate the effects of a "minimal" ANH in elective, coronary artery bypass graft.

Methods and Materials

After approval by the local Ethics Committee, written informed consent was obtained from all patients scheduled for elective CABG and thought to meet the eligibility criteria.

Exclusion criteria were left main coronary artery stenosis; left ventricular ejection fraction less than 40%; anemia (hematocrit <34% and hemoglobin <11.5 g/dL); pump time >2.5h; need for reoperation; history of hematological disorders; advanced chronic renal failure (serum creatinine >2 mg/dL); active chronic hepatitis; or cirrhosis.

One hundred one patients to undergo CABG surgery in October 2007 through March 2008 in our hospital were included in this prospective, randomized controlled trial to evaluate the merits and practicability of autologous blood transfusion.

By using a computer-generated random-number sequence, the 101 patients were prospectively randomized to one of the two groups: the ANH group (no = 54) and the standard care group (no = 47).

All patients had same protocol for anesthesia...
and surgery. On the morning of operation, the patients were premedicated with morphine, 5 µg/kg. Standard monitorings such as pulse oximetry, leads II and V5 of the ECG for heart rate and automated ST-segment trend analysis, continuous measurements of central venous pressures and mean arterial, end-tidal capnography, bispectral index analysis of the EEG (BIS A-2000 XP; Aspect Medical Systems;) and nasopharyngeal temperature were performed perioperatively.

Balanced anesthesia with propofol, fentanyl, midazolam, isoflurane, and pipecuronium was performed in all patients. Inhaled isoflurane (0.5 to 1% in the pre-bypass period), was administered to enhance cardiac protection before aortic clamping (anesthetic preconditioning). In the two groups, a similar depth of anesthesia was obtained by targeting bispectral EEG values between 40 and 60 arbitrary units.

In the ANH group, we used minimal ANH (representing 10% of patients’ blood volume). After the induction of anesthesia and before systemic heparinization, blood was withdrawn from a central vein by gravity into citrate-phosphate-dextrose collection bags. Simultaneous gelatin solution (1 mL for each 1 mL of blood withdrawn) was infused through a 16-gauge peripheral catheter on the opposite arm. The autologous blood was labeled and stored at the room temperature and reinfused intraoperatively when the transfusion criteria were met.

Cardiopulmonary bypass (CPB) and myocardial preservation strategies were uniform among the two participating surgeons. After heparinization (300 IU/kg), CPB including a membrane oxygenator and a circuit primed with a 2-L normal saline solution was performed using non-pulsatile flow (2.2 to 2.5 L/min/m²) and hypothermia (28 to 30°C). An α stat control for acid-base management was applied, and mean arterial pressure was targeted between 50 and 80 mm Hg with pharmacologic and pump flow manipulation as necessary.

All patients were operated on in our Institution with standardized techniques. The left internal mammary artery (LIMA) was isolated through an extra-pleural approach in all patients for left anterior descending artery (LAD) graft. The saphenous vein also was used for other grafts. The radial and the gastroepiploic artery were not used in any patient.

After achieving a nasopharyngeal temperature 37°C, weaning from CPB was performed by standard hemodynamic measurements. The pump flow was gradually reduced while the heart was progressively filled in order to optimize the preload-recruitable stroke volume and to reach a mean arterial pressure more than 70 mm Hg. The heart was electrically paced if it failed to maintain a heart rate more than 60 beats/min. Inotropes were not routinely administered during weaning from CPB.

At the end of CPB, protamine was administered to neutralize circulating heparin, and then in the ANH group, the whole autologous blood volume was reinfused. Allogeneic Packed red blood cells (PRBC) were transfused with hemoglobin <10 g/dL and hematocrit <30%.

Before closure of the chest, mediastinal and pleural drains were positioned, and low-grade suction was instituted.

Hemoglobin, and platelet count, were measured in blood samples obtained before the induction of anesthesia; at arrival in the intensive care unit (ICU) after completion of the reinfusion of autologous blood; 24 and 48 h after surgery; and before discharge from the cardiac intensive care unit. During surgery, hematocrit, hemoglobin and electrolytes and blood gasses were monitored in serial samples drawn for blood gas determinations (nova biomedical, phox plus).

All data were analyzed using statistical software (version 16 for Windows; SPPS; Chicago, IL). Values were expressed as mean (±SD). Dichotomous variables were compared by the χ² statistic or Fisher exact test, as appropriate, and quantitative variables were compared with unpaired Student t test. Differences were considered statistically significant with p values less than 0.05.

Results

Demographic, preoperative characteristics and operative data are shown in Table 1. No significant differences were observed between groups with regard to age, sex, body surface area, and preoperative left ventricular ejection fraction.
Also, the number of grafted coronary arteries, as well as the duration of aortic cross-clamping and CPB, preoperative hemoglobin, hematocrit and platelet count, were comparable (Table 2). Mean removal of blood in the ANH group was 490 ± 50 mL. No patient in the ANH group experienced complications related to normovolemic blood withdrawal.

Hemoglobin concentration preoperatively and postoperatively did not differ among groups. Significant decrease in the number of red blood cell units transfused per patient (1.39 ± 1.0 and 2.55 ± 1.9 units; p < 0.0001) in the ANH group versus the control group was observed (Fig. 1). Conversely, chest tube output, postoperative hemoglobin and platelet count did not differ between two groups, but a significantly larger number of patients in the control group required allogeneic transfusions.

The total number of PRBC units transfused was significantly more in the control group (120 vs. 75; P = 0.001). Percentage of patients in whom allogeneic red blood cells were transfused was 44% in study group

<table>
<thead>
<tr>
<th>Variable</th>
<th>ANH group (n = 54)</th>
<th>Control group (n = 47)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>55±12</td>
<td>58±9</td>
<td>0.149</td>
</tr>
<tr>
<td>Sex: male/female (%)</td>
<td>46:8 (17.3)</td>
<td>40:7 (17.5)</td>
<td>0.991</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.45</td>
<td>71.90</td>
<td>0.224</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.8±0.14</td>
<td>1.7±0.19</td>
<td>0.148</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>46±6</td>
<td>47±6</td>
<td>0.725</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.7±1</td>
<td>13.2±1</td>
<td>0.069</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>40±4</td>
<td>39±4</td>
<td>0.089</td>
</tr>
<tr>
<td>Platelet count (mm3)</td>
<td>230981±62</td>
<td>257361±10</td>
<td>0.123</td>
</tr>
</tbody>
</table>

### Table 1
Demographic data, Preoperative and operative characteristics of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>ANH group (n = 54)</th>
<th>Control group (n = 47)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>55±12</td>
<td>58±9</td>
<td>0.149</td>
</tr>
<tr>
<td>Sex: male/female (%)</td>
<td>46:8 (17.3)</td>
<td>40:7 (17.5)</td>
<td>0.991</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.45</td>
<td>71.90</td>
<td>0.224</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.8±0.14</td>
<td>1.7±0.19</td>
<td>0.148</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>46±6</td>
<td>47±6</td>
<td>0.725</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.7±1</td>
<td>13.2±1</td>
<td>0.069</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>40±4</td>
<td>39±4</td>
<td>0.089</td>
</tr>
<tr>
<td>Platelet count (mm3)</td>
<td>230981±62</td>
<td>257361±10</td>
<td>0.123</td>
</tr>
<tr>
<td>Preoperative treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β blockers (%)</td>
<td>60</td>
<td>62</td>
<td>0.654</td>
</tr>
<tr>
<td>ACE inhibitors (%)</td>
<td>31</td>
<td>31</td>
<td>0.996</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>16</td>
<td>18</td>
<td>0.256</td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>78</td>
<td>79</td>
<td>0.086</td>
</tr>
<tr>
<td>Grafted coronary arteries (n)</td>
<td>3±0.8</td>
<td>3±0.7</td>
<td>0.137</td>
</tr>
<tr>
<td>Duration of CPB (min)</td>
<td>75±21</td>
<td>75±25</td>
<td>0.898</td>
</tr>
<tr>
<td>Aortic clamp (min)</td>
<td>116±29</td>
<td>121±31</td>
<td>0.46</td>
</tr>
<tr>
<td>Removed autologous blood</td>
<td>490±50</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Data are presented as mean (95% confidence interval) unless otherwise indicated.
ANH = acute normovolemic hemodilution, BSA = body surface area; LVEF = left ventricular ejection fraction.

### Table 2
Postoperative data and perioperative allogeneic blood transfusions

<table>
<thead>
<tr>
<th>Variable</th>
<th>ANH group (n = 54)</th>
<th>Control group (n = 47)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest tube drainage, mL/48h</td>
<td>871±48</td>
<td>975±59</td>
<td>NS</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10±1</td>
<td>11±1</td>
<td>NS</td>
</tr>
<tr>
<td>Platelet count (mm3)</td>
<td>170804±69</td>
<td>178428±70</td>
<td>NS</td>
</tr>
<tr>
<td>Patients transfused with PRBC (n, %)</td>
<td>23, 44*</td>
<td>35, 76</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of PRBC transfused per patient (n)</td>
<td>1.39 ± 1.0*</td>
<td>2.55 ± 1.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total FFP (U)</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Total Platelet concentrate (U)</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Total number of PRBC transfused (n)</td>
<td>75*</td>
<td>120</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Data are expressed as mean±SD unless otherwise indicated.

# p < 0.05 between two groups.
PRBC = packed red blood cells; FFP = fresh frozen plasma.
more than three units whereas in the ANH group no patient received more than three unit of PRBC.

All patients in each group who required re-exploration for excessive bleeding were excluded from study. No patient was transfused with platelet concentrates or fresh frozen plasma (FFP).

PRBC = packed red blood cells; ANH = acute normovolemic hemodilution.
In the ANH group, the autologous blood was reinfused after CPB in all the patients as the transfusion threshold was reached.

Discussion

The application of minimal ANH decreased allogeneic blood exposure in patients undergoing CABG. This effect was essentially related to a reduction in perioperative allogeneic blood product use. This result was obtained without any increase in early postoperative morbidity or mortality. The results of this investigation demonstrate that minimal ANH prior to on-pump CABG reduced the number of red blood cell units transfused per patient and the total number of transfused PRBC. This is the first study to evaluate the effects of minimal ANH on allogeneic blood requirement in patients submitted to CABG surgery under CPB. Mean withdrawal blood was 490±50 mL. Although intraoperative masking was not possible, the ICU staffs were blinded to allocation to group, perioperative medical care was standardized, and similar clinical and physiologic end points were achieved in the two groups. Preoperative cardiac condition and intraoperative surgical treatment were also comparable.

Use of minimal ANH in present study resulted reduction in the number of patients transfused with donor blood. Accordingly, we observed a reduction in the number of PRBC units transfused. Because blood collected by ANH is stored at room temperature and is usually returned to the patient within eight hours of collection, there is little deterioration of platelets or coagulation factors.

Our results are very similar to those of Jalali et al. They used ANH and concluded that the use of ANH can reduce the need for PRBC and FFP by 58% and 74%, respectively. In present study the percentage of patients in whom allogeneic red blood cells were transfused was 44% in study group versus 76% in control group and any of patients did not need to FFP or platelet concentrates transfusion.

In our study the total blood loss was similar in the two groups of patient and the 24 h chest tube output, postoperative hemoglobin, and platelet count did not differ between the two groups. Most of the blood loss occurred during surgery or in the first postoperative hours, and the blood-sparing properties of ANH are mainly related to increased dilution of the intraoperative blood loss, leading to a smaller net loss of red blood cells. A clinical analysis of patients who had undergone minimal ANH (representing 15% or less of patients’ blood volume) estimated that only 100 mL of RBCs (the equivalent of 1/2 unit of blood) was saved under these conditions.

Whole blood withdrawal and administration of crystalloid or colloid solution decreases arterial oxygen content, but compensatory hemodynamic mechanisms and the existence of surplus oxygen delivery capacity make ANH safe. Sudden decrease of RBC concentration lowers blood viscosity, thereby decreasing peripheral resistance and increasing cardiac output. Some studies demonstrated that acute preoperative hemodilution attenuates the deleterious effects of aortic cross-clamping and improves myocardial recovery in patients undergoing CABG. In our study because of the relatively small degree of hemodilution and the attention paid to maintain normovolemia, no patient in this series experienced intraoperative myocardial ischemia, and the outcomes and postoperative complications did not differ between the two treatment groups. As suggested by some authors, more profound hemodilution might lead to serious complications, such as metabolic acidosis, peripheral edema, pulmonary and neurological sequel, and, especially in coronary patients, myocardial ischemia.

In present study, to assess the pure effect of minimal ANH on allogeneic blood requirement, we select the low risk patients and excluded the high risk patients who needed reoperation due to inadequate surgical hemostasis. Also the patients were monitored and assessed for postoperative acute myocardial infarction, on the basis of ECG abnormalities and a significant increase in myocardial enzymes, but no patients in two groups had evidence of postoperative myocardial ischemia.

In conclusion, minimal ANH can lead to a significant reduction in the number of patients who require allogeneic blood transfusions. The optimal value of hematocrit levels before CPB remains unknown. Further studies are warranted to confirm these results, to test the efficacy of this simple procedure in higher-risk patients with poor ventricular function and those requiring complex cardiac surgery.
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COMBINATION THERAPY IN THE PREVENTION OF PONV AFTER STRABISMUS SURGERY IN CHILDREN: GRANISETRON, ONDANSETRON, MIDAZOLAM WITH DEXAMETHASONE

WALEED RIAD* AND HESHAM MAROUF**

Summary

Background: Pediatric strabismus surgery is commonly associated with higher incidence of postoperative nausea and vomiting (PONV). Mixtures of different classes of antiemetics have been used successfully to decrease the incidence of PONV but there was no agreement on the optimal combination. The aim of this study was to investigate the effect of granisetron, ondansetron, midazolam combination with dexamethasone in the prevention of PONV following strabismus repair in pediatric population.

Method: Healthy 100 children ASA class I and II aged 4-12 years, scheduled for elective strabismus surgery, were enrolled in this study.

No premedications were given anesthesia was induced by inhalational technique using sevoflurane, nitrous oxide and oxygen mixture. After induction, fentanyl and atracurium were given and an endotracheal tube was inserted. Patients were randomly divided into four groups which received intravenously either: Placebo, or a combination of granisetron 10 µg/kg⁻¹, ondansetron 50 µg/kg⁻¹, midazolam 50 µg/kg⁻¹, plus dexamethasone 0.5 mg/kg⁻¹ after induction of anesthesia and before start of surgery. All episodes of PONV during the first 24 hours after anesthesia were recorded.

Results: The incidence of postoperative nausea was 48%, 8%, 12% and 0% while the incidence of vomiting was 52%, 12%, 4% and 0% in placebo, granisetron, ondansetron, midazolam and dexamethasone combination groups respectively. No difference was detected between combination groups (P value >0.05).

Conclusion: Prophylactic administration of either of either granisetron, ondansetron, midazolam combined with dexamethasone markedly decreases the incidence of PONV following strabismus surgery in pediatrics. All combinations are equally effective.

Key words: PONV, Granisetron, Ondansetron, Midazolam, Dexamethasone, strabismus surgery

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Introduction

Post-operative nausea and vomiting (PONV) is one of the most frequent distressing complaints following surgery under general anesthesia. The incidence of PONV in day-case patients ranges from 8% to 45%. For some patients PONV is even more distressing than postoperative pain.

PONV may increase hospital expenditure by prolongation of hospital stay, and management of vomiting related complications such as dehydration, electrolyte disturbances, and pulmonary aspiration. Pediatric strabismus surgery is commonly associated with higher incidence of PONV, it ranges between 40 and 90%.

A variety of methods have been tried in the management of PONV. Some anesthesiologist manage PONV with a single prophylactic anti-emetic given during surgery. There is, however, a growing trend towards the use of a combination of antiemetic therapy in moderate to high-risk patients. The optimal combination is yet to be universally agreed upon.

The role of serotonin receptors in drug-induced emesis has recently received increasing attention. Granisetron, a selective antagonist of serotonin receptor, has been proved to be effective in the prevention of PONV. Ondansetron, also a selective serotonin receptor antagonist, is well tolerated and effective in preventing PONV in adults and children. The anti-emetic effect of midazolam has been investigated by several investigators. Lee et al reported that in patients undergoing sevoflurane VIMA (volatile induction and maintenance of anesthesia), midazolam 2 mg given intravenously before the end of surgery was effective in decreasing the incidence of PONV. Unlugenc and colleagues reported that sub-hypnotic dose of midazolam was effective in treating PONV.

The efficacy of prophylactic dose of dexamethasone in reducing PONV after strabismus surgery and tonsillectomy in children has been reported.

The current study was designed to investigate the effects of either of granisetron, ondansetron or midazolam when either is mixed with dexamethasone, in the prevention of PONV following strabismus surgery in pediatric population.

Materials and Method

Following Hospital Research and Human Ethics Committee approval, 100 healthy children ASA class I aged 4-12 years, scheduled for elective strabismus surgery under general anesthesia, were enrolled in this prospective, randomized, placebo-controlled, double blind study. Exclusion criteria included children who had experienced retching or vomiting, or have taken an anti-emetic medications, antihistaminics, steroids, or psychoactive drugs within 24 hours before surgery, and children who gave a history of motion sickness, allergy or previous adverse experiences with anesthesia. Children with cardiovascular, respiratory, metabolic, and central nervous system disease were also excluded from the study.

Solid food was not allowed 6 hours before operation and clear liquids were permitted up to three hours before induction of anesthesia. No premedication was given to the children. Upon arrival to the OR, placement of routine monitors were established and baseline hemodynamic data were recorded after placement of routine monitors. Anesthesia was induced by inhalational technique using Sevoflurane, nitrous oxide and oxygen mixture. After induction, and establishment of intravenous line fentanyl 2 µg/kg-1 and atracurium 0.5 mg/kg-1 were given an endotracheal tube was inserted under the appropriate anesthesia depth and degree of relaxation.

In a double-blind manner, patients were randomly, divided into four groups (25 patients each), received either:

- (Group 1) - Placebo
- (Group 2) - Combination of Granisetron 10 µg/kg-1 plus Dexamethasone 0.5 mg/kg-1
- (Group 3) - Ondansetron 50 µg/kg-1 plus Dexamethasone 0.5 mg/kg-1
- (Group 4) - Combination of Dexamethasone 0.5 mg/kg-1 plus Midazolam 50 µg/kg-1

Maximum Dexamethasone dose given was 8 mg in all groups.

All drugs were delivered in equivalent volume in 5 ml syringe with a coded label. The anesthesiologist who anesthetized the patient and all involved nurses were unaware of the content of the syringe. The
study drugs were administered intravenously to all patients after induction of anesthesia and before start of surgery. Thereafter, anesthesia was maintained with 70% nitrous oxide, 30% oxygen with 0.5-3.0% inspired concentration of Sevoflurane. Ventilation was controlled mechanically to keep an end-tidal CO2 between 35-45 mmHg measured using an anesthetic/respiratory gas analyzer (Capnomac Ultima, Datex, Finland). Intraoperative fluid was (D5W in 1/4 strength NS) was administered at a standard rate defined as (one-half the deficit during the first hour, plus maintenance fluid). At the completion of surgery, muscle relaxant was reversed by a combination of 0.02 mg/kg⁻¹ atropine sulphate and 0.05 mg/kg⁻¹ neostigmine. Trachea was extubated when the child was fully awake and then transported to PACU for at least one hour until complete recovery, where assessment of vomiting was made by the recovery nurse and the attending anesthesiologist.

For the purpose of the current study, vomiting was defined as the forceful expulsion of liquid or solid gastric contents, while nausea defined as a subjective feeling which was reported by patients. No distinction was made between vomiting and retching (i.e., a retching event was considered a vomiting event).

Postoperatively, all children were admitted to the hospital where they remained for more than one day. Oral intake was not allowed for four hours after recovery from anesthesia. All episodes of nausea, retching and vomiting during the first 24 hours after anesthesia were recorded by nursing staff who had no knowledge of which treatment each subject had received. Also, parents were asked about episodes of nausea and vomiting and any other potential surgical or anesthesia related complications. If two or more episodes of vomiting occurred, a rescue dose of metoclopramide 0.2 mg/kg⁻¹ was given intramuscularly. Postoperative pain was treated with 1 mg/kg⁻¹ rectal diclofenic sodium.

Statistical analysis

The results were analyzed using SPSS version 14 (SPSS Inc., Chicago, IL, USA). Power analysis indicated that 25 patients are required per each group based on 85% incidence of PONV in strabismus surgery if no prophylaxis is given with an anticipated reduction in the incidence of emesis up to 25% which was the therapeutic outcome for dexamethasone when given as a sole prophylaxis agent. The alpha error was set at 0.05 and Type II error was set at 0.20. Statistical analysis was done using Kruskal-Wallis Test (Nonparametric ANOVA). If Kruskal-Wallis Test was significant, Dunn’s Multiple Comparisons Test

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n = 25)</td>
<td>Granisetron Dexamethasone Combination (n = 25)</td>
<td>Ondansetron Dexamethasone Combination (n = 25)</td>
<td>Midazolam Dexamethasone Combination (n = 25)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>6.7 (2.9)</td>
<td>6.6 (2.1)</td>
<td>7.3 (2.5)</td>
<td>8.3 (3.9)</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>14 (56%)</td>
<td>14 (56%)</td>
<td>13 (52%)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>11 (44%)</td>
<td>11 (44%)</td>
<td>12 (48%)</td>
</tr>
<tr>
<td>No. of operated muscles (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4 (16%)</td>
<td>1 (4%)</td>
<td>4 (16%)</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>2</td>
<td>19 (76%)</td>
<td>15 (60%)</td>
<td>18 (72%)</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>3 or 4</td>
<td>2 (8%)</td>
<td>9 (36%)</td>
<td>3 (12%)</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>60 (18)</td>
<td>40.6 (22,2)</td>
<td>62 (21)</td>
<td>57 (26)</td>
</tr>
<tr>
<td>Oculocardiac reflex requiring atropine (%)</td>
<td>3 (12%)</td>
<td>10 (40%)</td>
<td>2 (8%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Data expressed as a mean and standard deviation (SD) or number and percentages.
* P value = 0.01
was used to compare different groups. For all tests of significance, a $P$ value of 0.05 was used as the level of significance. Data were presented as a mean and standard deviation (SD) or number and percentages.

**Results**

The demographic and clinical data of the 100 enrolled children are shown in Table 1. There was no difference among the groups with regard to age, sex, duration of surgery, number of operated muscles. The incidence of oculocardiac reflex was significantly higher in Granisetron-Dexamethasone group ($P$ value = 0.01).

The data relating to PONV during the study are presented in Fig. 1. The incidence of PONV was significantly greater in the Placebo Group 1 compared to other combination groups ($P$ value <0.01) Patients in the Placebo group had incidence of nausea and vomiting of 48% and 52% respectively, while the same incidence was 8% and 12% in the Granisetron-Dexamethasone Group 2. Children of Ondansetron-Dexamethasone Group 3 reported 16% nausea and 4% vomiting. Neither nausea nor vomiting was observed in midazolam-dexamethasone combination Group 4. No difference recorded between combination groups ($P$ value >0.05). No major respiratory or hemodynamic adverse effects were observed in the studied groups.

**Discussion**

The main finding of the present study was that there were no significant differences between different combinations groups in reducing PONV after strabismus surgery in pediatric patients. Combinations of drugs have become a proven strategy for prevention of PONV with good response, as compared to monotherapy. Different classes of anti-emetics with different mechanisms of action were shown to act independently when given prophylactically and therefore can be combined to enhance anti-emetic efficacy.

The combination of granisetron and dexamethasone had been used in both adult and pediatric populations. The present work in a pediatric population showed an incidence of 8% nausea and 12% vomiting in children of granisetron-dexamethasone Group 2. Fujii and associates reported that prophylactic use of this mixture produced 2% incidence of PONV during the first 24 hours following thyroidectomy in 130 female patients. However the dose of granisetron in Fujii report was 40 µg/kg-1 compared to 10 µg/kg-1 used for the present work. The same result was reported following middle ear surgery in adult and in children undergoing inguinal hernia and phimosis surgery. The reported frequency of PONV was 7% after the use of 40 µg/kg-1 granisetron and 4 mg dexamethasone combination in pediatric subjects undergoing strabismus repair, tonsillectomy and adenoidectomy.

The present work showed an incidence of 16% and 4% for postoperative nausea and vomiting, respectively, for ondansetron-dexamethasone combination. Splinter et al reported that low-dose ondansetron plus dexamethasone was a more effective prophylactic antiemetic when compared with dexamethasone alone following strabismus repair. They used 150 µg/kg-1 dexamethasone together with ondansetron 50 µg/kg-1 and the incidence of PONV was 9%.

Although the minimum effective dose of dexamethasone for the prevention of PONV was suggested to be 2.5 mg in a recent study, an 8 to 10 mg dose of dexamethasone was most frequently used. In the current trial the same dose of ondansetron was used but the dose of dexamethasone increased to 0.5 mg/kg with a maximum of 8 mg. Peach and colleagues reported that the efficacy of the smallest dose combination (dexamethasone 2 mg with ondansetron 2 mg) did not significantly differ from that of larger dose combinations (dexamethasone 4 mg with ondansetron
Combination Therapy in the Prevention of PONV After Strabismus Surgery in Children: Granisetron, Ondansetron, Midazolam with Dexamethasone

4 mg) in women who had day-surgical gynecologic laparoscopy21.

Midazolam is commonly used as a premedicant to relieve anxiety. Previously it was suggested that midazolam may have a role in the management of PONV. Di Florio and Goucke22 studied the effect of intravenous midazolam infusion on persistent PONV on twenty patients aged 18-82 years. They reported that low-dose intravenous infusion of 1.0 mg h\(^{-1}\) midazolam after a 1 mg IV bolus was determined to be safe and effective treatment for resistant PONV in adult population. Splinter et al23 found that midazolam and droperidol at a dosage of 50 µg/kg\(^{-1}\) appear to have a similar effect on vomiting after strabismus surgery. The reported incidence of PONV following single intravenous injection of 2 mg midazolam was 3.3% in adult patients undergoing abdominal or gynecological procedures11. Palmer and Cameron24 reported the effectiveness of intravenous midazolam-clonidine infusion for treatment of cyclical vomiting syndrome in a 12 years old child24. Our combination of midazolam and dexamethasone produced good response.

Conclusion

Prophylactic administration of granisetron, ondansetron, midazolam combined with dexamethasone decreases the incidence of PONV following strabismus surgery in pediatric population. No recorded differences between different combinations.
References


PROSEAL LARYNGEAL MASK AIRWAY IN INFANTS AND TODDLERS WITH UPPER RESPIRATORY TRACT INFECTIONS: A RANDOMIZED CONTROL TRIAL OF SPONTANEOUS VS PRESSURE CONTROL VENTILATION

APARNA SINHA*, BIMLA SHARMA** AND JAYASHREE SOOD***

Implication statement

Laryngeal masks, especially ProSeal have made it possible to deliver pressure control ventilation with PEEP without requiring paralysis in infra umbilical surgeries, thereby obviating the need for endotracheal intubation and minimizing the associated adverse respiratory events. This randomized prospective study was conducted to assess the influence of mode of ventilation on adverse respiratory events in infants and toddlers having upper respiratory tract infection, when using ProSeal™ laryngeal mask as the airway device.

Abstract

Background: ProSeal LMA (PLMA), one of the advanced supraglottic devices has been successfully used to provide both spontaneous and controlled ventilation in children with upper respiratory tract infection (URTI). URTI does not imply restriction of disease to upper respiratory tract; it has been shown to produce pulmonary dysfunction. PEEP has been shown to improve oxygenation in such cases. This randomized prospective study was designed to compare postoperative adverse events associated with spontaneous respiration (SR) and pressure control ventilation (PCV) with PEEP in infants and toddlers with URTI when using PLMA as an airway device.

Methods: In the present study, 90 children, 6 months-2 years, scheduled for infra umbilical surgery were randomized to receive either SR or PCV with PEEP of 5cm H2O. Patients with risk of aspiration, bronchial asthma, anticipated difficult airway, snoring, passive smoking, morbid obesity, coexisting pulmonary and cardiac disease, lower respiratory tract infection, fever >38°C and sneezing, were excluded. At emergence, airway secretions, coughing, breath holding, bronchospasm, upper airway obstruction or laryngospasm (LS) were assessed.

Results: The adverse events were significantly higher in spontaneously breathing patients. Score of adverse events was 6.33±1.6 in PCV and 7.7± 2.2 in SR group (P=0.001). The mean SpO2 (%) in PACU was 96.5±2 in PCV and 94.4±1.37 in SR (P = 000).

Conclusion: Pressure control ventilation with PEEP using PLMA is associated with lower incidence of adverse events in comparison to spontaneous respiration in infants and toddlers with upper respiratory tract infection undergoing infra umbilical surgeries under general anesthesia.

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Introduction

Upper respiratory tract infection (URTI) is a frequently encountered clinical condition and has remained a matter of debate and concern to the pediatric anesthesiologists all over the world. The inception of laryngeal mask airway (LMA) has changed the conduct and outcome of anesthesia over last few decades particularly in patients with URTI.

Most previous studies have not been consistent with the type of airway device, age of subjects, anesthetic technique, type of surgery and mode of ventilation used in patients with URTI. Homer et al have shown that adverse events are affected by the airway device employed, that is, device used and the timing of its removal for the management of the case. Some previous studies ascertain the usefulness and performance of LMA over tracheal tube (TT) and facemask (FM) and show that use of laryngeal mask airways has significantly lowered the incidence of postoperative sore throat; while others demonstrate no clinically significant difference between the devices.

PLMA has challenged the assumption that TT is the only way to provide positive pressure ventilation (PPV). Recently, use of pressure-control ventilation in nonparalysed patients has been popularized with the use of laryngeal mask airways in pediatric patients and has been shown to improve oxygenation. No previous study compares the different modes of ventilation using PLMA in children with URTI.

We hypothesized that mode of ventilation has influence on postoperative adverse respiratory events in preschool children with URTI when using ProSeal LMA as airway device.

Patients and Methods

After approval of Hospital Ethics Committee and parents’ written informed consent we selected 90 consecutive children, 6 months to 2 years, having acute URTI and who met the exclusion and inclusion criteria for this randomized prospective study. Each patient’s parents was interviewed and patient examined in detail to determine presence of any symptoms suggestive of URTI. We used criteria defined by Tait and Knight: sore or scratchy throat, rhinorrhea, congestion, malaise, nonproductive, cough, fever <38°C and laryngitis.

Identification of two or more of these symptoms was declared as having URTI. All patients were scheduled to undergo infra umbilical surgery under general anesthesia (GA).

Patients with history of asthma, risk of aspiration, difficult airway, snoring, passive smoking, morbid obesity, coexisting pulmonary and cardiac disease, fever >38°C and evidence of lower respiratory tract infection, were excluded from the study. No child was premedicated and baseline oxygen saturation was obtained with room air. Any child with SpO2 <95% in preoperative area was excluded from the study.

They were randomized to receive either SR or PCV. All patients in PCV group received a PEEP of 5 cm H2O. The nurse in preoperative area allocated the patients into groups using computer generated random numbers. No muscle relaxant was used for any patient.

All cases were conducted in same period of the year for 3 consecutive years which are winter months in this country.

Anesthesia was induced using O2 and N2O and 8% sevoflurane using uniform flows for all patients. The anesthetic was titrated to allow spontaneous respiration for children in SR group whereas in PCV group were ventilated using pressure control ventilation and PEEP of 5 cmH2O was applied. In the PCV group the pressure limit was set at 15 cmH2O and the respiratory rate was adjusted to maintain the PeCO2 between 4.6 and 5.8 kPa (35–45 mmHg). Anesthesia was maintained using 1-2% sevoflurane in oxygen and nitrous oxide mixture. PLMA was inserted by anesthetist with experience of more than 500 cases of PLMA insertion. It was in accordance with manufacturer’s instructions. After PLMA placement, caudal block was administered. Paracetamol suppository was inserted per-rectally in all patients. Any patient developing a rise of heart rate by more than 20% at skin incision, received fentanyl citrate 1ug/kg, and was excluded from the study. At emergence, O2 and air mixture was used. Patients requiring more than one attempt at PLMA insertion were not included in the study. Pulse oximetry (SpO2), electrocardiography (ECG), respiratory rate, end-tidal CO2 (EtCO2) and automated blood pressure (NIBP), were monitored for all patients.

The values were mean of readings taken every five minutes throughout the period. During emergence,
the PLMA was removed inside the operation theatre at onset of swallowing in all patients by the anesthetist conducting the case. On removal, the device was observed for any evidence of blood.

A co-anesthesiologist who was blinded to mode of ventilation made all observations for adverse events at removal of PLMA and in the PACU. The respiratory adverse events that were evaluated were: presence of airway secretions, coughing, breath holding, bronchospasm and upper airway obstruction or laryngospasm (LS). These events were assessed and graded in accordance with details in Fig 1. All children with bronchospasm received nebulization with salbutamol in the PACU. No antiemetic was used in any patient and they were kept in the PACU till discharge readiness.

The observations were graded for their severity from 1 to 3 using the scale similar to one published by Levy et al. Score 1: mild or no signs, 2: moderate and 3: severe. An experienced anesthesiologist, who was blinded to the mode of ventilation made all observations. The mean scores, which ranged from minimum of 3 to maximum of 15, were used for comparison. The mothers were contacted telephonically to find about any respiratory adverse events upto 24 hrs after discharge.

Statistics

The primary variable was the mean adverse events score. Demographic data and incidence values were compared using chi-square test. The collected data was analysed using analysis of variance i.e. ANOVA. Mann-Whitney U-test and Wilcoxon W-tests were applied for nonparametric data. P value <0.05 was considered statistically significant. From preliminary data, we calculated with alpha-set at 0.05, that 90 patients would give a statistical power of 82% to detect 20% difference in mean respiratory adverse events score between the PCV and SR groups. Secondary variables were SpO2 in PACU and PetCO2. The data are expressed as mean ± standard deviation. Software SPSS Inc Chicago IL, USA 12.0 version, was used for the analysis.

Results

A total of 7 patients (6 of PCV group, and 1 of SR group) could not complete the study. Of these 4 patients required a second attempt at PLMA insertion and 3 patients had inadequate analgesia.

The demographic profile, general characteristics; baseline SpO2 and their distribution into the PCV and SR type of ventilation, are listed in Table 1. However in the PACU, the SpO2 (%) in the SR group (mean 94.5, range 89-96, median 94) was lower than the values than the PCV group (mean 96.5, range 90-100, median 97), achieving statistical significance.

The incidence of adverse events was significantly higher in SR (7.75±2.2) as compared to PCV (6.33±1.7) group; P = 0.001. All adverse events were significantly higher in SR group (Table 2, 3). Most adverse events in both groups were of mild degree (Table 2). The mean PetCO2 during intra operative period was 41.3±3.9 in SR and 36.6±4.4 in PCV group (P = 0.000). In contrast to 17% patients in PCV group, 41% in SR
Table 1
Demographic profile and general characteristics

<table>
<thead>
<tr>
<th></th>
<th>PCV</th>
<th>SR</th>
<th>Level of Significance (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>39</td>
<td>44</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.5±0.6</td>
<td>1.3±0.5</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>10.9±2</td>
<td>9.8±1.8</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>33/6</td>
<td>40/4</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Duration (minutes)</td>
<td>61.4±24</td>
<td>77±22</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Baseline SpO₂%</td>
<td>97</td>
<td>96.6</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>

M/F: Male/Female, PCV: Pressure Control Ventilation, SR: Spontaneous Respiration.

Table 2
Adverse respiratory events of PCV and SR groups

<table>
<thead>
<tr>
<th></th>
<th>BREATH HOLDING</th>
<th>SECRETIONS</th>
<th>BRONCHOSPASM</th>
<th>LS</th>
<th>COUGH</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD (PCV/SR)</td>
<td>25/13</td>
<td>36/31</td>
<td>29/22</td>
<td>36/31</td>
<td>26/23</td>
</tr>
<tr>
<td>MODERATE (PCV/SR)</td>
<td>10/27</td>
<td>2/11</td>
<td>9/18</td>
<td>3/12</td>
<td>10/17</td>
</tr>
<tr>
<td>SEVERE (PCV/SR)</td>
<td>4/4</td>
<td>1/2</td>
<td>1/4</td>
<td>0/1</td>
<td>3/4</td>
</tr>
<tr>
<td>P-value</td>
<td>0.003</td>
<td>0.036</td>
<td>0.110</td>
<td>0.039</td>
<td>0.236</td>
</tr>
</tbody>
</table>

The figures in the table represent number of patients in PCV/SR group.
PCV: pressure control ventilation, SR: spontaneous respiration, P>0.05=NS: not significant; P<0.05 = significant. LS is Laryngospasm.

Table 3
Comparison of various events between the two modes of ventilation

<table>
<thead>
<tr>
<th></th>
<th>PCV</th>
<th>95% Confidence Interval Lower/Upper</th>
<th>SR</th>
<th>P value</th>
<th>95% Confidence Interval Lower/Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>COUGH</td>
<td>1.08±0.3 (0.04)</td>
<td>1.02/1.14</td>
<td>1.32±0.6 (0.07)</td>
<td>0.011</td>
<td>1.21/1.43</td>
</tr>
<tr>
<td>BREATHE HOLDING</td>
<td>1.46±0.7 (0.10)</td>
<td>1.31/1.61</td>
<td>1.8±0.6 (0.09)</td>
<td>0.019</td>
<td>1.68/1.93</td>
</tr>
<tr>
<td>BRONCHOSPASM</td>
<td>1.28±0.5 (0.08)</td>
<td>1.17/1.39</td>
<td>1.77±1.5 (0.23)</td>
<td>0.06</td>
<td>1.44/2.10</td>
</tr>
<tr>
<td>SECRETIONS</td>
<td>1.10±0.4 (0.06)</td>
<td>1.02/1.19</td>
<td>1.34±0.6 (0.08)</td>
<td>0.030</td>
<td>1.22/1.46</td>
</tr>
<tr>
<td>LARYNGOSPASM</td>
<td>1.4±0.6 (0.10)</td>
<td>1.27/1.55</td>
<td>1.5±0.6 (0.08)</td>
<td>0.40</td>
<td>1.39/1.65</td>
</tr>
<tr>
<td>PETCO₂</td>
<td>36.6±4.4 (0.70)</td>
<td>35.67/37.56</td>
<td>41.3±3.9 (0.59)</td>
<td>0.000</td>
<td>40.48/42.16</td>
</tr>
<tr>
<td>PACU* SpO₂ (%)</td>
<td>96.5±2 (0.33)</td>
<td>96.09/96.99</td>
<td>94.4±1.37 (0.20)</td>
<td>0.000</td>
<td>94.11/94.70</td>
</tr>
<tr>
<td>NEBULIZATION</td>
<td>7/39 (17%)</td>
<td>9.6/25.3</td>
<td>18/44 (41%)</td>
<td>0.013</td>
<td>32/54</td>
</tr>
<tr>
<td>ADVERSE EVENTS SCORE (mean)</td>
<td>6.33±1.6 (0.25)</td>
<td>5.99/6.68</td>
<td>7.75±2.2 (0.32)</td>
<td>0.001</td>
<td>7.28/8.22</td>
</tr>
</tbody>
</table>

PCV: Pressure Control Ventilation, SR: Spontaneous Respiration. Nebulizations is with salbutamol. Values in parenthesis are Standard error mean. P<0.05 = significant
A total of 16 patients required assisted ventilation after removal of PLMA of which 13 were in SR group. The minimum SpO₂ experienced during study was 89% (SR group, immediately after removal of PLM). There was no evidence of device malposition, dislodgement or air leak in any patient; however blood was seen on device of 4 patients, 3 of which belonged to PCV group.

There was no difference in the two groups at discharge readiness.

Discussion

URTI does not imply restriction of disease to upper respiratory tract; it has been shown to produce pulmonary dysfunction as well changes in oxygen saturation9,10. PEEP has been shown to improve oxygenation in such cases. Our results show that the overall incidence of adverse events is significantly higher in children having acute respiratory tract infection undergoing surgery under spontaneous respiration when using PLMA as airway device.

Schreiner et al in a case-control study showed that younger age group is an independent risk factor for adverse events particularly laryngospasm, however no clear age cut-off was defined. No particular anesthetic technique or airway devices were used in any of the previous studies. Different anesthetic agents including thiopentone, propofol, halothane and sevoflurane have been described in the previous studies. Most previous studies have lacked uniformity with respect to type of surgery and few of these studies included patients undergoing surgery on airway, which could be an independent factor predisposing to adverse respiratory events11. However all our patients underwent infra-umbilical surgery and no airway manipulation other than insertion of airway device was required.

Cohen et al in their longitudinal study showed there is 2-7 times increased chances of respiratory complications in patients with acute URTI undergoing surgery12 and that the respiratory events increased by 11 times due to instrumentation of trachea.

PLMA, one of the advanced supraglottic devices has been successfully used to provide both spontaneous and controlled ventilation in children. Its use has been shown to lower incidence of coughing, sore throat, improved oxygen saturation and reduced anesthetic requirements for airway tolerance13.

Tait et al5, compared incidence of perioperative respiratory complications associated with TT and LMA. All their patients had acute but uncomplicated URTI and were allowed only spontaneous respiration and the agent used in all their cases was halothane. In our study however, sevoflurane was used for all patients there was no tracheal instrumentation.

Our results showed that individual events, namely secretions, breath holding, bronchospasm and coughing all of which could be precursor to laryngospasm, were seen more often in spontaneously breathing children and that PCV was associated with lower incidence of adverse respiratory events.

Goldman and Roettger demonstrated that application of PEEP of 5 cm H₂O with PCV under GA improves gas exchange when the PLMA is used, as evidenced by a significantly higher mean PaO₂. This could explain the higher SpO₂ seen in patients on PCV in our study.

Several studies have shown increased incidence of arterial desaturation in children suffering from acute URTI which responds rapidly to oxygen supplementation and also that this desaturation is more rapid following apnea9,11,14,15. In our study, we observed that the incidence of desaturation was higher for spontaneously breathing children in comparison with patients on PCV. All patients responded to oxygen supplementation in post anesthesia care unit (PACU).

In a study on lambs suffering from parainfluenza virus infection, Dueck et al found that the peak airway pressure (PAP) does not significantly change after infection but there is development of shunt at a higher FRC after infection. However, its influence on outcome of anesthesia as well as surgery remains uncertain. URTI has been shown to produce fall in FRC, development of shunt at higher FRC and many more changes in lung volumes and diffusion capacity16-24.

Conventionally, tracheal tubes have been used to provide positive pressure ventilation but the introduction of PLMA has challenged this assumption. Supra glottic devices in form of laryngeal masks,
particularly PLMA has made it possible to deliver PCV with PEEP without having to paralyze the patient, more so in infraumbilical surgeries, thereby obviating need for endotracheal intubation and minimizing adverse respiratory events in children particularly when URTI is present. There is a case report of laryngeal edema associated with use of PLMA, in an adult having suspicion of URTI. If general anesthesia is required despite URTI, the evidence is that the use of LMA significantly reduces the risk compared to intubation. The role of PLMA in children with symptoms suggestive of URTI, so far has remained unclear. Nevertheless it offers distinct advantages of permitting effective ventilation without air-leak and gastric distension, and providing ability to apply PEEP.

Although coexistence of URTI was seen to be associated with high incidence of adverse events, most of these were mild and no serious or life threatening complication was encountered in any of our patients. We conclude that Pressure control ventilation with PEEP using PLMA was accompanied with lower incidence of adverse events and this may be preferred mode of ventilation in infants and toddlers with upper respiratory tract infection undergoing infraumbilical surgery under general anesthesia.

References
CASE REPORTS

SONOGRAPHIC DIAGNOSIS OF CATHETER MALPOSITION IN A PATIENT WITH POSTOPERATIVE PLEXUS LESION AFTER RIGHT INTERNAL JUGULAR VEIN CATHETERIZATION

- Case Report -

WERNER TIEFENTHALER*, GREGOR K WENNING**, HANNES GRUBER*** AND ARNULF BENZER****

Abstract

Purpose: Postoperative brachial plexus lesion has been reported only rarely after catheterization of the right internal jugular vein (RIJV), and then is usually considered to be the result of puncture hematoma.

Clinical features: We here present the case of plexus brachialis injury after catheterization of the RIJV with ultrasonography showing direct compression of the plexus brachialis by a central venous catheter without evidence of puncture hematoma.

Conclusion: Every case of plexus brachialis injury after catheterization of the RIJV should be followed up by an emergency sonogram to rule out hematoma or catheter malposition.

Running head: Sonographic diagnosis of catheter malposition after RIJV catheterization.

Implication Statement

Ultrasonography should be performed in every case of brachial plexus lesion after catheterization of the right internal jugular vein to preclude damage to the plexus brachialis.

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Introduction

The scenario is not uncommon and familiar to many anesthetists. Following a surgical intervention with complication-free intraoperative course, the patient wakes up with nerve damage that primarily can not be associated with the surgical intervention or the general anesthesia procedure. Analysis of the ASA Closed Claims Database in 1999 showed “nerve damage” to be one the most common reasons for claims to indemnification.

Central venous cannulation through the right internal jugular vein (RIJV) is widely used in the management of patients scheduled for major surgery, but reports on injury of the Plexus brachialis after RIJV puncture are very rare, with such damage generally ascribed to puncture hematomas or patient malpositioning.

Case Report

A 30-year-old female with an unremarkable medical history (ASA I) was scheduled for correction operation of thoracolumbar kyphotic spinal deformity (TH3-L2).

After inducing general anesthesia the patient was positioned 15° head-down with the head turned 30° to the left for introduction of a central venous catheter (ARROW International) via the RIJV. Uneventful cannulation of the RIJV was performed via the approach described by Bazaral and Harlan using the Seldinger technique.

For surgery the patient was positioned prone with her arms abducted 70° and the arm position controlled and noted every 30min. After emergence, the patient reported pain and paresthesia of the right arm. The puncture point for the RIJV catheter was unremarkable. Neurological examination revealed the picture of a Plexus brachialis lesion primarily involving the axillary and musculocutaneous nerve with diminished shoulder abduction and elbow flexion and reduced sensitivity on the outer side of the shoulder.

An urgently performed neurosonogram showed the RIJV catheter to press against the right side of the root of C6 with hardly any hematoma (Fig.1). The catheter was immediately removed and the patient was treated conservatively with physical therapy. Paresis and paresthesia began to improve twelve weeks after surgery with full recovery twelve months after the initial event.

Discussion

Analysis of the ASA Closed Claims Database had showed perioperative nerve injury to still be a significant and constant source of injury (15%-16% of all lawsuits), with injury of the brachial plexus (i.e. due to patient positioning, regional block, surgical trauma or preexisting injury) at 20% being the second most common cause of damage (Nervus ulnaris 28%)1,5. In light of the similar anatomic-topographic situation it is, however, surprising that the ASA Closed Claims Database indeed lists claims for indemnification after Plexus brachialis anesthesia, but no reports on damage involving catheterization of the RIJV.

Likewise, an ASA Closed Claims Database study published by Domino et al. in 2004 on typical complications when introducing a central venous catheter does not even mention the possibility of
damage to the Plexus brachialis when catheterizing the RIJV. Since this study only included claims for which a central venous catheter was explicitly named as the primary damaging event and a Plexus brachialis lesion can occur as the result of patient malpositioning, unrecognized puncture-induced damage to the Plexus brachialis could erroneously be ascribed to "malpositioning".

The potential danger posed to the nerves by the anatomic course of the Plexus brachialis because of the particular patient position (i.e. abduction of the arms, which stretches the nerves) required for the surgical intervention, is a well-known fact and malposition as a possible cause of nerve damage cannot be ruled out with guarantee even in our patient. First doubts about the exclusivity of this malpositioning theory were already voiced in 1982 by Lederman et al., who found brachial plexus lesions in 23 out of 421 patients undergoing coronary artery bypass graft surgery with a correlation between the site of jugular vein cannulation and the side affected in 17 patients, thereby indicating the possibility of a puncture trauma during central venous catheterization. Their results were confirmed by a prospective analysis of 531 patients undergoing cardiac surgery with sustained brachial plexus injury in 5% of the patients and a correlation between the side of plexus brachialis lesion and the side of internal jugular vein cannulation in 73% of the patients.

Anesthetists should be aware of the potential for this complication in general and should realize that even after uneventful catheterization of the RIJV, catheter malpositioning cannot be excluded by clinical inspection alone. The recommendation to use ultrasound guidance devices when introducing a central venous catheter into the RIJV is thus further underscored, because such devices permit the RIJV to be reached by the shortest possible route, with the least possible danger for the surrounding (nerve) structures. Every case of postoperative injury to the plexus brachialis after catheterization of the RIJV should be followed up by an emergency sonogram to rule out hematoma or catheter malposition.

Acknowledgements

The authors would like to thank Julia Wanschitz and Wolfgang Löscher for their invaluable assistance.

References

INNOVATIVE LIGHTED STYLET
- Succeeds Where Conventional Lighted Stylet Fails -

MANISH JAIN*, AMIT GUPTA**, MUNISH GARG***, BHAVNA RASTOGI*** AND HIMANSHU CHAUHAN***

Introduction

Nasal intubation is an obvious choice for temporomandibular joint (TMJ) ankylosis surgery (Fig. 1). Adequate surgical access and better fixation makes RAE (Ring-Adair-Elwin) nasal tube a preferred choice. Conventional lighted stylet does not support RAE intubation due to short length of its stylet (Fig. 2). Our innovative lighted stylet can easily help in RAE tube insertion in these cases (Fig. 3). It is simple to make and can be easily assembled from materials commonly available in the operating room.

Fig. 1
Orthopantomogram (panorex view) showing TMJ ankylosis
Case Report

A 22 year old female was admitted to our hospital with temporomandibular joint (TMJ) ankylosis and was posted for gap arthroplasty (Fig. 1).

Preoperative investigations revealed hemoglobin 11.3 gm%, total leucocyte count (TLC) 9500/ cmm, differential leucocyte count (DLC) P82 L17 E1, blood sugar 110mg%, blood urea 35mg/dl, ECG and chest x-ray were normal.

Preanaesthetic check up revealed BP 114/70 mm Hg, pulse rate 84/min and weight 52 kg. Mallampatti (MP) grading could not be assessed as she barely had any mouth opening. She was accepted for anesthesia as ASA grade I with anticipated difficult airway.

Preanaesthetic check up revealed BP 114/70 mm Hg, pulse rate 84/min and weight 52 kg. Mallampatti (MP) grading could not be assessed as she barely had any mouth opening. She was accepted for anesthesia as ASA grade I with anticipated difficult airway.

On the day of surgery, patient was premedicated with glycopyrrollate 0.2 mg i.v., midazolam 2.0 mg i.v., and butorphanol 2.0 mg i.v. For securing airway, awake nasotracheal intubation with RAE (Ring-Adair-Elwin) nasal tube was planned with innovative lighted stylet as conventional lighted stylet had failed to reach the tip of RAE tube (Fig. 2, Fig. 3). Patient was thus prepared for awake nasal intubation. After explaining procedure to the patient, upper airway was anesthetized using 10% xylocaine spray. Bilateral superior laryngeal nerve block and intratracheal instillation of xylocaine was done for anesthetizing lower airway. After proper lubrication, RAE tube with innovative lighted stylet was put through right nostril and using light glow as guide, we succeeded in performing nasotracheal intubation in first attempt. Confirmation of correct tube placement was done by auscultation of bilateral breath sounds and using a capnograph. Inj. propofol 2.0mg/kg i.v. was given to induce anesthesia and maintained using inj. vecuronium bromide 0.08mg/kg, oxygen, nitrous oxide and isoflurane. At the end of surgery, patient was extubated after reversal using inj. neostigmine 2.5 mg and inj. glycopyrrollate 0.4 mg i.v. Postoperative period remained uneventful.
**Discussion**

Difficult airway is always a challenge for the anesthesiologist. To overcome these difficulties, various gadgets and equipments have been developed.

Our patient had TMJ ankylosis because of which she had no mouth opening making direct laryngoscopy unfeasible. Under this tight situation the options open for securing airway were: fiberoptic bronchoscopy (FOB), blind nasal intubation, tracheostomy, and intubation using lighted stylet.

Although FOB is a gold standard for securing airway in these patients, this instrument was not available in our Institution. Lighted stylet intubation is especially useful in situations where FOB is unavailable or difficult to perform because of secretions or blood in airway or when patient’s head cannot be flexed or extended.

Compared with blind nasal intubation, nasal intubation with lighted stylet has been shown to require less time and fewer attempts. Blind intubation has got high failure rates and there are also high chances of airway trauma.

Although tracheostomy was a feasible option, however, considering the postoperative morbidity associated with this technique, this option was kept only for emergent situation.

Lighted stylet aided intubation was the option selected. This technique uses a bright glow which guides the tube into trachea and can be used for nasal or oral intubation in patients whose larynx cannot be visualised by direct laryngoscopy.

Preformed tube (RAE) was chosen to secure airway over conventional endotracheal tube, as it is non kinkable, does not come into the surgical field and has better fixation which reduces the risk of unintended extubation. However, when conventional light wand was inserted into RAE tube, it could not reach the tip of tube because of its short length (Fig. 2). Hence, we innovated the lighted stylet which could reach the tip of RAE tube (Fig. 3) and were able to intubate the patient without encountering any difficulty.

In conclusion, intubation of trachea using lighted stylet is easy, safe, effective and rapid alternative method of airway management. Our innovative lighted stylet has an added advantage that it can be used to intubate trachea with RAE tube where conventional lighted stylet fails.
References

AN UNUSUAL CASE OF A PATIENT WITH EXTREME FIXED NECK FLEXION PRESENTING FOR EMERGENCY ABDOMINAL SURGERY

Michael Oleyar* and Steven M Neustein**

Abstract

Patients with a known difficult airway for intubation who present with intestinal obstruction are at an increased risk for receiving general anesthesia. It may be necessary to perform an awake fiberoptic intubation, or possibly a tracheostomy if an awake intubation cannot be performed. In some cases, an awake tracheostomy may not be possible due to the anatomy. We report a case in which a patient with extreme fixed neck flexion deformity in whom a tracheostomy would not have been possible, presented for emergency abdominal surgery.

Case Report

A 77 year-old man presented for emergency herniorraphy of an incarcerated left inguinal hernia with small bowel obstruction. He was complaining of nausea and vomiting. Past medical history included arthritis, hypertension, Parkinson’s disease, enlarged prostate and colorectal cancer s/p chemotherapy and radiation therapy. Medications included finasteride, carbidopa/levodopa, and mirtazapine.

On physical exam, his neck was in a 90 degree flexed position, and was immobile. He did have a good mouth opening, and his airway classification was Mallampati 3. His thyromental distance was 6 cm. His abdomen was distended, and he had an incarcerated left inguinal hernia.

Once in the operating room, he was propped up on a ramp created with pillows and padding.

Fig. 1
The patient is positioned for surgery, with padding to stabilize the head in a vertical position. The chin is juxtaposed on the chest. The nasotracheal tube is in position.
Glycopyrrolate 0.2 mg was administered to decrease secretions. Airway topicalization was accomplished with the use of 4% lidocaine by nebulizer and then atomizer. It was not possible to perform a cricothyroid puncture for tracheal anesthesia, due to the extreme neck flexion. The nares were prepped with lidocaine/phenylephrine.

The nasal passageway was then dilated with a 6.0 nasal airway which had been lubricated with 2% viscous lidocaine. Following removal of the nasal airway, a 7.0 ID soft nasotracheal tube (Portex, Kenne, NH) was passed via the nares into the pharynx. While standing in front of the patient, the fiberscope was passed through the endotracheal tube. Once the patient’s vocal cords were visualized, an epidural catheter was advanced via the working channel of the fiberscope, and 4 ml of 4% lidocaine was administered via the epidural catheter. The fiberscope was then advanced into the trachea, and the endotracheal tube was passed over the fiberscope into the trachea. General anesthesia was then induced. Following completion of surgery, the patient was extubated, and had a good recovery. A photograph of the patient following tracheal intubation and induction of anesthesia can be seen in the Fig. 1.

Discussion

Extreme neck flexion may cause difficulty with endotracheal intubation. We have described an unusual case of a patient with a severe fixed flexed neck deformity, presenting for emergency surgery. A tracheostomy was not possible. A cricothyroid puncture for transtracheal topicalization was also not possible.

Awake fiberoptic intubation appeared to be the safest technique. The technique of passing an epidural catheter through the working channel of the fiberoptic bronchoscope was utilized, which has been previously described.

References

LOSS OF CONSCIOUSNESS SECONDARY TO LEAD POISONING

Reza Shariat Moharari*, Mohammad Reza Khajavi**, Mahdi Panahkhahi*, Mojtaba Mojtabedzadeh*** and Atabak Najafi**

- Case Reports -

Abstract

Diagnosis of lead toxicity could be difficult in IC setting because of overlap of signs and symptoms with other diseases. This is a report of two Iranian patients (father and son) with severe level of whole blood lead concentration, developing into unconsciousness.

Introduction

The use of lead and its environmental contamination has increased dramatically since the beginning of the Industrial Revolution. However, environmental and occupational exposure to lead as well as the severity of lead poisoning have decreased due to government regulations and increased public health awareness of the problems associated with lead. New forms of non-occupational poisoning have emerged and poisoning due to drug addiction has been reported in few studies.

Inorganic lead affects the central and peripheral NS, hematopoietic systems, kidney, GIT, liver, myocardium and reproductive capacity.

We present two cases (Iranian father and son), with severe level of whole blood lead concentration, developing into unconsciousness,

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Case 1

A 27 year old worker, with a history of colicky abdominal pain for two months accompanied with weakness and constipation, was admitted to the internal medicine ward. Patient was an opium addict. Few days after hospitalization, patient showed signs of icter and a considerable reduction in the level of consciousness, in the form of delirium and hyperirritability. As a result patient was moved to the ICU.

On physical exam. revealed normal vital signs of BP 135/86, HR 68/min and T 37.5 deg. C. Patient manifested generalized abdominal pain without guarding. CV and respiratory examinations were normal. Neurologic exam. revealed tremor, hyperirritability and delirium. Motor and sensory exam. were normal. ECG, chest and abdominal radiography, abdominal US, upper GI endoscopy, and CT-scan of abdomen and brain, were all normal.

Lab tests revealed anemia of Hb 9g/dl, total bilirubin 6.5 mg/dl with domination of indirect component, and an increase in liver enzymes ALT 138u/l, AST 102 u/l (N = ALT u/l ≤41, AST ≤37 u/l). Blood lead level was 154 ug/dl (N ≤25ug/dl).

Symptoms gradually improved after a five day course of treatment with BAL 75mg/m² IM Q4h and Ca Na₂ + EDTA 1500 mg/m²/d (continuous infusion) started four hours after BAL injection.

Case 2

A 68 year old worker with a month’s history of abdominal pain, icter, insomnia, weight loss and anorexia, admitted to internal medicine ward. Loss of consciousness, confusion and coma occurred a week after admission.

Patient had a positive history of diabetes mellitus, cigarette smoking and opium addiction.

On physical exam. vital signs were normal with BP 140/85 and HR 65/min. and T 37 deg. C. He manifested abdominal pain without tenderness. The CV and respiratory exam. were normal. He had an altered mental status. Upper and lower extremities were paralyzed, atonic with absent deep tendon reflexes ECG, chest and abdominal radiography, abdominal US, brain and abdominal CT-scan, were normal. Lab tests revealed anemia of Hb 6.5 g/dl, elevated liver enzymes ALT 40 u/l, AST 88 u/l and total bilirubin 6.5 mg/dl, with indirect component dominancy. HBSAg, HCV Ab and HIV tests were normal. Lead level in whole blood was 180 mg/dl.

Patient did not respond to a five day treatment with BAL and CaNa₂ + EDTA, and died due to CV collapse.

Discussion

Up till the present, few cases of lead poisoning due to usage of lead contaminated opium have been reported. We report on two patients (Iranian father and son) who had been hospitalized manifesting common symptoms of; icter, abdominal pain, impaired consciousness and anemia. Patient’s relatives hypothesized the possibility of lead poisoning due to usage of opium processed in a lead-based bowl.

The older patient (Case 2) had shown rare occurrence of neuropathy and encephalography symptoms in the form of paralysis with absent deep tendon reflexes and decreased level of consciousness.

In the accurate determination of lead content, blood samples must be collected with lead-free equipment. For reliable results, tests should be done in Labs. experienced in lead analysis, with intra laboratory quality control and atomic absorption spectrometry. The diagnosis of lead poisoning is based on elevated blood levels (defined as equal or greater than 25 ug/dl). Chelation therapy is needed in severe cases to decrease blood lead levels faster, thereby facilitating clinical improvement.

The patients’ blood samples (arterial and venous), were sent to the reference lab., and in parallel chelation therapy was started.

Test results indicated a high level of lead in the blood samples (≥100ug/dl). Further questioning of patients’ relatives, hypothesized that patients used to add lead to opium in order to increase its weight, and that it was probable that they had used their own product by mistake. This hypothesis was confirmed by sending the opium sample to the reference lab. who reported that the lead content was higher than the normal standard recognized by the FDA.

The younger patient had responded positively
to the treatment and left the hospital with informed consent before completion of the normal term of treatment. The older patient, however, who is diabetic, died due to CV collapse in four days after start of chelation therapy.

Sources of lead, other than occupational exposures, such as lead contaminated opium should be considered, in the differential diagnosis of loss consciousness of opium addicted patients.

**Acknowledgement**

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**References**


ACUTE RESPIRATORY DISTRESS SYNDROME: RAPID AND SIGNIFICANT RESPONSE TO VOLUME-CONTROLLED INVERSE RATIO VENTILATION

- A Case Report -

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Abstract

Pulmonary complications following cardiopulmonary bypass (CPB) are relatively common, with up to 12% of patients experiencing acute lung injury (ALI). The treatment for ALI or acute respiratory distress syndrome (ARDS) is primarily supportive with specific modes of mechanical ventilation. We report a 46-year-old man with ARDS after cardiac surgery whose arterial oxygenation was surprisingly improved 1 hour after using volume-controlled inverse ratio ventilation (VC-IRV).

Key words: pulmonary complication, CABG, treatment of ARDS.

Introduction

Pulmonary complications following cardiopulmonary bypass (CPB) are relatively common, with up to 12% of patients experiencing acute lung injury (ALI). The overall goals of mechanical ventilation in ARDS are: to maintain acceptable gas exchange and to minimize the occurrence of adverse effects associated with its application.

A growing consensus currently supports the use of low tidal volume ventilation, with positive end expiratory pressure (PEEP). Current clinical practice with known or suspected lung injury is, however, to limit inflation pressure. The inverse ratio ventilation (IRV) is a mode of mechanical ventilation in which the inspiratory time is prolonged (I>E) and has the advantage over the conventional use of (E ≥ I and extrinsic-PEEP) in that unacceptable increases in peak airway pressures and peak alveolar pressures can be avoided. 

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Case Report

A 46-year-old man, with a 5 year history of ischemic heart disease, hypertension and severe opium addiction and a 15 year history of heavy smoking, with EF = 50% and three vessels disease, was operated for coronary artery bypass graft (CABG) surgery, under cardiopulmonary bypass (CPB). The operation was uneventful.

After operation, in the ICU, because of bleeding with chest tube drainage in place, patient was sedated. Following reduction of drainage, weaning of patient from ventilator was gradually started. The day after, patient was completely weaned and extubated. Thirty six hours after extubation, however, he suddenly had an acute onset of severe arterial hypoxemia resistant to oxygen therapy. Meanwhile, the hemodynamics were stable, ECG did not show arrhythmia or ischemia, echocardiography did not show evidence of left ventricular failure. At this time (arterial pressure of oxygen) PaO₂/FIO₂ (fraction of inspiratory oxygen) was<100 (Table1-ABG1).

The patient was rapidly intubated, sedated and ventilated with conventional ventilator support that is usually used following surgery (Volume cycled, SIMV, RR = 12/min, Vt = 10cc/kg, FiO₂ = 50%, I:E = 1:2, PS = 15 cm H₂O, PEEP = 5 cm H₂O) following cardiac surgery (Table1-ABG2).

Chest x-ray revealed bilateral infiltration of the lungs (3 quadrant at first and 4 quadrant 1 hour later). (chest-x-ray 1 and 2).

Based on Murray lung injury score that awards points for affected quadrants on chest x-ray, PaO₂/FiO₂ ratio, amount of PEEP applied and static compliance of the lungs (Table 2) our patient’s score was greater than 2.5, which confirmed severe ARDS. The ventilator’s settings were therefore changed to high PEEP level with low tidal volume. With this setting arterial oxygenation was improved, PaO₂ reached to 61-63 mmHg and O₂ saturation reached to 93-94% (Table 1-ABG3).
The same ventilation was maintained for the following 48 hour, but PaO₂ did not increase and emphysema began to show.

With this development, the ventilator’s settings were modified to deliver inverse ratio ventilation (IRV) with reduction in ventilator rate and PEEP discontinued. An hour later, PaO₂ reached up to 115 mmHg and arterial O₂ saturation (SaO₂) of 98% (Table 1-ABG 4).

Weaning of patient was started, sedative drugs were tapered and surprisingly in 8 hour patient’s status normalized and he was extubated. Emphysema was reduced in 48 hour. Patient was discharged from ICU with acceptable ABG (Table 1-ABG 5 & 6), chest-x-ray (chest-x-ray 3) and stable hemodynamics (MAP = 83mmHg, HR = 87 beat/min, no serious arrhythmias and EF = 45%).

Discussion

Patients undergoing cardiac surgery experience physiologic stresses from anesthesia, surgical manipulation, and CPB. ARDS may develop as a sequel of CPB, or, more commonly, in the postoperative patient with cardiogenic shock, sepsis, or multiple organ failure.

The treatment for ALI or ARDS is primarily supportive with mechanical ventilation, a procedure allowing time for treatment of the underlying cause of lung injury and for natural healing. Low tidal volume ventilation should be applied to all patients with ARDS unless more efficacious strategy is demonstrated.

For more than two decades, PEEP has been used to improve arterial oxygenation in patients with ARDS. Indeed, several recent studies have found improved hemodynamic performance and fewer pulmonary complications using high PEEP levels with tidal volumes as low as 6 ml/kg in these patients.

Due to the increased physiologic dead space of patients with ARDS, ventilator rates greater than 20-25 breath/min are often required to normalize PaCO₂ and pH, unless excessive intrathoracic gas trapping occurs, leading to development of auto-PEEP which has the potential of adverse effects including barotraumas, hemodynamic instability, increased work of breathing, and decreased efficiency of diaphragmatic...
contractility. We also used this method (tidal volume = 6 ml/kg, PEEP + 8-15 cm H2O, ventilator rate + 18-20 breath/min) on our patient but it could not increase PaO2 to more than 69-74 mmHg.

Because of the preceding event and the start of emphysema (adverse effect of auto-PEEP), we changed the mode to volume-controlled-inverse ratio ventilation (VC-IRV). Other investigations have concluded that the effect of reduced expiratory time on end-expiratory lung volume, pressure and arterial oxygenation during volume-controlled VC-IRV, is similar to the use of PEEP. However, a growing oxygenation during volume-controlled-inverse ratio ventilation (VC-IRV), is on end-expiratory lung volume, pressure and arterial oxygenation with using of high PEEP levels and low tidal volume, but with the use of VC-IRV, oxygenation was rapidly and significantly improved while acceptable peak airway pressure was maintained.

Although beneficial effects of VC-IRV are known, and studies have been directed on the late effects of this mode of ventilation, yet the rapid and significant effect on oxygenation has not been reported.

**Conclusions**

In a situation where acceptable arterial oxygenation cannot be achieved with PEEP less than 15 cmH2O, or when the use of PEEP is associated with excessive plateau pressure, the volume-controlled inverse ratio ventilation (VC-IRV) is recommended.

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MANAGEMENT OF NEONATAL massive anterior mediastinal teratoma

- A Case Report -

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Abstract

We report a challenging case of a newborn with a massive anterior mediastinal teratoma (MT), occupying nearly the right hemithorax, presenting at birth with life threatening respiratory distress (RD). Optimal approach and outcome was achieved with a coordinated, multidisciplinary approach.

Key Words: Mediastinal, Teratoma, Neonate, Anesthesia, Airway

Introduction

Teratomas are tumors composed of multiple tissues containing at least two of three germ-layer derivatives foreign to the part of the body in which they arise1. Mediastinal Teratoma is uncommon in infants and children, constituting 7 to 11% incidence2,3,4. In newborn period, these tumors can cause life threatening respiratory obstruction and must be promptly diagnosed and treated if the patient is to survive3.

Case Report

A term baby boy (39 weeks), was a product of an unbooked 30y old (G2 P1 + 0) mother with a history of prolonged rupture of membrane, for more than 24 hours, delivered by emergency (LSCS) due to failure to progress. Neoborn had a birth weight of 4.06 kg and an Apgar Score of 5 and 8 at 1 and 5 minutes, and had no dysmorphic features.
Following delivery, the baby had marked respiratory distress (cord pH 7.24), he was resuscitated, ventilated and shifted to NICU. In NICU, chest X-ray revealed widened cardiac silhouette and a leftward mediastinal shift (Fig. 1). Cardiac evaluation revealed tiny patent ductus arteriosus and patent foramen oval which could not explain the severity of respiratory distress.

CT scan showed huge multiloculated anterior mediastinal cystic mass (6.26.8 x cm); with multiple calcifications suggestive of a teratoma, causing significant displacement and shift of the mediastinum to the left side and posterior displacement of the heart and lungs (Fig. 2).

The diagnosis based on radiological finding was congenital anterior mediastinal teratoma, which needed urgent surgical excision. Laboratory workups were within normal limits and Alpha-fetoprotein was 1210 mg.

Pre-operatively the patient was maintained intubated (ETT size 3), sedated, SIMV mode with FiO2 30%. Two intravenous accesses in both arms (22G). Right thoracotomy was performed on day four, patient was positioned in left lateral decubitus position, connected to two pulse oximetries, ECG, EtCO2, respiratory parameter, temperature, and NIBP monitoring.

Balanced anesthesia was used, combination of sevoflurane, fentanyl 5 µg followed by another 5 µg rocuronium (3 mg initially then 2 mg.h-1). Mechanical ventilation was maintained by pressure support mode using RR 30 per minutes.

Through 4th intercostal space (Fig 3) and after meticulous dissection from the great vessels and trachea, a cystic mass was completely excised. Lung expansion was synchronized with the movements of the surgeon, and there was no complication with minimal blood loss of 10 ml.

During the progress of surgical excision of the mass (Fig. 4), an increasing airway pressure and hypoxia were noted: oxygen saturation dropping to 60-75% on two occasions that necessitated interruption of surgery, managed by using manual ventilation in the first occasion, and on second occasion by ETT
suction which resulted in some thick mucus secretions blocking the airway. This was followed by a dramatic increase oxygen saturation up to 96% and maintaining meanwhile, normocapnia. In addition, during surgical traction on the mass tachycardia and decrease in blood pressure were noted, mostly related to compression on major blood vessels. That was well managed well with bolus of fluid plus the maintained fluid at 25ml/h, with urine output 2 ml/kg/h.

Following surgery the patient was send back to NICU, intubated and ventilated with stable hemodynamics: BP 85/40 mmHg and 140 b.p.m., \(\text{SpO}_2\) 96%.

Pathology revealed a lobulated 6 x 6 cm, 78 g mass. Histology confirmed an encapsulated immature cystic teratoma with muscle and cartilage, and primitive neuroepithelium with no malignancy (Fig. 5).

Up to 14\textsuperscript{th} postoperative day, there were two incidences of failure to ETT extubation, one week apart. This raised a high suspicion of a pressure effect of this huge mass which can lead to tracheomalacia. Diagnostic Rigid bronchoscope (3 mm) was done at day 16. It showed normal tracheobronchial patency with no evidence of tracheomalacia. A decision was made to ETT extubation in O.R. under observation. The oxygen saturation was well maintained by nasal cannula oxygen support, and patient was sent back to NICU, where he initially was maintained on nasal CPAP, then to room air within 4 days. The baby tolerated full oral feeding, and was discharged home on the 28\textsuperscript{th} day of life.

He is currently followed-up in Pediatric Oncology, Neonatology Clinic, Pediatric surgery Clinic for more than one year. He gained weight, doing well and is free of symptoms.

\textbf{Discussion}

In infants and children, mediastinal teratomas are uncommon, constituting 7 to 10\% of all teratomas\textsuperscript{1,2} In newborns, however, immature teratomas are rare and constitute less than 1\% of all mediastinal teratomas.

This case of MT was presented at birth with respiratory distress and without fetal diagnosis. It was fully investigated until the diagnosis of anterior mediastinal teratoma was established.

Two reported series from Middle East tackled this issue but one included a neonatal MT\textsuperscript{3}, and another exclusively MT analysis in patients ranging 5-56 years of age with a mean age of 29 years;10 females and 4 males\textsuperscript{4}. Imaging plays a very major role in the pre-
operative diagnosis of these conditions and proper pre-operative resuscitation dramatically improves the outcome of surgery. This holds true in the absence of antenatal intrauterine fetal diagnosis or immediate postpartum surgery.

The credit for the successful outcome of this case is the role played by the modern medical imaging in the diagnosis, surgical, anesthesia and neonatal intensive care modern advances.

References
ACUTE NORMOVOLEMIC HEMODILUTION IN SICKLE CELL PATIENT

- A Case Report -

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Abstract

Sickle cell disease patients with relatively high hemoglobin (≥12 g/dl) and those who have elevated alloimmunizations antibodies with rare phenotype subgroups, are problems challenging anesthesiologists. Acute Normovolemic Hemodilution (ANH) is rarely used in the perioperative management of homozygous sickle cell disease (SCD) in patients undergoing surgery. We hereby present a case in which ANH was used successfully.

A 22 year old male patient with known homozygous sickle cell disease undergoing orthopedic surgery, underwent Acute Normovolemic Hemodilution (ANH) because of the absence of blood and suitable blood donors and high hemoglobin level. Just before establishing spinal anesthesia, a 400 ml blood was extracted from patient and then replaced by 6% Hydroxyethylstarch HES solution. The surgery was performed uneventfully under spinal analgesia. Patient was discharged 48 hours later. A week later, his follow up visit showed no complications and his lab work returned to basic levels.

We recommend the ANH technique as an on hand tool in the perioperative anesthetic management of sickle cell disease patients who have high Hb S with relatively high Hb levels, and in those special patients who have no blood available because of high alloimmunization antibodies or rare phenotype blood groups.

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Introduction

Sickle cell anemia is one of the main hemoglobin disorders responsible for anemia requiring blood transfusion therapy in the Eastern Province of Saudi Arabia.

We report a case of a homozygous sickle cell-beta thalassemia disease scheduled for an orthopedic surgery who had undergone an Acute Normovolemic Hemodilution (ANH) technique.

Sickle cell disease patients with relatively high hemoglobin (≥12 g.dl) with unavailable blood, and those patients who have elevated alloimmunization antibodies with rare phenotype subgroups, pose challenging problems to the anesthesiologist.

The conundrum presented here is the use of ANH in a sickle cell patient with high Hb S and relatively high Hb levels, when no blood is available.

Case Report

A 22 year old male scheduled for intra medullary femur nail removal and with a history of homozygous sickle cell disease-Beta thalassamia, had a mild course of the disease (few painful attacks, two hospital admissions for non sickle cell complication and had not received any blood transfusion previously) His preop. CBC revealed Hb 12.7 gm %, Hct 34.8%, hemoglobin electrophoresis of Hb S 76.5, HbF 15.4 and Hb A2 4.8 and blood group of B positive. Blood and suitable donors were both unavailable as reported by the Blood Bank.

After consultation with the surgeon and explaining the technique of ANH to the patient and obtaining his informed written consent, the decision was taken to go ahead with the intraoperative ANH, the aim being to reduce the viscosity to a hematocrit level of nearly 30 %, and later to restransfuse the autologous blood previously obtained, by the end of surgery.

To estimate the allowable hemodilution required, the allowable blood phlebotomy (ABP) was calculated in accordance to the Bourke & Smith equation:

\[
\text{ABP} = \frac{\text{Estimated blood volume} \times (H_o - H_r)}{Htm}
\]

\[H_o = \text{hematocrit at time of operation}\]

\[H_r = \text{recommended hematocrit}\]

\[Htm = \text{mean of hematocrit} (H_o + H_r)/2\]

The calculated ABP in our patient turned out to be 450 ml. 400 ml was of autologous blood was therefore collected in a bag, labeled, signed showing patient’s name, medical record number and autologous blood label attached, was kept inside the OR at normal room temperature. 500 ml 6 % Hydroxymethylstarch HES solution then replaced the autologous blood. Meanwhile 1000 ml L/R solution was started as a preload before spinal analgesia was commenced, Following optimization of patient’s condition with warm IV fluid, face mask oxygenation at 4 L/min and thermal blanket, a successful spinal analgesia was performed at L 3-4 interspinous space, using 12.5 mg of heavy marcaine with 25 ug fentanyl.

The procedure passed uneventfully with stable CV parameters and oxygen saturation. Ephedrine 10 mg IV was administered to treat mild hypotension which had occurred subsequent to the spinal analgesia. The estimated blood loss was around 300 ml. By the end of surgery, the previously collected autologous blood was administered slowly. Postoperatively, there was good oxygenation and monitoring parameters. Patient was discharged in good condition 48 hours later. A cell-phone contact was maintained around the hour. A week later, the follow up visit showed no complications and his lab work returned to basic levels.

Discussion

Sickle cell anemia and thalassemia major are the main hemoglobin disorders responsible for anemia that requires regular blood transfusion therapy in the Eastern Province of Saudi Arabia. The perioperative management of sickle cell patients is a conundrum between aggressive intervention and therapeutic nihilism, with little scientific data to support any approach.3.

Partial exchange transfusion is highly indicated for patients with high Hb S and relatively high hemoglobin and hematocrit levels for the purpose of improving their oxygen carrying capacity and decreasing the incidence and frequency of sickle crisis.

The simple allogenic blood transfusion increases the risk of disease transmission, transfusion reaction,
reduces immunity and increase viscosity\textsuperscript{4,5}. However, the autologous blood transfusion decreases transfusion in patients undergoing elective procedures\textsuperscript{6}.

The entertained management must be carefully discussed with the patient, explaining the benefits of ANH and the adverse events of allogenic blood transfusion that may possibly occur.

Few publications\textsuperscript{7-11} have reported good conditions on transfusing autologous sickle blood, allowing good lab results (Fig. 3, Table 1) with minimum blood loss during surgery. The work supported by Weiskop\textsuperscript{12} encouraged us to use autologous blood transfusion in this case. Contrary to our management, however, Shulman et al\textsuperscript{13}, exchanged one-volume whole blood

\begin{table}[h]
\centering
\caption{Perioperative Laboratory Data}
\begin{tabular}{|l|c|c|c|}
\hline
Parameter & Preoperative & Post ANH & 24 hours Postoperative \\
\hline
Rectic count & 5.6 & 6.0 & 5.0 \\
NR (0.7-2.5\%) & & & \\
Hb level (gm.dl) & 12.3 & 11.0 & 10.9 \\
Hct & 37.8 & 34.3 & 33.8 \\
PT (11-14 sec) & 11.1 & 13.6 & 12.5 \\
Control 12.1 sec & & & \\
aPTT (25-38 sec) & 29.9 & 37.6 & 28.9 \\
Control 32.0 sec & & & \\
\hline
\end{tabular}
\end{table}

\textsuperscript{aPTT} = activated partial thromboplastin time  \\
Hb = hemoglobin  \\
Hct = hematocrit  \\
PT = Prothrombin Time  \\
NR = Normal range

\textbf{Fig. 3}

\textit{Hemoglobin Electrophoresis shows perioperative stability}
after initial partial exchange transfusion before initiation of CPB.

Most sickle cell anemia patients undergo transfusion therapy in order to prevent complications. Despite its efficacy, transfusion therapy is limited by its alloimmunization\textsuperscript{14}.

On the medical side, sickle cell disease patients scheduled for surgical procedure, can have their hemoglobin level increased by the use of iron rich food, and oral iron supplements etc.. The improved Hct level will facilitate ANH to be done by the anesthesiologist.

To our knowledge after literature search, our case was the first homozygous sickle cell patient who underwent ANH uneventfully. We emphasize ANH as a convenient tool in the perioperative anesthetic management of homozygous sickle cell patients who have high Hb S and relatively high Hb levels.

The technique of ANH opens a new door optimization of patient’s condition, reduction of transfusion of allogenic blood not only in sickle cell patients, but also in those patients who have no blood available because of high alloimmunization antibodies or have rare phenotype blood groups. It is essential that assessment of the benefit-ratio of the management be made very clear to the patient.

The present single case though successful, brings out the need to a prospective double-blinded randomized study on sickle cell disease patients, to prove the benefits of ANH technique.

References
INTRA-OPERATIVE EPIDURAL CATHETER MIGRATION INTO SUBARACHNOID SPACE LEADING TO MASSIVE SUBARACHNOID INJECTION OF MORPHINE

-A Case Report-

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Introduction

Epidural catheter (EC) migration is well documented entity in literature. However, most of these reports are consistent with introduction of Tuohy needle, either partially or completely, into intravascular, subdural and subarachnoid spaces prior to the placement of catheter. We report an intra-operative delayed migration of epidural catheter into subarachnoid space after apparently normal needle placement and negative test dose.

Key words: Subarachnoid, Epidural, Test dose

Case Report

Austin Moore prosthesis insertion was planned under combined spinal epidural anesthesia (CSE) technique in a 78 year old man with a fracture neck of right femur. Epidural catheter (EC) insertion technique consisted of right lateral position and midline approach at L3-4 interspace. Epidural space was identified on first attempt with 18G Tuohy needle (Portex) by loss of resistance to saline technique. Subarachnoid block (SAB) was done with 27G Whitacre needle via needle through needle technique and 8.75 mg of hyperbaric bupivacaine with 25 µg of fentanyl was injected.

A multi-orifice EC was introduced 5 cm into the epidural space and secured with adhesive dressing at 10 cm mark after negative aspiration for blood and CSF.
Patient was turned left lateral after attaining T₈ sensory block and surgery was started. Block regressed to T₁₀ level after 70 minutes. Epidural test dose was given after negative aspiration for CSF and it was negative. At this juncture, surgeon started hammering the prosthesis. Epidural top up was withheld to prevent hypotension which follows application bone cement (polymethyl methacrylate). Surgeons finished fixation of prosthesis by 20 minutes. The block by that time regressed to T₁₁ level and bupivacaine 0.25% 10 ml with 3 mg morphine was injected through EC.

The BP immediately dropped to 60/40 mmHg from 110/60 mmHg and HR sank to 38/min. Patient was resuscitated with intravenous 0.5L ringer lactate, 0.5 L 6% hydroxy ethyl starch, mephentermine boluses and atropine. Level of block was noted up to T₉. The EC aspiration resulted in a free fluid with some difficulty, and the fluid was confirmed to be CSF by the presence of precipitation with thiopentone and glucose estimation. EC was noted to have migrated inwards by less than 0.5 cm with 11 cm mark visible outside. EC was removed and patient was shifted to high dependency unit.

As expected, patient became increasingly drowsy with drop of respiratory rate to 8/min and oxygen saturation to 88%. Naloxone infusion was started at the rate of 1 µg/kg/hr after bolus of 200 µg to which patient responded with improved sensorium and saturation. Naloxone infusion continued for next 24 hours. Rest of the post-operative course was uneventful.

Discussion

Migration of EC into intravascular, subdural and subarachnoid spaces is of common clinical occurrence with incidence showing wide variation between 21 to 43%1-3. It is considered clinically significant if movement is more than 1 cm into the space or 2 cm outwards2,3. Intravascular and subarachnoid migration can have catastrophic consequences, whereas many failures have been attributed to outward migration1-3,4. An appropriate fixation technique such as subcutaneous tunneling2, suturing4, adhesive devices and Lockit EC clamp3,6 have been used to reduce its incidence.

Routine test dose of 60 mg lignocaine with 15 µg of epinephrine does not always ensure correct placement as in our case and each dose should be considered as a test dose given in increments7. In our experience, interpretation of an epidural test dose can be sometimes difficult when CSE is performed by needle through needle technique. As SAB is done prior to insertion of EC, subarachnoid placement cannot be ruled out by a standard test dose unless anesthesiologist is very careful about sensory block level. It is almost impossible to detect a subdural placement because a subdural block and receding SAB share common characteristics. This problem does not arise if SAB is done after epidural catheter insertion by an epidural needle with side to side or double space approach.

Hypotheses such as sub-atmospheric pressure in epidural space exaggerated by movement/ respiration and gripping action by ligamentum flavum propelling the catheter inwards as patients straighten their backs from the flexed position, have been used to explain catheter migration8,9. In our patient there is a probability of catheter migration during hammering of prosthesis as aspiration and test dose were negative before that. The other factor supporting this hypothesis is the fact that catheter moved less than 0.5 cm which is clinically insignificant. Considering the fact that EC cannot penetrate an intact dura10 the EC in our patient was most probably placed in subdural space during insertion which migrated to subarachnoid space during prosthesis insertion.

As there is no full proof method to diagnose or prevent SA migration of EC, we omit morphine while administering drugs through EC for the first time and prefer to use local anesthetics at highest concentration possible to achieve surgical anesthesia. Once SA migration is clinically ruled out by the first epidural dose, we proceed to inject morphine either with first top up or in between.

Conclusion

Epidural catheter may migrate into subarachnoid space in the intra-operative course of event even if test dose and aspiration were negative. It may be advisable to omit morphine from first epidural dose to avoid massive subarachnoid administration of morphine.
References

Correct placement of epidural catheter has always been an enigma with varying degrees of success rates even in experienced hands owing to the blind nature of this procedure. We advice a simple test which can improve specificity and success rate in placing epidural catheter without using advanced gadgets.

After localizing the epidural space by loss of resistance or hanging drop technique, the catheter is inserted 5 cm into the epidural space, Touhy’s needle is removed and the following test performed in a stepwise fashion:

1) Negative aspiration is done to rule out intravascular or intrathecal placement of catheter.

2) The catheter is primed with 2 ml of 0.9% normal saline and catheter port splashed to get rid of excess saline. Next, the catheter is raised vertically at the level of mid-scapula in a sitting patient or approximately 1 foot above the level of insertion in a laterally positioned patient. If the catheter tip is positioned epidurally the fluid column will fall in a manner similar to CVP manometer.

3) During the fall of fluid column the patient is asked to cough voluntarily. While coughing the meniscus first halts, rises abruptly by 2-3 mm and then falls again. This occurs due to transmission of intrathoracic pressure into epidural space through valveless venous communications between intercostal and epidural veins.

4) If the catheter is now lowered below the level of insertion, the fluid column will start rising due to fluid moving out of epidural space followed by bubbles of air.

This free fall and rise of fluid level will not occur if the catheter is placed outside the epidural space, in an epidural vein or intrathecally. In the latter two circumstances the fluid level will continue to rise due to egression of blood or CSF seen at lower end of catheter.

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The changes in fluid level associated with catheter raising or coughing reflect free communication between epidural space and catheter and rules out misplacement or kinking of catheter. The above test barely takes two minutes to perform without using any additional equipment. The above technique has been described earlier in literature except the coughing test (step 3) which was our incidental observation in a patient coughing on O.T. table during the procedure\textsuperscript{1,2}.

In an event of inadvertent dural puncture, localize a cephalad epidural space, perform negative aspiration until air bubbles appear in catheter followed by cough test to confirm epidural placement. Though the chances of false negative results (i.e. catheter in epidural space but does not seems to be there) are higher in this scenario due to loss of negative pressure of epidural space from leaking CSF, a violent coughing will still evoke pressure changes in epidural space and catheter fluid column.

The disadvantage of this technique is that it requires an awake and cooperative patient for stepwise assessment and is difficult to perform in pediatric patients. Moreover it cannot confirm the level of catheter tip placement as compared to specific muscle group contraction done by electrical stimulation test\textsuperscript{3,4}.

At our centre we have used this technique successfully in 50 patients with only two failures where the effect was patchy and delayed, probably due to migration of catheter anteriorly in epidural space.

We recommend using this simple technique routinely in clinical practice. It can be really helpful in patients with anticipated difficult epidural procedure (e.g. obesity) where correct catheter tip placement is sometimes confirmed only after achieving the effect.

References

UNILATERAL SPINAL ANESTHESIA COMBINED WITH LOCAL ANESTHESIA FOR PTOSIS SURGERY

D YUKSEL1, Y OFLU2, O CUVAS3 AND S DUMAN4

Frontal suspension surgery is the most common procedure for congenital blepharoptosis with poor levator muscle function. In view of long term cosmetic results, frontal suspension with autogenous fascia lata is a gold standard surgery1,2.

A 46-year-old patient with bilateral ptosis and poor levator function was scheduled for ptosis surgery. Frontal suspension surgery with autogenous fascia lata1,2 was planned under general anesthesia. Patient had a history of type-II diabetes mellitus and poor control of blood glucose level. He was a heavy smoker and had decreased breath sounds bilaterally on chest examination. We decided to perform unilateral spinal anesthesia instead of general anesthesia for harvesting of fascia lata3 due to patient’s systemic problems and reluctance to general anesthesia. Spinal anesthesia was performed at the L4-5 interspace using a 25 G Quincke needle with the patient placed in the lateral decubitis position and lying on the operated side. Two mL of 0.5% hyperbaric bupivacaine was injected. The patient’s position was maintained for 15 min after injection, then he was turned to supine and fascia lata graft was taken. Five mL of 1% lidocaine was infiltrated into the operative site in both eyes, and frontal suspension was performed by using Crawford technique under local anesthesia2.

Unilateral spinal block produces a more restricted spinal anesthesia and has less cardiovascular side effects when compared to bilateral spinal anesthesia4.

Anesthesiologists and ophthalmologists are not used to performing a central nerve block combined with local anesthesia for an ophthalmic surgery. On the other hand, dissection of fascia lata can be done by using unilateral spinal anesthesia in adult patients with risk for general anesthesia. By this way, complications due to general anesthesia are decreased and adjustment of lid level can be performed more accurately under local anesthesia.
References


ERRATUM

(a) In Vol. 20, No. 1, Feb. 2009, Article “Is I-Gel a new revolution among supraglottic airway devices? Page 53, Dr. Aslam Rizvi has been listed as MD, Resident. The correct status is DA, Resident (Diploma in Anaesthesiology).

(b) In Vol. 20, No. 2, June 2009, Article “Robotic laparoscopy radical cystectomy: Inhalational vs Total intravenous analgesia: Pilot Study” page 257-263, Table 3, page 260, heading of the first column “Growth hormone (mg/ml⁻¹), should read “Growth hormone ng/ml).

(c) In the following three articles (both under CONTENTS & REVIEW ARTICLES), published in Vol. 20, No. 2, June 2009, where Alan Kaye is listed as a co-author:

1. Anesthetic care of the patient with obstructive sleep apnea  p. 143
2. Current perioperative management of the patient with HIV p. 167
3. Modern strategies for the anesthetic management of the patient with Diabetes p. 187

The name Alan Kaye should read Alan D. Kaye
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