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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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“For some must watch, while some must sleep” 

(Hamlet-Act. III, Sc. ii)
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It is indeed a great pleasure for me to carry the Torch of learning and become the new forth Editor-In-Chief specially at the auspicious occasion of the launching of the February issue of Volume 20, No. 1, 2009, where new improvements have been implemented to promote our Journal its citation and readership.

Of the new improvements, I am happy to inform you that our Journal has become available electronically in the form of a link to the American University of Beirut (aub) which can be accessed at the following website www.aub.edu.lb/meja. Our projectional aspirations is to increase the Journal’s citation index and improve its impact factor. To archive the articles published back to year 2000 is also one of our projects.

For the past 42 years, the Journal has taken the shape of a book designed with the National Lebanese Flag. With the release of the February 2009 issue, however, the Journal appears in its new format and new design. The size of the Journal has now assumed international dimensions with double-column printing, a process designed to increase number of publications per issue while maintaining costs at reasonable levels. The cover design depicts the historical poppy flower, first planted in the Middle East, that has been and still is, used to ease the pain of mankind over the past millennia. The Cedar Tree depicts the Republic of Lebanon with its unique geographical location between East and west.

I would like to take this opportunity to welcome the New Editorial Board, a well certified and qualified group who will continue to work hard in promoting and improving the Journal to better and higher levels.

In accomplishments like this, one cannot but give credit and gratitude to the founder, Dr. Bernard Brandstater, (Professor and Chairman 1958-1969) and first Editor-In-Chief, (1966-1969) who back in June 1966, lit the Torch of learning, had the dream and early recognized the significance of creating a platform to encourage publication, research and exchange of opinions of colleagues widely scattered across the vast Middle East. With pride, pleasure and confidence, those dreams have not only become true, but over the years, through the dedicated efforts of succeeding Executive Editorial Boards and the contributors around the World, the Journal has become intercontinental.

I would also like to offer special thanks to Dr. Anis Baraka (Ex-Chairman and Professor of Department of Anesthesiology (1974-2008) and third Editor-In-chief (1978-2008) who was most instrumental in supporting, contributing and promoting the Journal internationally. I also congratulate him for his recent appointment to the position of Emeritus Professor of Anesthesiology, effective Jan. 2009, an honor well deserved.

Special appreciation is offered to Dr. Fouad Salim Haddad second Editor-In-Chief (1970-1978) and later as Executive Editor (1978-    ) for his incessant dedication to the Journal.

We take pride in having an affiliated Journal to our Department. We welcome all contributors and readers around the world and do appreciate their input, past and present, and hope for their continued support for many years to come.

In closing, the Middle East Journal of Anesthesiology (MEJA), a Torch of learning that has and is still fulfilling its objectives, has succeeded in putting Republic of Lebanon, the American University of Beirut and the Department of Anesthesiology, on the world map of anesthesia.

Ghassan E. Kanazi, MD, ABA
ABA Critical Care & Pain Medicine
Editor-In-Chief
Chairman and Associate Professor
Department of Anesthesiology
SIR ROBERT REYNOLDS MACINTOSH, 1897-1989
- The First Professor of Anaesthesia in UK -

Sir Robert Macintosh was the first holder of a full time University Chair of Anaesthesia in Britain. It is doubtful whether anyone has contributed so much to the basic principles underlying the safe practice of anesthesia.

Sir Robert Macintosh was nominated as the Chairman of the Nuffield Department of Anaesthesia in Oxford, founded in 1937. His theme of clinical and academic practice was based on the triad of science safety and simplicity. Those who came from every corner of the globe to study anesthesia in Oxford under the leadership of Sir Macintosh had learned the rational basic and essentially the practical approach to anesthesia which has characterized that Department from its earliest days. The love of Macintosh of clinical anesthesia and his drive for clear simple thinking, made learning opportunities under his Chairmanship both a delight and a privilege.

Sir Robert Macintosh was a quiet and very modest man, with a sparkling sense of humor, and was always supportive to the trainees and associates that worked in his Department. During his career, Macintosh published many books, and designed many equipments that had the greater impact on the practice of anesthesia. During our daily practice in the operating room, we must always remember Sir Robert Macintosh whenever we induce anesthesia, and use the Macintosh laryngoscopy blade for tracheal intubation.

Sir Robert Macintosh traveled all over the World to lecture and demonstrate anesthesia. We, in the Arab World, were honored when he accepted our invitation to visit Lebanon and Egypt. He traveled to our area in 1965 with his EMO (Epstein-Macintosh-Oxford) air-ether vaporizer and Oxford inflating bellows, when he demonstrated simple but safe anesthetic techniques based on the use of air-ether that could be used in any environment. During his visit to the American University of Beirut, Lebanon, aged 68 yrs, he enjoyed swimming in the Mediterranean sea and watching the fantastic Casino show. At the Casino gala dinner, Mrs. Fouad Salim Haddad was seated beside him, and she commented after dinner that it surprised her that the very modest man beside her was the great Sir Robert Macintosh.

At that time, I was a Faculty of the American University of Beirut, and was honored to escort Sir Robert Macintosh and share with him a cabin on a boat sailing from Beirut to Alexandria, Egypt (Fig. 1). Throughout this trip which lasted 24 hours, I was privileged to discuss with Sir Robert many subjects including the use of EMO air-ether vaporizer. However, I never thought at that time, that Lebanon, the Cedar land, which was considered Switzerland of the Middle East will be after 5 years the site of a tragic war that lasted 15 years, and that the EMO air-ether vaporizer of Macintosh will be our anesthetic apparatus during these tragic
events when we became short of oxygen and other anesthetic supplies (Fig. 2).

Fig. 1  
Dr. Anis Baraka and Sir Robert Macintosh

Fig. 2  
Dr. Anis Baraka using the EMO air-ether vaporizer for anesthesia during the tragic events in Lebanon

Sir Robert Macintosh died in Radcliffe Infirmary, Oxford on the 28th of August 1989, at the age of 91. We will never forget Sir Robert Macintosh, the symbol of modesty and the godfather of science, simplicity and safety of clinical anesthesia practice.

References


Anis Baraka, MD, FRCA (Hon)  
Emeritus Professor of Anesthesiology  
Emeritus Editor-in-Chief  
Middle East Journal of Anesthesiology
Needs Assessment

Clinical practice has changed over recent decades, especially in obstetrical care and in neonatal management. An appreciation of current guidelines physiological considerations, equipment modalities, and therapeutic interventions, is necessary to provide successful neonatal resuscitation.

Introduction

The transition from a fetus to a neonate involves complex changes in physiology. A delay in these adaptations can result in significant neonatal morbidity and mortality. In the United States, 10% of newborns require some assistance with breathing and about 1% require extensive ventilatory assistance. Furthermore, anesthesiologist’s practice in a spectrum of facilities with varying levels of care. Smaller practices or rural settings can limit consistent practices. Thus, it is vital for all clinical anesthesiologists and delivery room personnel to understand the physiological adaptation of the newborn, ensure proper preparation and maintenance of equipment (Table 1), perform an adequate risk assessment to predict possible resuscitative needs, and respond appropriately with resuscitation efforts.
resistance to flow on the pulmonary side of the circulatory system. As a result, a large portion of the right ventricular output is shunted across the ductus arteriosus bypassing the pulmonary circuit. Thus, the fetal lungs play no role in intrauterine gas exchange.1

In order for the neonate to assume the responsibility of extrauterine gas exchange, there has to be an elimination of fluid from the lungs, production of surfactant and stimulation of the respiratory center1. Compression of the thoracic cage during the passage through the birth canal lays a limited role in the removal of fetal lung fluid. On the other hand, sodium channels in alveolar epithelial cells are thought to play the main role in the elimination of fluid from the fetal lungs3. Their expression is largely regulated by developmental changes during the last few weeks of pregnancy and hormonal changes associated with labor. Reabsorption of sodium through the sodium channels creates an osmotic gradient leading to clearance of a large portion of fetal lung fluid. This process allows for air to fill the lungs and leads to the establishment of an air-fluid interface. The surfactant lining the alveoli reduces surface tension and prevents collapse of the alveoli. The maturation of alveoli and capillary networks along with surfactant production allows for the commencement of gas exchange1-3.

The process of spontaneous breathing begins with the initial stimulation of the respiratory center and further contributes to fetal adaptation to the outside environment1-2. Asphyxia, a collective term given to hypercapnea, respiratory acidosis and hypoxia, along with tactile and thermal stimuli associated with labor and delivery are believed to play a role in switching on the respiratory center1-2.

The initiation of ventilation and inflation of lung volumes contributes to an increased systemic vascular resistance, decreased pulmonary vascular resistance, increased arterial partial pressure of oxygen (PaO₂) and decreased partial pressure of carbon dioxide (PCO₂)1-2. Failure of any of these processes can result in neonatal problems such as transient tachypnea of newborn and respiratory distress2.

Cardiovascular Adaptations

As a result of low systemic vascular resistance in utero, 40% of cardiac output is received by the placenta.
and there is right to left shunting of blood across the foramen ovale and ductus arteriosus. Clamping of the umbilical cord significantly increases systemic vascular resistance and contributes to a functional closure of the foramen ovale within the first few minutes of birth. A left to right reversal of the shunt across the ductus arteriosus results. Because it takes days to weeks for the ductus arteriosus to anatomically close, there may be a right to left reversal of the shunt anytime pulmonary vascular resistance rises above systemic. Several states can predispose the infant to this reversal during this “transitional phase”. Conditions such as meconium aspirations can result in a more persistent fetal circulation.

Metabolic Adaptations

In utero, the fetus depends on a continuous supply of glucose from the placenta. Around 36 weeks gestational age there is a rapid increase in the amount of glycogen stores. The onset of labor causes a surge in adrenaline, noradrenaline and glucagon and a decrease in insulin allowing for mobilization of the glycogen stores. These stores can be depleted more quickly if demand is high. As a result, an inadequate supply of available glucose substrate can lead to hypoglycemia.

Thermoregulation

Intrauterine temperature regulation is a passive process requiring no energy expenditure on the part of the fetus. In utero, thermoregulation depends upon maternal transfer of heat via the placenta and uterus. Therefore, transitioning to the outside world poses a serious problem to the neonate in regards to regulating body temperature. At birth, in addition to being cold and wet, neonates have thin skin, a high body surface area to mass ratio, limited insulation and metabolic reserves and an inability to shiver. As a result, the temperature drops suddenly after birth.

In order to survive in the extrauterine environment, one important physiological adaptation newborns have in place is the ability to rapidly increase body temperature by non-shivering thermogenesis (NST), which is initiated minutes after birth. NST is an oxygen dependent process that relies on an uncoupling protein specific to brown adipose tissue. Prior to birth, inhibitors of non-shivering thermogenesis, mainly adenosine and prostaglandin E2, allow the fetus to accumulate a sufficient amount of brown adipose tissue. After birth the presence of brown adipose specific uncoupling protein allows for heat production by uncoupling ATP synthesis in the mitochondria during fatty acid oxidation.

Thus, a distressed newborn with hypoxemia is unable to produce a sufficient amount of heat because the decreased PaO2 results in reduced nonshivering thermogenesis. Common practice in the care of newborns stresses they be kept dry and warm at birth. Hypothermia increases metabolic rate resulting in increased oxygen and energy consumption. Cold stress can also cause a shift from aerobic to anaerobic metabolism resulting in further tissue hypoxia and metabolic acidosis. Finally, prolonged hypoxemia and metabolic acidosis can cause persistent pulmonary hypertension and is one example of transitional circulation returning the infant to its previous fetal circulation and increasing hypoxia. Therefore, preventing excessive heat loss is vital in neonatal resuscitation especially if there is respiratory compromise.

Risk Assessment

The anticipation of resuscitative needs can be determined by performing a thorough assessment of risk. By evaluating maternal and fetal risk factors in addition to intrapartum and postpartum events, the need for resuscitation can be identified in more than half of all neonates. There are several methods used to evaluate fetal well being during the intrapartum period. The primary purpose of these methods is to detect hypoxic ischemia in the fetus, which can result in significant morbidity and mortality in the neonate. Thus, information gathered from the intrapartum assessment can be utilized to determine the possible need for resuscitative measures.

Fetal Heart Rate Monitoring

There are two commonly used methods for assessing intrapartum fetal heart rate: continuous electronic fetal heart rate monitoring (EFM) and intermittent auscultation (IA). The latter form is more tedious for nursing staff and used in some centers for low risk pregnancies. Electronic fetal heart monitoring, which records fetal heart rate changes relative to
Acoustic stimulation is a less invasive alternative whereby an electronic device placed on the mother’s abdomen sends sounds to the baby. In either situation, if the fetal heart rate increases to greater than 15 beat per minute above baseline for more than 15 minutes, a pH of 7.20 is likely.

**Biophysical Profile Score**

Studies have shown some benefit in using the Biophysical Profile Score in conjunction with non-reassuring fetal heart rate monitoring. Biophysical profile score provides a direct and accurate measure of normal tissue oxygenation by combining sonographic assessments of (1) fetal breathing movements, (2) heart rate reactivity, (3) gross body movements and (4) fetal tone with (5) amniotic fluid volume. Each parameter is given a score of 0 (if criteria are not met) or 2 (if criteria are met) with 0/0 being the lowest attainable score and 10/10 being the highest. A score of >8 out of 10 indicates normal tissue oxygenation, a score of 0-4 out of 10 suggests significant acidemia and a high risk of asphyxia within one week if there is not intervention. A score of 6 out of 10 is equivocal and

### Table 2
The five criteria of the APGAR score

<table>
<thead>
<tr>
<th>Score:</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance (skin color)</td>
<td>blue (whole body)</td>
<td>blue extremities, pink body</td>
<td>normal</td>
</tr>
<tr>
<td>Pulse (heart rate)</td>
<td>absent</td>
<td>&lt;100 bpm</td>
<td>&gt;100 bpm</td>
</tr>
<tr>
<td>Grimace (irritability)</td>
<td>no response to stimulation</td>
<td>grimace or weak cry</td>
<td>sneeze/cough/pulls away</td>
</tr>
<tr>
<td>Activity (muscle tone)</td>
<td>no movement</td>
<td>some flexion at joints</td>
<td>full body movement</td>
</tr>
<tr>
<td>Respiration</td>
<td>absent</td>
<td>weak/irregular</td>
<td>strong</td>
</tr>
</tbody>
</table>

Adapted from: Manning FA. Fetal biophysical profile. *UpTo Date* 15.3. May 3, 2006.

### Table 3
Biophysical Profile Tests and Criteria

<table>
<thead>
<tr>
<th>Biophysical Profile Test</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(0 points for any criteria not met)</td>
</tr>
<tr>
<td>Nonstress Test</td>
<td>2 points if reactive</td>
</tr>
<tr>
<td>Fetal Breathing Movements</td>
<td>2 points if one or more episodes of rhythmic breathing for greater than 20 seconds within a 30 minute period</td>
</tr>
<tr>
<td>Fetal Tone</td>
<td>2 points for one or more episodes of extension of extremities or spine with subsequent return to flexion</td>
</tr>
<tr>
<td>Amniotic fluid volume</td>
<td>2 points if a single pocket of fluid measures greater than 2 cm in vertical axis</td>
</tr>
<tr>
<td>Fetal Ultrasound</td>
<td>2 points for two or more discrete body or limb movements in 30 minutes</td>
</tr>
</tbody>
</table>
should be closely evaluated in the context of amniotic fluid volume (Table 3).

**Fetal Pulse Oximetry**

Fetal pulse oximetry is another method currently used for intrapartum fetal assessment in the presence of non-reassuring fetal heart pattern. Three systems have been developed for commercial use. The OB Scientific sensor is shaped like a tongue depressor and can be placed along the fetal torso during a vaginal exam, with or without rupture of the membranes. Nonin Medical system incorporates the pulse oximeter into the fetal scalp electrode. Finally, the Nellcor sensor is directed to lie against the fetal temple or cheek after rupture of the membranes. A fetal SpO₂ >30%, which is the oxygen saturation above which acidosis is unlikely to occur, can be considered reassuring while a SpO₂ <30% may be associated with acidosis. If SpO₂ <30% persist longer than 10 minutes, this may predict a scalp pH of 7.20 less and demand the need for intruterine resuscitation or expedited delivery.

**Fetal Scalp pH and Umbilical Cord Blood Gas**

The fetal scalp pH and umbilical cord blood gas analysis are two methods used to determine fetal acid base status. A fetal scalp pH <7.2 for two consecutive readings indicates significant fetal distress and imminent need for delivery. In the United States, the use of fetal scalp sampling has declined and is not available in many obstetrical departments, primarily due to technical difficulties in performing the procedure and other inherent limitations.

On the other hand, umbilical cord blood gas analysis is considered to be the gold standard for evaluating fetal acid base status and uteroplacental function. It measures values for pH, pCO₂ and base excess from the umbilical artery and vein. The umbilical artery depicts fetal and immediate neonatal acid base status while the umbilical vein depicts maternal status. The umbilical artery base excess is considered to be the most direct measure of fetal metabolic status. A base excess greater than –12 mmol L⁻¹ and a pH <7.10 suggests significant metabolic acidosis and is a sign of fetal compromise. With a pH of less than 7.10 there is an increased risk of intracranial hemorrhage, seizures, respiratory distress syndrome and death.

**Fetal Doppler Ultrasound Study**

The Doppler ultrasound study is a method for evaluating fetal well being often used in conjunction with the BPP score. Fetal Doppler studies utilize the flow velocity waveforms and pulsatility indices as diagnostic and prognostic evaluators of fetal adaptation. There are four main types of Doppler studies used to evaluate maternal, fetal and placental circulation. Uterine artery Doppler is often used in the second trimester to assess the effect of maternal circulation on the fetus. Information gathered can be useful in predicting pre-eclampsia and intrauterine growth retardation. The umbilical artery Doppler assesses the effects on placenta deficiency on multiple organ systems in the fetus in addition to intrauterine growth retardation. If abnormal flow is detected, further evaluation of fetal systemic circulation with either middle cerebral artery or ductus venosus Doppler studies is warranted. In response to hypoxia, the middle cerebral arteries dilate to preserve flow to the brain, “brain sparing effect”. Loss of the brain sparing effect seen as reduced middle cerebral artery flow on the Doppler, signifies a critical event and can result in fetal demise. Doppler of the ductus venosus is used to predict right heart failure in the hypoxic fetus. Therefore, reversal of flow in the ductus venosus Doppler is often seen as an ominous sign.

**Effects of Maternal Drugs on Neonate**

**Regional anesthesia**

Regional anesthetic techniques such as epidurals, spinals and combined epidural–spinals are the preferred methods of providing labor analgesia and anesthesia for cesarean sections. Although these methods provide excellent pain control with limited exposure of the fetus to drugs, there are still some concerns associated with their use.

Due to temporary sympathectomy caused by the anesthetic, a transient period of mild maternal hypotension is relatively commonly associated with regional analgesia. However, prolonged severe maternal hypotension often results in significant impairment in uteroplacental perfusion and places the infant at risk.
to acidemia\textsuperscript{16}. Therefore, efforts should be made to prevent maternal hypotension such as placement in the left lateral position (to reduce aortocaval compression), utilizing lower leg compressive stocking, and intravenous fluid loading\textsuperscript{15}.

Ephedrine and phenylephrine are currently the drugs of choice to treat maternal hypotension\textsuperscript{15}. Ephedrine is the drug most commonly used and is often associated with fetal tachycardia and fetal acidosis. The prophylactic use of ephedrine does not reliably prevent maternal hypotension and should be reserved for treatment. For maternal patients with significant cardiac disease, phenylephrine is the drug of choice. Also, phenylephrine is associated with lower catecholamine concentration in the neonate and improved acid base status in comparison to ephedrine\textsuperscript{15}.

**Systemic Drugs**

Although the use of epidural analgesia and combined spinal-epidural techniques are increasingly used as methods of pain control in labor, systemic medications such as opioids are still widely used\textsuperscript{15}. The initial effect of opioids seen during the intrapartum period is decreased fetal heart rate variability and decreased gross fetal movements\textsuperscript{16}. The effects of their use during the postpartum period include neonatal respiratory depression and decreased alertness, reversible with naloxone.

Meperidine is a commonly used systemic opioid in labor analgesia worldwide\textsuperscript{15,16}. Babies at the greatest risk of respiratory depression are those born within one to five hours after meperidine is given. Additionally, those born to mothers who received multiple doses of meperidine are also at increased risk. Repetitive administration of meperidine results in an accumulation of its metabolite, normeperidine, in both the mother and fetus. Normeperidine is associated with seizures and depressed respiratory status in neonates that is not reversed by naloxone\textsuperscript{16}.

**General Anesthesia**

General anesthesia is still used for cesarean sections in special situations when regional techniques are contraindicated as in coagulopathies, severe maternal hemorrhage, hypotension, or in failure of the regional anesthetic, and severe fetal distress when there is no time to perform a regional technique\textsuperscript{15}. An important aspect related to neonatal outcome associated with general anesthesia is the time between the induction of anesthesia and delivery time\textsuperscript{15,16}. This represents the total time of fetal exposure to maternally administered medication and is associated with lower Apgar scores (Table 2) and increase in the base deficit (i.e. neonatal acidosis). An additional factor is time from uterine incision to delivery of the baby. The longer the incision to delivery time the greater the likelihood of fetal asphyxia leading to respiratory depression. In order to prevent these complications, the induction to clamp time should be less than ten minutes and the uterine incision to delivery time should be less than three minutes\textsuperscript{15}. In a crisis situation where the mother cannot be intubated or ventilated, a cesarean section under local anesthesia should be considered.

Additionally, though the mechanism is thought to be linked to serum cortisol suppression, the use of etomidate as an induction agent in mothers undergoing cesarean sections is associated with neonatal hypoglycemia\textsuperscript{15}. Therefore, close monitoring of the neonate’s glucose is warranted. It should be noted that inhalational agents have a reduced minimum alveolar concentration in pregnancy as well as in the neonate. All of the common utilized inhalational agents, e.g. desflurane, sevoflurane, and isoflurane, have been used successfully in both pregnancy and in neonates.

**Overview of Steps of Neonatal Resuscitation**

Neonates born at term, who have clear amniotic fluid with no signs of meconium, are actively breathing and crying and have muscle tone require routine care, including drying, providing warmth and clearing the airways by simply wiping with a towel\textsuperscript{12,14}. One the other hand, neonates not meeting these requirements should be assessed for the initial steps of resuscitation. An Apgar score at different time periods post delivery is particularly useful and is common practice in many parts of the world.

The sequences of steps involved in neonatal resuscitation are (1) initial steps in stabilization, (2) ventilation, (3) chest compression, and (4) medications\textsuperscript{12,14}. Each step is allowed 30 seconds for completion\textsuperscript{12}. The decision to progress to the next category is based on the cumulative assessment of
respirations, heart rate and color. For example, gasping
and apnea may serve as an indication for assisted
ventilation. Increasing or decreasing heart rate may
suggest an improvement or worsening in overall
condition. Finally, central cyanosis may serve as an
indication of decreased cardiac output, hypothermia,
acidosis or hypovolemia necessitating further
resuscitative efforts13 (Figure 1).

**Provide warmth**

Thermoregulation is a critical component of the
initial resuscitative effort. This can be accomplished
by simply placing the neonate under a radiant
warmer. The infant should be uncovered to allow
for full visualization and adequate heat transference.
Thermoregulation is particularly important in very low
birth weight preterm infants12. Infants weighting less
than 1500 grams are placed at a significantly increased
risk of hypothermia. Thus, it is recommended that the
infant be covered in plastic wrapping in addition to
being placed under a radiant warmer.

There has been some concern about hyperthermia,
particularly in infants born to febrile mothers, resulting
in respiratory depression, seizures and cerebral
injury2. Therefore, the goal in neonatal resuscitation is
to achieve normothermia by adequately monitoring the
temperature, thus avoiding iatrogenic hyperthermia12.

**Position Head and Clear Airways**

Once the neonate has been placed underneath
a radiant warmer, the baby should be positioned on
the back or side with the neck slightly extended in
a “sniffing position”14. Then, the airway should be
cleared as determined by whether or not meconium
is present. If meconium is not present, simple wiping
the nose and mouth with a towel or suctioning with
a bulb syringe or suction catheter is appropriate. It is
important to remember to suction the mouth prior to
the nose to ensure that there is nothing present in the
mouth that would cause the neonate to aspirate. Also,
it is important to avoid vigorous or deep suctioning
to prevent a severe vagal response which can lead to
bradycardia or apnea14.

If meconium is present but the baby is vigorous,
as defined by a heart rate greater than 100 beats per
minute, appropriate respiratory effort and muscle tone,
simply suctioning the mouth and nose with a bulb
syringe or large bore suction catheter is appropriate14.

Severe aspiration pneumonia can be a sequela of
meconium aspiration before delivery, during birth or
during resuscitation11. Therefore, if meconium is present
and the infant shows poor respiratory effort and muscle
tone and has a heart rate less than 100 beats per minute,
direct suctioning of the trachea is recommended and

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American Heart Association (AHA) Guidelines for
Cardiopulmonary Resuscitation (CPR) and Emergency
Cardiovascular Care (ECC) of Pediatric and Neonatal Patients:
Neonatal Resuscitation Guidelines American Heart Association,
American Academy of Pediatrics Pediatrics 2006; 117; e 1029-e
1038 DOI: 10.1542/peds. 2006-0349.

**Initiation of Resuscitation**

The initial steps in stabilizing the neonate
involves minimizing heat loss, positioning the head
in “sniffing” position to open the airway, clearing the
airways, and stimulating the infant12.
should occur immediately following birth. This is done by performing direct laryngoscopy and inserting a 12 French (F) or 14 F suction catheter to clear the mouth and posterior pharynx, followed by insertion of an endotracheal tube, then attaching the tube to a suction source and slowly withdrawing the tube as suction is applied. This latter step should be repeated until either very little meconium is recovered or a need to proceed with resuscitative efforts is dictated by the heart rate.

**Dry and Stimulate Baby**

Once the airway is cleared the neonate should be dried thoroughly to prevent further heat loss and then repositioned. If the neonate still does not have appropriate respiratory effort, additional tactile stimulation in the form of gently slapping or flicking the soles of the feet or gently rubbing the newborn’s trunk and extremities can be performed. It is important to note that if the newborn has primary apnea (e.g. when asphyxiated, an infant responds with an increased respiratory rate) any form of stimulation will stimulate breathing. However, if the neonate has secondary apnea (e.g. when asphyxia is allowed to continue after primary apnea) the infant responds with a period a gasping respirations, falling heart rate, and falling blood pressure. The infant takes a last breath and then enters the secondary apnea period. The infant will not respond to stimulation and death will occur unless resuscitation begins immediately and no form of stimulation will trigger the baby’s respiratory effort and positive pressure ventilation should be initiated immediately13.

**Evaluate Respiration, heart rate and color**

Finally, the last step in the initial resuscitative efforts involves an evaluation of respiration, heart rate and color14. The neonate should have good chest movements and should not be gasping. Gasping is indicative of ineffective respiratory effort and requires the use of positive pressure ventilation. Additionally, the heart rate should be greater than 100 beats per minute (bpm), determined by feeling for a pulse around the umbilical cord or auscultating the left chest wall. If the heart rate is less than 100 bpm, positive pressure ventilation should be administered. Finally, color should be assessed by looking at the neonate’s lips and trunk for signs of central cyanosis. Central cyanosis indicates hypoxemia and supplemental oxygen should be given. If the neonate remains cyanotic after the administration of supplemental oxygen, positive pressure ventilation should be administered even if the heart rate is greater than 100 bpm. If ventilation is adequate and the baby continues to have central cyanosis, a congenital cyanotic heart defect or persistent pulmonary hypertension should be considered13. Peripheral cyanosis (acrocyanosis) is a normal finding in the newborn.

**Assessment and Management of Airway**

**Airway Assessment**

As previously mentioned, properly assessing and managing the airway of a newborn involves clearing the airway, properly positioning the neonate in sniffing position to open up the airway and monitoring for satisfactory respiratory effort. In addition to evaluating respirations, heart rate and color should also be carefully monitored because an abnormality in any one of these vital signs usually improves with ventilation. Thus, in neonatal resuscitation, providing adequate ventilation of the compromised newborn is the most crucial and effective step13.

**Supplemental Oxygen**

Supplemental oxygen is recommended whenever the neonate is breathing, has a heart rate greater than 100 beats per minute, but has central cyanosis13. Free flow oxygen, which is passively blowing oxygen over the baby’s nose, may be given by an oxygen mask, flow inflating bag and mask, T-piece resuscitator, or oxygen tubing, with the latter being the least reliable method. (see discussion on devices) In order to ensure that the neonate receives a high concentration of oxygen, the mask should be held close to the face, but not so tight as to cause a build up of pressure similar to Continuous Positive Airway Pressure (CPAP) or Positive End Expiratory Pressure (PEEP). If using oxygen tubing, the hand should be cupped around the tubing and baby’s face13. It is also recommended that administering unheated dry air at a flow rate greater than 10 L/min for an extended period of time be avoided. A flow rate of 5 L/min is usually sufficient
during initial resuscitative efforts.

The standard approach to oxygen delivery in neonatal resuscitation has been to use 100% oxygen. However, growing evidence suggest that resuscitating with room air (21% oxygen) may be just as effective as 100% oxygen. According to current recommendations, there is insufficient evidence to recommend a specific concentration of oxygen and/or oximetry goal during the initial resuscitative efforts in term neonates. Therefore in term infants, it is recommended that O₂ 100% continue to be used.

On the other hand, concerns have been raised over the adverse effects of reactive oxygen intermediates which may potentially injure lung and tissues, especially in premature infants. Thus, it is currently recommended that preterm infants are resuscitated with less than 100% oxygen, achieved by using an oxygen blender which allows for the mixing of oxygen and air from a compressed source to deliver a desired oxygen concentration. In infants with congenital heart disease such as single ventricle disorders, resuscitation with 100% oxygen can be detrimental to tissue perfusion. In general, the goal should be to maintain oxygen saturations between 85-95%, with 70-80% being acceptable during the first few minutes of life.

Supplemental oxygen is also recommended in neonates requiring positive pressure ventilation. Indications for positive-pressure ventilation with supplemental oxygen are infants who remain apneic, have a heart rate of <100 beat per minute after 30 seconds and/or continue to have central cyanosis after supplemental oxygen delivery.

Initial ventilation strategies in term infants

Studies have shown that in an infant who is apneic or gasping, administering positive pressure ventilation at a rate of 40-60 breaths per minute with 100% oxygen is usually effective in achieving a heart rate greater than 100 beats per minute. The average initial peak pressures required to successfully ventilate an unresponsive term or preterm infant ranges from 30-40 cm H₂O, although 20 cm H₂O may be effective. It is recommended to use the minimum amount of pressures necessary to achieve adequate ventilatory response which is primarily indicated by a rapid improvement in heart rate. If there is no increase in the neonate’s heart rate, chest wall movement should be assessed, the head and facemask should be repositioned, airway cleared and suctioned. After several failed attempts at assisted non-invasive ventilation, intubation is indicated.

Initial ventilation strategies in preterm infants

The lungs of preterm infants are more easily injured by large inflation volumes, yet tend to be more difficult to ventilate. The same strategies used to initiate positive pressure ventilation in term infant may be employed in neonates as well. If positive pressure ventilation is required during the initial stabilization of a preterm infant, initial inflation pressure of 20-25 cm H₂O is usually adequate. Continuous positive airway pressure, about 4-6 cm H₂O should also be considered in neonates who are demonstrating signs of poor respiratory effort and/or cyanotic. As in term infants, if after several failed attempts of assisted ventilation the neonate should be intubated.

Ventilation Devices

Ventilation of the neonates lungs can be achieved using several different devices: self-inflating bags, flow-inflating bags, T-piece resuscitator, laryngeal mask airways, and endotracheal tube. Self-inflating bags are the most commonly used manual ventilation device due to accessibility. They contain a pop off safety valve with a limited inflation pressure of 35 cm H₂O. However, when the bags are used vigorously, the pop off valves are not very effective. Bags of more than 450 ml have been shown to provide more consistent ventilation volumes. Obviously, these larger bags are designed for adults and would be inappropriate in the newborn. Positive end-expiratory pressure (PEEP) may be administered if a PEEP valve is attached but cannot be used to deliver CPAP. Also self-inflating bags cannot be used to deliver free-flow oxygen.

Flow inflating bags or anesthesia bags only fill when there is a source of compressed gas. They do not have a fixed safety pop off valve but may be used with or without manometer to regulate pressure. PEEP or CPAP can be administered using flow inflating bags and is controlled by an adjustable flow valve. Flow inflating bags can be used to deliver free-flow oxygen.
and are preferable in newborn resuscitation.

T-piece resuscitator is an apparatus that is designed to not only control flow but also limit pressure. Compressed gas is delivered at a user determined pressure through one of the ports. The pressure delivered is depicted on the manometer. Target inflation pressures and inspiratory times are more consistently achieved with T-piece devices versus flow-inflating or self-inflating bags. There are some commercially available T-pieces which also allow for the maintenance of positive end-expiratory pressure between inflations. Finally, the T-piece can also be used to deliver free-flow oxygen.

The laryngeal mask airway (LMA) is capable of applying effective ventilation in situations where bag mask ventilation has been ineffective and endotracheal intubation is not possible in near or full term infant. Traditionally the size 1 is used. Currently there is not enough evidence to recommend its use as a primary airway in neonatal resuscitation, the setting of meconium stained amniotic fluid, delivery of drugs via the trachea, or when chest compressions are required.

Endotracheal tube placement is indicated for meconium suctioning of the trachea, mechanical ventilation after ineffective bag-mask ventilation, coordination of chest compression with ventilation, administration of epinephrine, and special resuscitative circumstances (i.e. congenital diaphragmatic hernia).

Endotracheal intubation may take place at various points during resuscitation. In order to minimize hypoxia associated with intubation, the neonate should be pre-oxygenated, given free-flow oxygen and the procedure should be limited 20 seconds. Pre-oxygenation may not be possible if the reason for intubating is for suctioning of meconium. Usually a straight blade is preferred for the procedure. The No. 1 blade is used for term, No. 0 for preterm and No. 00 for extremely preterm. The size of the endotracheal tube chosen is based on weight of the neonate.

Table 4: Endotracheal Tube Size in Neonate

<table>
<thead>
<tr>
<th>Tube size (mm)</th>
<th>Weight (g)</th>
<th>Gestational age</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>&lt;1000</td>
<td>&lt;28</td>
</tr>
<tr>
<td>3.0</td>
<td>1000-2000</td>
<td>28-34</td>
</tr>
<tr>
<td>3.5</td>
<td>2000-3000</td>
<td>34-38</td>
</tr>
<tr>
<td>3.5-4.0</td>
<td>&gt;3000</td>
<td>&gt;38</td>
</tr>
</tbody>
</table>

Adapted from AAP/AHA Neonatal Resuscitation. 5th Ed.

Chest Compression

Ventilation is vital to resuscitation efforts. Since, chest compressions can potentially compete with effective ventilation, it is important to ensure that assisted ventilation has been optimized prior to the start of chest compressions. Chest compressions are indicated when the heart rate is less than 60 beats per minute despite adequate ventilation with supplemental oxygen for 30 seconds. Chest compressions should occur at a rate of 90 per minute with a ratio of compression to ventilation of 3:1 (90:30). Compressions should be delivered on the lower third of the sternum at a depth one third the anterior posterior diameter of the chest. There are two possible methods which can be employed: the 2 thumb-encircling hands and 2 finger method. The 2 thumb-encircling hands method is recommended because it is less tiring and allows for better depth control. However, the 2 finger may be preferred when access to the umbilicus is required for the placement of an umbilical catheter. Respirations, heart rate and color should be reassessed approximately every 30 seconds. Coordinated chest compression and ventilations should be sustained until the spontaneous heart rate is greater than or equal to 60 beats per minute. Furthermore, simultaneous delivery of chest compressions and ventilation must be avoided.

Administration of Medications

Bradycardia in a newborn is usually attributed to inadequate lung inflation and hypoxemia. Thus, in neonatal resuscitation efforts, the use of drugs is rarely indicated because the most important step in correcting bradycardia is establishing adequate ventilation. However, if medications are required, they can be given by three possible routes: umbilical vein, endotracheal tube and intraosseous, in that order.
Epinephrine

If the heart rate remains less than 60 beats per minute despite adequate assisted ventilation for 30 seconds and chest compression for an additional 30 seconds, the administration of epinephrine, a cardiac stimulant and peripheral vasoconstrictor, is indicated. The current recommended dose of epinephrine is 0.01 to 0.03 mg/kg intravenous and a higher dose of 0.3 to 0.1 mg/kg if given endotracheal. Epinephrine may be given through the endotracheal tube to allow for faster administration while IV access is being obtained. It is important to note that the safety and efficacy of the endotracheal use of epinephrine has not been evaluated; further reinforcing preference for the intravenous route.

Blood Volume Expanders

Blood volume expanders such as 0.9% NaCl, Ringer’s lactate and O Rh-negative packed red blood cells are seldom indicated unless there is clear evidence of acute blood loss or shock such as weak pulse, poor perfusion, pale skin, and an infant who is responding poorly to other resuscitative efforts. In general, the recommend dose of 10 ml/kg should be given over 5 to 10 minutes to avoid the risk of intraventricular hemorrhage.

Naloxone

Naloxone reverses neonatal respiratory depression associated with maternal opioids given during labor. Currently, naloxone is not recommended for use in the initial resuscitative efforts in infants with respiratory depression. Heart rate and color should first be restored through supportive ventilation prior to the use of naloxone. The preferred route of administration is 0.1 mg/kg intravenous or intramuscular. Naloxone has a shorter half-life than opioids that may be present in the neonates system. Therefore, the neonate should be closely watched for recurrence of respiratory depression and given additional doses as needed. It is important to note that naloxone should not be given to an infant born to an opioid addicted mother because it may precipitate acute withdrawal and seizures.

Neonatal hypoglycemia

Although there has been an association between hypoglycemia and poor neurological outcome, currently there have been no clinical trials demonstrating a poor outcome in hyperglycemic infants. Based on current availability of evidence, the AAP recommends maintaining glucose in the normal range. The optimal range of blood glucose values has not been clearly defined by the AAP.

Post Resuscitation

Although vital signs may have normalized, neonates are at continued risk for deterioration after resuscitation efforts. Therefore, the infant should be maintained in an environment which will allow for attentive monitoring and can provide preventative care.

Discontinuing of Withholding Resuscitation

When should resuscitative care be withheld or discontinued? According to the AAP Neonatal Resuscitation Guidelines, care should be withheld in cases of significant prematurity <23 weeks, birth weight <400 grams and congenital anomalies associated with early deaths such as anencephaly and trisomy 13. In situations when the prognosis is uncertain and morbidity rate is very high, the parental desire to initiate or continue life supportive measures should be considered.

Studies have shown that infants without signs of life after 10 minutes of resuscitation have an increased mortality rate and risk of severe neurodevelopmental disability. Therefore, discontinuing continuous and adequate resuscitation after 10 minutes, if there are no signs of life, is justifiable.
Summary

Although only 10% of neonates born in the United States require resuscitation, availability of well trained personnel skilled in neonatal resuscitation can result in a significant decline in neonatal morbidity and mortality. One important aspect of performing a successful resuscitation is having a good understanding of the complex dynamics of fetal/neonatal physiology and the adaptations that must be made to transition to extrauterine life. This knowledge will allow one to better serve the resuscitative needs of the neonate. Performing a risk assessment by evaluating maternal and fetal risk factors is important. Review of medical history including medications, may reveal other medical conditions (e.g. gestational diabetes, preeclampsia, etc.). Once the need for resuscitation is recognized, easy access to equipment, medication and supplies can result in a successful resuscitative effort.

References

WEGENER’S GRANULOMATOSIS

PAUL ROOKARD*, JACKLYN HECHTMAN**, AMIR R BALUCH***, ALAN D KAYE**** AND VINAYA MANMOHANSINGH*****

Abstract

The immunopathologic disease, Wegener’s granulomatosis, presents a challenge to the anesthesiologist due to multisystem involvement resulting in potential abnormalities of the airway, respiratory, circulatory, renal, and central/peripheral nervous systems. It is a systemic vasculitis of small, medium and occasional large arterial involvement. A familiarity with the proper approach to perioperative management is essential. Additional considerations must be made as problems arise from immunosuppressant and corticosteroid treatment.

Keywords: Wegener’s, granulomatosis, vasculitis, immunosuppressant, airway lesion.

Introduction

Wegener’s Granulomatosis (WG), is an uncommon immunopathologic disease characterized by necrotizing granulomatosis in the upper and lower respiratory tracts combined with glomerulonephritis. It was first described by Klinger in 1933 and by other investigators such as Rossle in 1933, Wegener in 1936 and 1939 and Ringertz in 19471. It is a systemic vasculitis of small, medium and occasional large arterial involvement. Arterioles as well as venules have also been implicated in the pathogenesis2-6. This rare disease has an estimated prevalence of 3 per 100,000 persons affected. While much more common in whites when compared to blacks, the disease shows no gender affinity with 1:1 male to female ratio. Presentation before adolescence is uncommon, and although the mean age of onset is approximately 40 years, it can be found at any age7.
Case Report

A 51-year-old, black female, weighing 68 kg and measuring 170 cm, without any significant medical or surgical history was flown in by air ambulance from the British Virgin Islands and presented with a four week history of bilateral lower extremity edema accompanied by hematuria, fever, and rash. She received hemodialysis, vancomycin, prednisone, and furosemide for acute renal failure. She went into respiratory failure and required intubation and ventilator support shortly after, with settings of 50% fraction of inspired oxygen, a respiratory rate of 18 breaths per minute, and a tidal volume of 600 mL prior to air ambulance. She has no known allergies. She denied use of nicotine, alcohol, or drugs. Family history was positive for lymphoma, brain tumor, and gastric cancer.

Physical exam revealed a middle-aged female, awake and comfortable on ventilator support. She was afebrile with a blood pressure of 131/78 mmHg, a heart rate of 97 beats per minute, and an O₂ saturation of 100%. Pulmonary exam revealed mild bilateral rhonchi throughout all fields. The rest of the exam was unremarkable.

Laboratory data showed a white blood cell count of 10.8 x 1,000/mL, hemoglobin of 9.2 g/dL, hematocrit of 27%, and platelets of 99,000/mL. Metabolic panel revealed sodium of 138 mEq/L, potassium of 4 mEq/L, chloride of 104 mEq/L, Bicarbonate of 27 mEq/L, blood urea nitrogen of 42 mEq/L, and creatinine of 3.7 mg/dL. Albumin was 1.9 g/dL. Autoimmune serologies revealed positive ANA greater than 1:1280 and ANCA greater than 100 along with low levels of complement. Cardiolipin antibody was negative. Prothrombin time was 14.7 seconds, partial thromboplastin time was 34 seconds, and INR was 1.5.

Chest radiography revealed bilateral interstitial infiltrates. Echocardiogram revealed mildly elevated pulmonary pressure. A renal biopsy was performed and showed sclerosing crescentic glomerulonephritis.

After renal biopsy, the patient was taken for right lung biopsy by video assisted thoracoscopic surgery. Arterial blood gas showed pH of 7.45, pCO₂ 44 torr, pO₂ 79 torr, CO₂ of 30 mmol/L, and an O₂ saturation of 40%. Assist control ventilation settings included a respiratory rate of 18 breaths per minute, a tidal volume of 500 mL, FiO₂ of 100%, and a PEEP of 5.

After application of routine monitors, the patient was pre-oxygenated and administered 2 mg midazolam as well as cistarcurium 20 mg IV. General anesthesia was induced with 100 mg fentanyl. The patient was intubated with a double lumen tube (DLT) to allow collapse of the left lung. After biopsy, the DLT was exchanged for an 8.0 cuffed ETT. The patient was escorted out of the operating room with packed red blood cells infusion, stable vital signs, and a triple lumen catheter placed in the left subclavian vein.

Tracheostomy was performed 9 days later with a delay due to an elevated partial thromboplastin time of 53.1 seconds and platelets of 28/mL. After 4 units of platelets and 2 units of fresh frozen plasma, PTT shortened to 29.4 seconds and platelets increased to 44/mL. After routine monitors were applied, the patient was pre-oxygenated and administered 12 mg cistarcurium in 3 equal doses over thirty minutes. Tracheostomy was performed without complication. Assist control ventilation was set to 18 breaths per minute with a tidal volume of 500 mL, a PEEP of 8, and an FiO₂ of 50%, and the patient was escorted to the ICU.

The rest of the hospital course was uneventful. The patient tolerated tracheostomy collar well, continued with hemodialysis three times per week, was administered IV methylprednisolone and monthly cyclophosphamide, and plans for psychiatric and rehabilitation therapy were coordinated.

Clinical Manifestations

Involvement of the upper airways occurs with a 95% prevalence in WG patients. They often present with severe upper respiratory tract findings. In addition to paranasal sinus pain and drainage, these findings can include purulent or bloody discharge not necessarily associated with nasal mucosal ulceration. In addition to an upper respiratory tract contribution to the disease, lower respiratory tract symptoms may be present and may include cough, dyspnea, and hemoptysis in 85-90% of patients. Chest x-ray findings are varied but can include alveolar opacities, diffuse hazy opacities, nodules (may cavitate) and pleural opacities. The second most common clinical manifestation occurs in...
the kidneys in 77% of patients. This common trait of WG can manifest as acute renal failure with microscopy revealing red cells, red cell casts, and proteinuria without evidence of immune complex deposition on biopsy2.

While WG is known for upper and lower airway involvement with associated kidney manifestations, any area of the body may be affected. Among others, eye and skin involvement occur with a relatively high frequency. Eye involvement occurring in 52% of patients ranges from mild conjunctivitis to dacrocystitis, episcleritis, and other pathology. Consequently, these pathologies may lead to proptosis. Skin lesions can occur as papules, vesicles, palpable purpura, ulcers or subcutaneous nodules [Table 1].

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Manifestations</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>Conjunctivitis, episcleritis, nasolacrimal duct obstruction, proptosis, retinal vasculitis, corneal ulceration, optic neuropathy, diplopia, uveitis</td>
<td>9, 10</td>
</tr>
<tr>
<td>Nervous</td>
<td>Cranial nerve abnormalities, external ophthalmoplegia, mononeuritis multiplex, central nervous system mass lesion, hearing loss</td>
<td>9</td>
</tr>
<tr>
<td>Heart</td>
<td>Myocarditis, pericarditis, conduction system abnormalities</td>
<td>9</td>
</tr>
<tr>
<td>Skin</td>
<td>Palpable purpuric, hemorrhage, vesicular ulcerative lesions</td>
<td>11</td>
</tr>
<tr>
<td>Joints</td>
<td>Arthritis, myalgias, arthralgias</td>
<td>9</td>
</tr>
<tr>
<td>Others areas that may show involvement</td>
<td>GI and GU tracts, subglottis or trachea, thyroid, parotid glands, breast, liver</td>
<td></td>
</tr>
</tbody>
</table>

WG is also known for having nonspecific symptoms such as night sweats, malaise, fatigue, arthralgias, anorexia, and weight loss. Fever can be present but often represents an underlying infection as opposed to the primary disease process2. WG may present, rarely, with tumor-like masses outside the lung instead of parenchymal lung nodules. If these cases are not recognized, unnecessary surgeries may ensue12.

There can be misleading similar renal lesions without the necessary systemic problems of Wegener’s. These patients are considered to have microscopic polyarteritis. Others with no systemic symptoms may be presumed to have idiopathic necrotizing glomerulonephritis; however, both of these disorders may develop the classic respiratory tract lesions13 or possess antineutrophil cytoplasmic antibodies (ANCAs) resulting in a similar and possibly exact picture of WG14-15.

**Lab Findings**

Aberrant hematologic lab values are most notable, evidenced by a markedly elevated erythrocyte sedimentation rate (ESR), normocytic normochromic anemia, leukocytosis, and thrombocytosis. Mild hypergammaglobulinemia (particularly of the IgA class) is also a characteristic lab finding2.

**Diagnosis**

Diagnosis is confirmed by biopsy demonstrating necrotizing granulomatous vasculitis. The biopsy of a nasopharyngeal lesion, if present, is preferred since this method is less invasive. However, If this lesion is not present or unable to be biopsied, an affected organ, such as the kidney or lung, may be biopsied. The renal biopsy is preferable because it is easier to perform and more often diagnostic than a lung biopsy. The results are distinct showing segmental necrotizing glomerulonephritis with little or no immunoglobin deposition (pauci-immune)16. The diagnosis is also suggested by the presence of circulating ANCs that are usually directed against proteinase 3 (c-ANCA). A range of 65% to over 90% of patients with Wegener’s granulomatosis are positive for ANCA14-15,18.

Differential diagnoses include other vasculitides (e.g. microscopic polyarteritis), Goodpasture’s syndrome, tumors of the upper airway of lung, and infectious processes. These host of infections include histoplasmosis, mucocutaneous leishmaniasis, rhinoscleroma, lymphomatoid granulomatosis and the spectrum of midline destructive diseases. Special attention must be paid to anti-glomerular basement membrane (GBM) antibody disease because this pathology may present similarly to Wegener’s as it manifests with both renal and pulmonary components17.
**Pathogenesis**

Histopathologic hallmarks of WG are necrotizing vasculitis of small arteries with granuloma formation that may be either intravascular or extravascular. The complex process begins with an inflammatory event. Later, a highly specific pathogenic immune response follows where previously unavailable epitopes of neutrophil granule proteins come into play. This mechanism is responsible for the generation of the high serum titer of autoantibodies (or ANCA)se). These ANCAse are then directed against the primary granules of neutrophils and monocytes, with proteinase-3 (PR3) and Myeloperoxidase (MPO) being most commonly targeted antigens\(^{19-22}\). The lung involvement generally appears as multiple, bilateral, nodular cavitary infiltrates. On the other hand, upper airway lesions, usually in the sinuses and nasopharynx, often reveal inflammation, necrosis and granuloma formation, with or without vasculitis\(^2\).

The pathogenesis of Wegener’s may involve a lack of alpha-1 antitrypsin (AAT) which in vivo is the primary inhibitor of PR3. Patients that have an AAT deficiency are at an increased risk for WG suggesting a role for the increased presence of PR3 at inflammation sites. Future research may establish a more concrete relationship\(^23-24\).

The coordination of ANCA production begins with an autoantibody response which subsequently produces ANCAse. Via the process of epitope spreading, the mechanism generalizes to the rest of a macromolecular protein complex. Since the process is antigen driven, the disease may be intricately linked to T cell activation. This observation is supported by the fact that patients with active WG have much higher levels of CD4+T cell and monocytic activation compared to normal individuals. Additionally, extremely high levels of the Th1 cytokines, TNF-alpha and interferon (INF)-gamma, are seen in patients with active Wegener’s. Furthermore, monocytes from these patients produce a large amount of interleukin-12, a major inducer of cytokines. Altogether these data suggest that IL-10, a monocyte antagonist, may inhibit the Th1 pathway in the disease as shown in vitro\(^25\).

“Primed” neutrophils are those with increased numbers of cell surface levels of membrane associated PR3. Once these neutrophils are primed, the ANCA\(\text{se} can bind causing abnormal constitutive activation through crosslinking of MPO and PR3 or by binding of Fe receptors. This pathway is supported by the observation that patients with ANCA-associated vasculitis demonstrate increased numbers of primed neutrophils in renal biopsy specimens with severity resembling the activity of the disease. Moreover, the interaction and upregulation of neutrophil activity by endothelial cells may play an important role in pathogenesis\(^26-30\).

Finally, recent animal models have shown evidence for the pathogenic potential of ANCAse. Two types of mice are employed: MPO knockout mice and recombinase-activating gene 2 (RAG-2) deficient mice. The RAG-2 deficient mice lack both T and B cells. In one model, MPO knockout mice were immunized with mouse MPO creating anti-MPO splenocytes and anti-MPO antibodies. RAG-2 deficient mice were injected with either anti-MPO splenocytes or control splenocytes (those producing no anti-MPO antibodies). Mice that received anti-MPO splenocytes developed clinical features of ANCA-associated vasculitides, whereas RAG-2 deficient mice that received the control splenocytes suffered only a “mild immune complex glomerulonephritis”. From this we can conclude that ANCAse have pathogenic potential and require a functioning immune system to mediate this pathology\(^31\).

**Treatment**

Aggressive immunotherapy is warranted in the case of WG since studies show that up to 90% of patients would die within two years without this treatment modality\(^2\). The mainstay of treatment that has reversed the drastic fatality numbers is cyclophosphamide combined with oral glucocorticoid. The current recommended dosage is 1.5 to 2 mg/kg per day of cyclophosphamide. Higher doses of 3-4 mg/kg per day may be given for several days to those that are acutely ill with severe disease. The dosage of cyclophosphamide should be adjusted to maintain the leukocyte count above 3000/µL while keeping an absolute neutrophil count above 1500/µL. The dose of corticosteroid for the first month is usually 1 mg/kg per day of oral prednisone. After clinical signs of disease remission throughout the first month, this dose
Antibody disease, or dialysis dependent renal failure. Cyclophosphamide resistance is rare with some experts citing that they never have seen a patient with a true form. Treatment is unclear, and simple adjustment of dose or monitoring of compliance oftentimes may ameliorate the “resistance”.

Drug side effects can be numerous from the above medications. The glucocorticoid side effects may include diabetes mellitus (8%), cataracts (21%), osteoporosis, and cushingoid features. Cyclophosphamide related side effects are more severe with at least 30% of patients developing cystitis. Bladder cancer will manifest in 6%, myelodysplasia in 2% and a high risk of permanent infertility in both women and men. Although the risk is low, a fatal complication of immunosuppressive therapy in WG is neumocystis carinii pneumonia (PCP), which occurs in as many as 6% of patients. Prophylaxis with trimethoprim-sulfamethoxazole at 160/800 mg three times weekly, may not only be cost saving but also life prolonging.

After the disease enters remission, maintenance doses utilizing different medications are employed in order to lessen the aforementioned toxicities. Methotrexate at 0.3 mg/kg per week may be administered orally in place of cyclophosphamide. If this drug is tolerated, and increased regimen can be administered and maintained for two years, then tapered down, and ultimately discontinued. Furthermore, azathioprine at 2 mg/kg per day can be given as an alternative to methotrexate. Additionally, since there are no head to head comparison studies of these two drugs, debate still exists as to which regimen is superior.

Monthly intravenous cyclophosphamide must be considered as an alternate regimen due to the toxic side effects of a daily cyclophosphamide dose. At present, studies have shown an equal or lesser effect of using monthly dosing. Another treatment option involves the use of a methotrexate-prednisone course of therapy. This modality has been shown to be efficacious in patients other regimens have been unsuccessful. The methotrexate was well tolerated with reversible GI disturbances, pneumonitis and oral ulcers reported in some cases. If using methotrexate, one must incorporate folic acid at 1-2 mg/day or folinic acid 2.5-5 mg/week (24 hours after taking methotrexate). Plasmapheresis, another alternative, may help those with severe pulmonary hemorrhage, anti-GBM antibody disease, or dialysis dependent renal failure. Cyclophosphamide resistance is rare with some experts citing that they never have seen a patient with a true form. Treatment is unclear, and simple adjustment of dose or monitoring of compliance oftentimes may ameliorate the “resistance”.

Drug side effects can be numerous from the above medications. The glucocorticoid side effects may include diabetes mellitus (8%), cataracts (21%), osteoporosis, and cushingoid features. Cyclophosphamide related side effects are more severe with at least 30% of patients developing cystitis. Bladder cancer will manifest in 6%, myelodysplasia in 2% and a high risk of permanent infertility in both women and men. Although the risk is low, a fatal complication of immunosuppressive therapy in WG is neumocystis carinii pneumonia (PCP), which occurs in as many as 6% of patients. Prophylaxis with trimethoprim-sulfamethoxazole at 160/800 mg three times weekly, may not only be cost saving but also life prolonging.

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If apparent manifestations of kidney failure are present, renal transplantation may be performed, although there is limited data as to long term outcomes. Case reports show that both renal and extrarenal manifestations may still occur. Even the ureter can become involved, possibly leading complications of stenosis and obstructive uropathy. In addition, relapse rates may be lower due to continued immunosuppression, but long term results in the “cyclosporine” era are unavailable.

Several alternative therapies and maintenance medications such as trimethoprim-sulfamethoxazole, mycophenolate mofetil, and cyclosporine have been
employed with varying success. Currently, no consensus has been reached on their benefit owing to the paucity of data. Future therapies utilizing anticytokines, anti-T/B cell antibodies, IV immunoglobulin, etoposide (chemotherapeutic agent), and 15-deoxyspergualin (immunosuppressant) are being studied with hopes of limiting remission and decreasing morbidity and mortality not only from the primary disease but also from the treatments themselves.

**Perioperative Anesthetic Considerations**

**Pre-operative assessment**

The approach to the patient with WG begins with a careful preoperative assessment which includes upper airway evaluation, chest x-ray, and if warranted pulmonary function tests (PFTs). Evaluation of the upper airway is used to recognize any ulcerating or obstructing lesions, as they are present in 95% of cases. Symptoms and complications secondary to these lesions include cough, dyspnea, hemoptysis, pleuritic chest pain, pneumothorax, and pulmonary hemorrhage. Chest x-ray may reveal nodules, cavitations, consolidation, effusions, pleural thickening, or hilar lymphadenopathy. PFTs may show reduced lung volumes complicated by obstructive airway disease patterns.

**Respiratory**

Patients with WG commonly have destructive lesions of the epiglottis. A thickened or fibrotic laryngeal wall may be present, which may result in a narrow lumen, with or without evidence of vasculitis. The laryngeal mucosal lining may be lost or even replaced by granulation tissue. Additionally, ulcerative or proliferative types of lesions commonly present with subglottic involvement.

Laryngoscopy should be used by the anesthesiologist to identify ulcers on the palate, pharynx, or epiglottis. Palatal or pharyngeal perforations may be observed, as well. Afterwards, careful planning and gentleness should be advised during the intubation to avoid bleeding from granulomas or displacement of brittle, ulcerated tissue down into the trachea or larynx. In fact, preoperative tracheostomy may be necessary if ulcers and lesions are extensive. Following extubation, edematous granulation tissue may obstruct the airway, therefore close observation postoperatively is compulsory. Finally, a regional anesthetic approach may be preferable to avoid airway instrumentation and its inherent complications in this population.

If vasculitis is present in the lungs, progression may lead to total occlusion of veins and arteries. Usually thin-walled cavities develop in the lower lobes, but thick-walled versions may grow secondary to central necrosis. These pulmonary changes may lead to increased dead space and mismatch of ventilation-perfusion. Furthermore, bronchial obstruction and/or destruction can lead to increased pulmonary shunting as well as arterial desaturation. For this reason, frequent suctioning of necrotic debris may be needed to keep the airway clear. Monitoring of arterial blood gases help assure that adequate oxygenation and ventilation occur. Even if a regional technique is employed, supplemental O₂ may be required.

**Cardiovascular**

Vasculitis of veins, peripheral arteries coronary arteries, granulomas, and necrotizing changes are included in the cardiovascular effects of WG. If coronary involvement is present, anesthetic management requires avoidance of intraoperative myocardial ischemia secondary to increased preload, afterload, heart rate, or coronary artery spasm. In cases with valvular heart defects or cardiomyopathy, hemodynamic status will determine the need for extensive monitoring and the use of adjuncts such as pacemakers and vasodilators. Digital arteritis and infarcts occurring at the tips of the digits may complicate the scenario. In these cases, the anesthesiologist use indwelling arterial lines with caution and limit the use of arterial punctures. Lastly patients on corticosteroid therapy are typically given a standard dose of 100 mg of hydrocortisone immediately prior to surgery to prevent an Addisonian hypotensive crisis as long term therapy will reduce the capacity of the body to respond to the stress of surgery.

**Renal**

Glomerular destruction along with extensive tubular atrophy occurs in patients with WG. Caution should be used when administering anesthetics and drugs that require renal excretion. The following drugs
have active or toxic metabolites that are dependent on renal excretion: opioids including morphine, meperidine, diazepam, and midazolam; muscle relaxants including: vecuronium and pancuronium; and the anti-hypertensive sodium nitroprusside. Rapid accumulation of these metabolites may place the patient in significant danger. Moreover, one can anticipate a decrease in renal clearance of highly ionized, lipid-insoluble agents. It follows that maintenance doses of highly protein bound anesthetic agents will be 30-50% lower. Loading doses, which often are more dependent on redistribution than elimination, oftentimes remain the same\cite{60}. Anesthetic agents that predominately depend on renal elimination are included in Table 2.

### Table 2

<table>
<thead>
<tr>
<th>Muscle Relaxants</th>
<th>Anticholinergic</th>
<th>Cholinergic</th>
<th>Cardiovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>gallamine</td>
<td>atropine</td>
<td>neostigmine</td>
<td>digoxin</td>
</tr>
<tr>
<td>pancuronium</td>
<td>glycopyrrolate</td>
<td>pyridostigmine</td>
<td>milrinone</td>
</tr>
<tr>
<td>pipecuronium</td>
<td>edrophonium</td>
<td>amrinone</td>
<td></td>
</tr>
<tr>
<td>d-tubocurarine</td>
<td></td>
<td>amphetamines</td>
<td></td>
</tr>
<tr>
<td>vecuronium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>doxacurium</td>
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</tbody>
</table>

Consideration must also be given to the possible depression of pseudocholinesterase activity following dialysis, the presence of hyperkalemia with resultant arrhythmias, hypertension, anemia, and coagulation defects, as in any patient with renal failure\cite{59}.

### Use of Succinylcholine

The depolarizing neuromuscular blocking agent, succinylcholine, is hydrolyzed by the plasma pseudocholinesterase enzyme (PSC). Conditions that reduce the activity of this enzyme may lead to prolonged action of succinylcholine and extended apnea. The cyclophosphamide used to treat WG patients inhibits PSC, possibly in a dose-dependant manner\cite{61}. There are other case reports of succinylcholine and even mivacurium causing prolonged apnea\cite{62,63}, but older case reports have described uncomplicated and successful use of succinylcholine in patients treated with cyclophosphamide, as well\cite{64}.

### Regional Anesthesia

WG patients may be candidates for regional anesthesia, for example, when procedures concerning the urogenital tract may be needed. Cases have been described where spinal anesthesia in WG patients were used with success.

Some concerns for general anesthesia may also be concerning for a regional approach. A WG patient with cardiac disease may also have peripheral neuropathy as part of their clinical picture\cite{65}. The neuropathy may be a sequela from underlying vasculitis of the vasa vasorum of peripheral nerves or in association with a necrotizing myopathy. A neurological assessment should be performed prior to anesthesia in these cases\cite{66}.

Complications from bleeding may be of concern for a regional technique, as well. This tendency to bleed may arise due to 1) cytotoxic therapy (cyclophosphamide or methotrexate) leading to thrombocytopenia, 2) circulating immune complexes leading to a low grade disseminated intravascular coagulation, or 3) complications from general vasculitis and granulomatous inflammation with cutaneous, meningeal, or spinal hemorrhages\cite{66}. Literature reports have also noted spontaneous subdural hemorrhage and spinal vasculature abnormalities as complications\cite{67,69}.

The anesthesiologist must weigh the risks and benefits of regional and general anesthesia when these cases arise. Platelet levels and clotting studies should be performed. If these return as normal and the patient has no neurological signs, it is likely that a regional approach will be without complications. Neurological deficits, if present, may suggest underlying vascular abnormalities or granulomatous infiltration of the cord. In these situations, computed tomography or magnetic resonance imaging is warranted before attempting spinal or epidural anesthesia\cite{66}.

### Conclusion

Wegener’s granulomatosis is a complex systemic autoimmune disease that presents many challenges to treatment. Although much success has come from current cyclophosphamide-corticosteroid treatments, vigorous relapse rates and high morbidity illustrate the need for continued study and treatment alternatives.
References

5. RAO-LEYVA F, RATLIFT NB, COSGROVE DM 3rd, HOFFMAN GS: Study of 52 patients with idiopathic aortitis from a cohort of 1,204 surgical cases [In Process Citation]. Arthritis Rheum; 2000, 43:901.
WEGENER’S GRANULOMATOSIS


Abstract

Objective: Electrocorticography (ECoG) may be used to guide epilepsy surgery. However, anesthetics can suppress epileptiform activity or induce confounding burst-suppression patterns and the relationship between ECoG results and seizure outcome is controversial. In this study, we evaluated the ECoG activity under several different anesthetics and examined the relationship between ECoG and outcome.

Methods: We retrospectively studied 44 patients who had ECoG during epilepsy surgery. Anesthesia was with fentanyl and isoflurane (n = 19), fentanyl and sevoflurane (n = 9), remifentanil and sevoflurane (n = 5), remifentanil and propofol (n = 9), and fentanyl with propofol sedation during local anesthesia (n = 2). Pre-resection ECoG was considered satisfactory if epileptiform activity was present and there was no burst-suppression. Post-resection ECoG was graded according to residual epileptiform activity: A (none), B (mild), C (moderate). Seizure outcome was graded: I (seizure free without medication), II (seizure free with medication), III (> 50% seizure reduction) or IV (< 50% seizure reduction). Grades I-III were considered beneficial.

Results: ECoG was satisfactory in 43 of the 44 surgeries, but one of the 11 recordings during propofol showed no epileptiform activity. Thirty-six of 37 patients (97%) with ECoG grade A or B and five of seven patients (71%) with ECoG grade C benefited from epilepsy surgery. Chi-squared, p > 0.05.

Conclusions: Satisfactory ECoG is possible using isoflurane or sevoflurane with nitrous oxide and fentanyl or remifentanil or using propofol and remifentanil. However, one of eleven ECoGs under propofol was negative for epileptiform activity. The amount of post-resection ECoG epileptiform activity does not significantly correlate with seizure outcome.

Keywords: Epilepsy surgery, anesthesia, electrocorticography.
Introduction

Despite the great advancement in medical treatment of epilepsy, quite large number of epileptic patients remain intractable to drug therapy. Epilepsy surgery can be a better choice for control of seizures in quite good number of these medication refractory patients1-4.

In the United States, it is estimated that 1500 patients undergo epilepsy surgery each year4. Intraoperatively, resection of the epileptogenic zone can be guided by electrocorticography (ECoG)6-8. The epileptogenic activity may be increased or masked by the effects of anesthetic drugs7-11.

In a retrospective study of twenty patients Tanaka et al7 reported the use of ECoG in 20 children undergoing epilepsy surgery under fentanyl and pancuronium with hyperventilation and found enhanced epileptiform activities in 17 patients. While Endo et al11 found that balanced neuroleptic analgesia using fentanyl and droperidol together with sevoflurane is not suitable for epilepsy surgery requiring ECoG. The relationship between intraoperative ECoG and seizure outcome is still controversial. Cascino et al12 reported that ECoG findings are not important determinants of surgical outcome in patients with non-lesional temporal lobe epilepsy. On the other hand, Stefan et al13 found that intraoperative ECoG contributes to a better delineation of epileptic activity and good postoperative outcome.

In this study, we evaluated the presence or absence of epileptiform activity and potentially confounding burst-suppression in pre-resection ECoG under several different anesthetics during epilepsy surgery and also examined the relationship between post-resection ECoG and seizure outcome.

Patients and Methods

Fourty four patients with intractable epilepsy who were referred for epilepsy surgery at Jordan University Hospital completed their surgical management from 1994 to 2005.

Data was collected on each patient by detailed review of preoperative, intraoperative and postoperative status. Preoperative data included age, sex, type, onset and duration of intractable epilepsy, psychological status and investigations like electroencephalograms (EEG), video EEG, brain computerized tomography (CT) and magnetic resonance imaging (MRI). Intraoperative data include the anesthetic techniques and monitoring, patient management during ECoG, post resection ECoG grades and type of surgical resection. Postoperative data include postoperative seizures outcome.

Presurgical localization of the epileptic zones were derived from the clinical features of the epileptic foci, scalp EEG, video EEG monitoring, invasive subdural EEG monitoring, brain CT and MRI imaging studies.

Epilepsy in all patients of this study, was refractory to two or more of the conventional antiepileptic drugs (AEDs), the frequency of seizures was not less than one per week and the duration of treatment was not less than 6 months before considering surgery.

The selection of patients for surgery was a joint decision between the neurologist, clinical neurophysiologist and the neurosurgeon. Patients were not premedicated before anesthesia. Three patients were premedicated with diazepam before surgery and were excluded from the study. Antiepileptic drugs were discontinued at least one day before surgery.

Twenty six males and 18 females were studied whose age distribution is shown in Fig. 1 and their clinical findings are summarized in Table 1.

Fig. 1
Age distribution of patients

Age Distribution of Patients
Pre-resection and post-resection ECoG recording was used in 44 patients.

Seven patients and 2 patients underwent pre-resection subdural and sphenoidal electrodes insertion respectively for more precise localization of the epileptic zone.

Temporal lobectomy was performed in 30 (68.2%) patients, (Table 2).

The presence or absence of epileptiform activity and burst-suppression was noted and that pre-excision ECoG was defined as satisfactory when epileptiform activity was found.

General Anesthesia Management and Intraoperative ECoG

Induction of general anesthesia was either inhalational with isoflurane and sevoflurane or intravenous with sodium thiopentone 2-4 mg/Kg or propofol 1-2 mg/Kg and fentanyl 2µg/Kg. Muscular relaxation was achieved by either atracurium or vecuronium and maintained by incremental doses of either drug to achieve one or two twitches on nerve stimulator. Arterial oxygen and carbon dioxide partial pressures were kept above 100 mmHg and between 30-35 mmHg respectively. Hypothermia during the

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**Table 1**

<table>
<thead>
<tr>
<th>Clinical data and results of investigations of 44 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Male/female</strong></td>
</tr>
<tr>
<td><strong>Type of seizures</strong></td>
</tr>
<tr>
<td>Complex partial</td>
</tr>
<tr>
<td>Complex partial with simple partial</td>
</tr>
<tr>
<td>Simple partial</td>
</tr>
<tr>
<td>Complex partial with secondary generalization</td>
</tr>
<tr>
<td>Generalized tonic clonic</td>
</tr>
<tr>
<td>Mixed types</td>
</tr>
<tr>
<td><strong>Age of onset of seizure</strong></td>
</tr>
<tr>
<td>Range (birth-45 years)</td>
</tr>
<tr>
<td><strong>Duration of seizure</strong></td>
</tr>
<tr>
<td>Range (0.5-25 years)</td>
</tr>
<tr>
<td><strong>Psychological status</strong></td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Decrease in cognitive functions</td>
</tr>
<tr>
<td>Mentally retarded</td>
</tr>
<tr>
<td><strong>Preoperative EEG findings</strong></td>
</tr>
<tr>
<td>A-Focal</td>
</tr>
<tr>
<td>Temporal activity</td>
</tr>
<tr>
<td>Extra temporal activity</td>
</tr>
<tr>
<td>B - Generalized activity</td>
</tr>
<tr>
<td><strong>CT and MRI examination</strong></td>
</tr>
<tr>
<td>Temporal structural lesions</td>
</tr>
<tr>
<td>Extra temporal lesions</td>
</tr>
</tbody>
</table>

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**Table 2**

<table>
<thead>
<tr>
<th>Surgical procedures done on 44 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedure</strong></td>
</tr>
<tr>
<td>Temporal lobe resection</td>
</tr>
<tr>
<td>Extra temporal lobe resection</td>
</tr>
<tr>
<td>Functional hemispherectomy</td>
</tr>
</tbody>
</table>

Fentanyl was used in 30 (68.2%) patients and isoflurane in 19 (43%) patients, (Table 3).

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**Table 3**

<table>
<thead>
<tr>
<th>Anesthesia management of 44 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of anesthesia</strong></td>
</tr>
<tr>
<td>General anesthesia</td>
</tr>
<tr>
<td>Local anesthesia</td>
</tr>
<tr>
<td>Maintenance of anesthesia</td>
</tr>
<tr>
<td><strong>During ECoG recording</strong></td>
</tr>
<tr>
<td>1. Fentanyl and Isoflurane</td>
</tr>
<tr>
<td>2. Fentanyl and Sevoflurane</td>
</tr>
<tr>
<td>3. Remifentanil and Sevoflurane</td>
</tr>
<tr>
<td>4. Remifentanil and Propofol during general anesthesia</td>
</tr>
<tr>
<td>5. Fentanyl and Propofol during local anesthesia</td>
</tr>
</tbody>
</table>

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procedure was prevented by using warm IV fluids, water heating matrix and keeping the operating room temperature between 24-26 °C. After craniotomy and exposure of brain surface and during the period of ECoG recording before and after surgical resection, anesthesia was maintained by one of the following:

- Fentanyl 0.5µg/kg incremental doses with inspired concentration of 0.5-1% isoflurane and 50% nitrous oxide in oxygen.
- Fentanyl 0.5µg/kg incremental doses with inspired concentration of 1-2% sevoflurane and 50% nitrous oxide in oxygen.
- Remifentanil infusion 1-4µg/kg/hour and inspired concentration of 1-2% sevoflurane and 50% nitrous oxide in oxygen.
- Propofol infusion 1-4mg/kg/hour with remifentanil infusion 1-4µg/kg/hour.

**Local Anesthesia Management For Awake Craniotomy**

Patients were initially deeply sedated with 2 mg/kg propofol and 1 µg/kg fentanyl intravenously and positioned on the operating table in the semilateral position. Propofol infusion was subsequently administered at a rate of 1-4 mg/kg/hr and 25 µg incremental doses of fentanyl. After that, local anesthesia infiltration of the scalp down into the temporalis muscle and infiltration of the pin sites for Mayfield head holder was done. 0.25-0.5% lignocaine with adrenaline 1:200000 was used. Deep levels of sedation were employed during Mayfield head holder fixation, during scalp incision, raising the bone flap and manipulation, transection or coagulation of meningeal vessels. Light levels of sedation and sometimes discontinuation of the propofol infusion were employed during ECoG recording and during cortical speech mapping for verbal communication with the patient.

ECoG recording during awake craniotomy was the same as during general anesthesia cases and electrodes were moved over the entire area of exposure.

ECoG recording was done using 23 SLE microscribe EEG machine and E9 flexible plate 15 electrodes. Ad Tech 4, 6 or 8 electrode strips were used according to the case. ECoG was recorded before resection to delineate the margins of resections and after resection to detect any residual resectable epileptic focus. Twenty minutes was the minimum duration of ECoG recording during general and local anesthesia.

Post-resection ECoG was graded according to Jay et al: (A) no residual epileptiform activity; (B) mild residual activity; (C) moderate residual activity; (D) unchanged from the pre-resection ECoG and (E) undetermined due to drug effect14.

The range of follow-up period was from 6 months to 7 years.

Postoperative seizure outcome was graded according to Kobayashi et al: grade I (seizure free without AED); grade II (seizure free on AED); grade III (> 50% reduction in seizure frequency); grade IV (< 50% reduction in seizure frequency); grade V (not improved) and grade VI (worse)15. A beneficial surgical result is defined as grade I-III seizure outcome.

Postoperative seizure outcome and post-resection ECoG grade were compared with chi-square analysis of proportions.

**Results**

No burst suppression or masking of epileptiform ECoG activity in 43 of 44 surgeries was observed regardless of the type of anesthesia. The epileptiform activity was absent in one patient under propofol anesthesia before resection. The was a 38 years old male patient scheduled for temporal lobectomy. The patient was suffering from long standing complex partial seizure with secondary general seizure and with frequency of 4 times/month. The preoperative video EEG revealed left temporal focus. General anesthesia was employed using remifentanil and propofol. During ECoG monitoring before resection, epileptic activity could not be recorded, surgical resection could not be done and the patient awakened from general anesthesia. Three days later, general anesthesia was employed again for temporal lobectomy using fentanyl and isoflurane, epileptic activity before resection was recorded and surgery was completed. The histological diagnosis was normal brain tissue.

Figure 2A, shows the ECoG with epileptic focus of a 21 years old male patient who was suffering from complex partial seizure of 17 years duration and
underwent left temporal lobectomy using fentanyl and isoflurane. Figure 2B, shows ECoG of the same patient after surgical resection without residual epileptiform activity.

Post-resection ECoG grades showed 17 patients with grade A, 20 patients with grade B and 7 patients with grade C.

Seizure outcome demonstrated that 6 (14%) patients are seizure free without AEDs, 16 (36%) are seizure free on AEDs and 19 (43%) patients had more than 50% reduction in the rate of seizures, (Table 4).

The chi-square analysis of proportions for ECoG and beneficial outcome grades is 2.80, p = 0.094 which is not significant.

### Table 4

<table>
<thead>
<tr>
<th>Post-resection grade* (Number of patients)</th>
<th>Postoperative seizure outcome grade**</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade A</td>
<td>Grade I</td>
<td>4</td>
</tr>
<tr>
<td>(17)</td>
<td>Grade II</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Grade III</td>
<td>7</td>
</tr>
<tr>
<td>Grade B</td>
<td>Grade I</td>
<td>2</td>
</tr>
<tr>
<td>(20)</td>
<td>Grade II</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Grade III</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Grade IV</td>
<td>1</td>
</tr>
<tr>
<td>Grade C</td>
<td>Grade II</td>
<td>2</td>
</tr>
<tr>
<td>(7)</td>
<td>Grade III</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Grade IV</td>
<td>2</td>
</tr>
</tbody>
</table>

* According to Jay et al [15]: A, no residual epileptiform activity; B, mild residual epileptiform activity; C, moderate epileptiform activity; D, unchanged from the pre-resection ECoG; E, undetermined due to drug effect.

** According to Kobayashi et al [16]: 1, seizure free without antiepileptic drugs; 2, seizure free on antiepileptic drugs; 3, more than 50% reduction in seizure frequency; 4, less than 50% reduction in seizure frequency; 5, not improved; 6, become worse.
Discussion

The aim of epilepsy surgery is to stop seizures or to reduce their frequency by removing the epileptogenic zone or focus. This requires presurgical evaluation and selection of patients suitable for this type of surgery16,17.

Routine scalp EEG usually provides interictal activity while ictal activity is usually obtained from short and long duration video EEG monitoring18.

Temporal lobe is a common site for epilepsy focus and temporal lobectomy is a common procedure for intractable epilepsy patients. Epilepsy surgery can be done under local or general anesthesia. ECoG monitoring is more difficult during general anesthesia since anesthetic agent can suppress electrical brain activity and epileptogenic activity9,10.

The present study has shown that satisfactory ECoG was obtained in 43 of the 44 surgeries done using different types of anesthetics and also 41 of 44 patients with post resection ECoG grade I -III benefited from epilepsy surgery.

Many anesthetic drugs used in ECoG-guided epilepsy surgery may stimulate or suppress epileptiform activity including alfentanil, fentanyl, remifentanil, sevoflurane, isoflurane, propofol and methohexitone19.

Wass et al19 found increase in epileptiform activity after bolus 2.5 µg/kg intravenous remifentanil. Hisada et al21 reported increase in epileptogenic activity by 1.5 MAC sevoflurane anesthesia. Sato et al20 found epilepsy spikes decreased significantly with administration of nitrous oxide.

Iijima et al22 found that the supplementation of nitrous oxide with sevoflurane suppressed epileptogenicity of sevoflurane in patients with epilepsy.

The effect of propofol on epileptiform activity during epilepsy surgery is controversial and reports of both pro-convulsant and anti-convulsant effects have been published24-33.

Hewitt et al26 reported increase in epileptic activity in 12 of 20 patients given boluses of propofol (range 40-200 mg) undergoing temporal epilepsy surgery and burst suppression was produced in the ECoG in all but two patients. Samra et al30 reported no increase in epileptiform activity after subanesthetic doses of a propofol in volunteers with complex partial seizures. Drummond et al8 reported in a case of awake craniotomy given low dose propofol sedation an increase in EEG beta (β) activities that obscure the epileptogenic activity in ECoG recording. Rampil et al9 reported suppression of epileptiform activity by propofol during epilepsy surgery.

Thirty three (75%) of our patients during intraoperative ECoG recording were given fentanyl and remifentanil with isoflurane and sevoflurane in 50% nitrous oxide in oxygen with adequate epileptiform activity recording. Despite reports of epileptiform activity suppression, we found satisfactory ECoG results regardless of the several types of anesthesia evaluated. In our study, we did not evaluate spike frequency or amplitude of ECoG that may be affected by some types of anesthetics more than others, and although ECoG was absent in one patient under propofol anesthesia, it is difficult to exclude other effects than propofol on ECoG since it is only one observation. Thirty patients in our study underwent temporal lobectomy and the present study has also shown that 41 (93%) patients benefited from epilepsy surgery using intraoperative ECoG.

Various studies have shown favorable and encouraging seizure control after temporal lobe epilepsy surgery2,5,34-36. Drake et al2 reported 9 of 16 (56%) patients are seizure free after temporal lobectomy and 6 of 16 (38%) patients had more than 50% reduction in the frequency of seizures. Other reports have shown 90% and 80% overall improvements after temporal and extra temporal respectively36.

In conclusion, our study has added further support to the literature that ECoG guided epilepsy surgery can be done with isoflurane or sevoflurane with nitrous oxide and fentanyl or remifentanil or using propofol and remifentanil, although, one of eleven ECoG was negative for epileptiform activity under propofol.
infusion. There was no statistically significant correlation between the amount of epileptiform activity on post-resection ECoG and seizure outcome, and it seems that detailed analysis of post-resection ECoG beyond simple spike abundance may be required to better predict resection outcome.

References

COMPARATIVE STUDY OF NEUROMUSCULAR BLOCKING AND HEMODYNAMIC EFFECTS OF ROCURONIUM AND CISATRACURIUM UNDER SEVOFLURANE OR TOTAL INTRAVENOUS ANESTHESIA

ASHRAF MOUNIR AMIN*, MOHAMMAD YOSRY MOHAMMAD* AND MONA FATHI IBRAHIM*

Abstract

Neuromuscular blockers (NMB) are important adjuvant to general anesthesia. Rocuronium bromide and cisatracurium besylate are considered relatively recently introduced non-depolarizing muscle relaxants.

Objectives: This study evaluates the enhancement of cisatracurium and rocuronium-induced neuromuscular block during anesthesia with 1.5 MAC sevoflurane or total i.v. anesthesia (TIVA), hemodynamic effects and side effects.

Methodology: 80 patients were randomly allocated into one of four equal Groups to receive either rocuronium (under sevoflurane or propofol TIVA) or cisatracurium (under sevoflurane or propofol TIVA). The NMB effects of rocuronium and cisatracurium were studied by constructing dose-effect curves. Acceleromyography (TOF-Guard) and train-of-four (TOF) stimulation of the ulnar nerve were used (2 Hz every 15 sec). Cisatracurium and rocuronium were administered in increments until depression of $T_1/T_0 > 95\%$ was reached. Hemodynamic effects of both muscle relaxants together with sevoflurane or propofol were assessed using thoracic bioimpedance.

Results: Depression of $T_1/T_0$ was enhanced under sevoflurane compared to TIVA. $ED_{50}$ and $ED_{95}$ values of both drugs were significantly lower under sevoflurane more than TIVA. Recovery index 25-75% and time to a TOF ration of 0.70 were prolonged significantly by sevoflurane compared to TIVA. Hemodynamically, rocuronium and cisatracurium did not exert significant changes, but the interaction of the relaxants and the anesthetic agents resulted in statistically significant decline in some hemodynamic parameters at certain periods which are not clinically significant and required no medications.

Conclusion: We conclude that the effects of rocuronium and cisatracurium are significantly enhanced during sevoflurane compared with propofol anesthesia and the recovery is lower.

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Introduction

Neuromuscular blockers (NMB) have become essential parts of the anesthetist armamentarium. They aid endotracheal intubation, mechanical ventilation, reduce anesthetic requirements, prevent patient movement without voluntary or reflex muscle movement, facilitate surgery, and decrease oxygen consumption.

In the development of new neuromuscular blocking drugs, the anesthesiologist is now provided with drugs that are almost free of unwanted effects, have a time course of action that allows great control of their activity and, in most cases, allows the anesthesiologist to substitute them for succinylcholine.1

In selecting a neuromuscular blocking agent, an anesthetist strives to achieve three competing goals: rapid adequate muscle relaxation, hemodynamic stability, and predictable complete return of skeletal muscle function.

Rocuronium bromide is a non-depolarizing muscle relaxant, with a short onset time, an intermediate duration of action and rapid recovery characteristics coupled with cardiovascular stability, with no histamine release or other side effects.2

Cisatracurium has an intermediate duration of action, potent and safe with excellent cardiovascular stability and without apparent histamine release.3

Sevoflurane is a fluorinated methyl ethyl ether that has less respiratory irritation, more hemodynamic stability and more rapid emergence in comparison to isoflurane.4 It has a low blood-gas solubility resulting in rapid uptake and elimination. These physicochemical properties allow a fast recovery, thus making it suitable for day case surgery.

Propofol (di-isopropylphenol) is a phenol which is insoluble in water. The short elimination half life and non cumulative properties of propofol should make this drug ideal for use in TIVA. Indeed propofol can be considered the best intravenous anesthetic available for TIVA.5

The neuromuscular blocking effects of muscle relaxants are enhanced by volatile anesthetics, a phenomenon called “potentiation”. Several reasons have been postulated as the causes of this potentiation: pre-junctional effects, increased blood flow to muscles during anesthesia, and a centrally mediated relaxation. Not all types of anesthetics enhance neuromuscular block to the same extent.6

Inhaled anesthetics augment the neuromuscular blockade from nondepolarizing muscle relaxants in a dose-dependent fashion, which may also depend on the duration of anesthesia.

Joo and Perks have shown that the use of volatile anesthetics results in lower ED50 and ED95 of neuromuscular blockade significantly in comparison to propofol.4 Underestimation of the enhancement of neuromuscular block by volatile anesthetics during short procedures could result in inadvertent prolonged duration of relaxation.

A new method for monitoring neuromuscular function consists of measuring acceleration of the thumb after stimulation of a peripheral motor nerve.7 This technique is based on Newton’s second law: Force = mass x acceleration.8

Thus if mass is constant, acceleration is directly proportional to force. Accordingly, after nerve stimulation, one can measure not only the evoked force but also the acceleration of the thumb.8

Acceleromyography is a simple method of analyzing neuromuscular function. One requirement is that the muscle be able to move freely. During a nondepolarizing neuromuscular blockade, good correlation exists between the TOF ratio measured by this method and the TOF ratio measured with a force displacement transducer.9 Also the precision of acceleromyography seems to be comparable to that of mechanical measurement.10

The aim of this study is to compare rocuronium to cisatracurium regarding intensity, duration of neuromuscular blockade and also the hemodynamic profile under sevoflurane or total intravenous anesthesia, as well as associated side effects.

Materials and Methods

This clinical study was conducted in Kasr et Aini University Hospital after obtaining local Ethics Committee approval and informed patient consent. Eighty adult patients of both sexes (ASA I and II) scheduled to undergo extra-thoracic moderate
elective general surgery were studied in a prospective, randomized study. Routine laboratory investigations included liver function tests, kidney function tests, complete blood picture, and coagulation profile.

Patients were randomly divided into 4 equal groups, (20 patients each). Group I (Rocuronium & Sevoflurane), Group II (Cisatracurium & Sevoflurane), Group III (Rocuronium & Propofol) and finally, Group IV (Cisatracurium and propofol). Exclusion criteria included cardiovascular diseases or drugs affecting hemodynamics, renal impairment, hepatic insufficiency, endocrine disease, neuromuscular disease or receiving drugs that interact with neuromuscular blockers and finally, difficult intubation patients grade III & IV.

All patients received midazolam 0.05 mg.kg\(^{-1}\) I.M. one hour before surgery. An intravenous line was secured in the arm opposite to that connected to the neuromuscular monitoring equipment. Anesthesia was induced with propofol 2-2.5 mg.kg\(^{-1}\) and fentanyl 1 µg.kg\(^{-1}\). Oxygen and nitrous oxide mixture (50:50%) were used in all Groups. Groups I and II patients were allowed to sustain spontaneous ventilation with a face mask with 2 MAC sevoflurane for 10-15 minutes, then rocuronium and cisatracurium were given in gradual incremental doses till reaching ED\(_{95}\) as judged by accelerograph. Groups III and IV patients received a standard propofol infusion at 6-12 mg.kg\(^{-1}\).h\(^{-1}\). Rocuronium and cisatracurium were given in gradual incremental doses till reaching ED\(_{95}\) as judged by accelerograph. The patients were anesthetized before operating the stimulator, as the stimulator could be painful to an awake patient.

Lungs were mechanically ventilated, followed by laryngoscopy and orotracheal intubation when ED\(_{95}\) was reached. Anesthesia was maintained in Group I and II with 2 MAC sevoflurane and with propofol, 100 µg.kg\(^{-1}\).min\(^{-1}\) in Groups III and IV. End-tidal PCO\(_2\) was adjusted to 32-36 mmHg, skin temperature above the monitored muscle were measured and maintained between 32°C and 35°C by passive warming (wrapping of the patient arm in a cotton blanket). The arterial pressure cuff was placed on the opposite arm.

When adductor response was reached to T\(_{25}\%\) (time to recovery of T\(_1\) to 25% of baseline), clinical relaxation was maintained by a second bolus of rocuronium (0.1 mg/kg) or cisatracurium (0.015 mg/kg) till the end of the operation.

**Neuromuscular Monitoring**

By the use of TOF-guard (biometer, Denmark) the following variables of neuromuscular block were obtained for all groups:

1. **Depression of T\(_1\) of the train-of-four:** Cumulative increments of 100 µg.kg\(^{-1}\) rocuronium were given in Groups I and III, while increments of 15 µg.kg\(^{-1}\) cisatracurium were given in Groups II and IV. The subsequent dose was administered after at least 3 min and only if three consecutive twitches of identical amplitude were demonstrated (steady state of onset). Increments were given until depression of the first twitch of at least 95% was achieved during sevoflurane or total i.v. anesthesia (equi-effective dose: identical end-point instead of identical doses).

2. **Cumulative dose-response curves:** They were obtained by non-linear regression in the four Groups, showing values of ED\(_{50}\), Ed\(_{95}\), Ed\(_{95}/ED_{50}\) ratio and the slope of the regression curve in the four Groups of the study.

3. **Clinical duration:** Time after injection of the last cumulative dose of muscle relaxant until 25% recovery of T\(_1\).

4. **Recovery index:** Time interval during which T\(_1\) recovered from 25% to 75% of control. Time to TOF\(_{0.7}\): Time required for return of TOF ratio to 0.7.

**Fig. 1**
The TOF-Guard connected to the patient before starting stimulation

TOF-Guard: It is a relatively new microprocessor controlled neuromuscular transmission monitor
based on accelerometry. Four supramaximal stimuli of 60 mA were given every 0.5 seconds (2HZ), and each set (train) is repeated by the monitor every 15 seconds to the ulnar nerve at the wrist. Electrodes are placed over the ulnar nerve on the medial side of the wrist. The transducer is positioned so that its flat side is placed on the finger in such a way that the movement is perpendicular. The temperature probe is placed over the skin of adductor pollicis muscle; it can read between 16.0 to 41.5 C°. The data are stored on a memory card and transferred to a computer (Fig. 1).

**Hemodynamics:** Hemodynamic parameters were monitored at; before administration of general anesthesia, after administration of general anesthesia and just before administration of muscle relaxant, then at 1, 3, 5, 10, 15, 20 minutes after muscle relaxant and then every 10 minutes up to 90 minutes. The following parameters were monitored: heart rate, mean arterial blood pressure (by Agilent M 1166A monitor), cardiac index and stroke index were monitored non-invasively by thoracic bioimpedance (BOMED/NCCO M3-R7) cardiodynamic monitor. Electrodes are applied to the patients’ neck and chest as shown in Fig. 2. After recovery data were measured, conventional doses of neostigmine 0.045 mg/kg with atropine 0.01 mg/kg were given, followed by continued hemodynamic and oxygenation monitoring and management of postoperative complications: e.g. pain, nausea and vomiting.

**Statistical Analysis**

Data were presented as mean (SD), or mean (95% CI), as appropriate. Statistical analysis was performed using the software package statistica® 5.0 for Windows®. Values were compared among the groups using analysis of variance (ANOVA) with post hoc Newman-Keul’s test. Repeated measures ANOVA were used for comparison of hemodynamic parameters. Chi-square test was used for analysis of categorical data. Statistical significance was set when \( P < 0.05 \).

Dose-response curves were constructed by non-linear regression using the known pharmacological model:

\[
\text{Response} = \frac{\text{Max}}{\text{Max} + \left(\frac{\text{Dose}}{\text{ED}_{50}}\right)^{\text{Slope}}}
\]

Where Max is the maximum possible response (100% in the present case), \( \text{ED}_{50} \) is the median effective dose and Slope is the slope of the regression curve. Both \( \text{ED}_{50} \) and Slope were estimated as regression parameters. \( \text{ED}_{95} \), the dose which produces the desired response in 95% of patients, was calculated from the equation of the regression curve.

The 95% confidence interval (CI) was calculated for \( \text{ED}_{50} \), \( \text{ED}_{95} \), the ratio \( \text{ED}_{95}/\text{ED}_{50} \), and the slope of the curve. If the experiment is to be repeated a hundred times under the same conditions, the calculated values of the previously mentioned parameters will fall within the 95% CI in 95 of these hundred times; i.e. it can be said with 95% confidence that the calculated values of the parameter will fall within the 95% CI.

**Results**

**Demographic data:** there was no significant difference among the four Groups of the study as regards age, weight, gender distribution, or duration or surgery (Table 1).

**Hemodynamic parameters**

**Heart rate:** Changes in heart rate are shown in Table 2. Significant changes at certain times of the study are marked with *. There was no significant difference among the four Groups at baseline as well as all through the study period. General anesthetic administration resulted in a non significant decrease of heart rate in the four Groups of the study.
Table 1
Demographic and operative data of patients in the four Groups of the study [mean (SD) or ratio].

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 20)</th>
<th>Group II (n = 20)</th>
<th>Group III (n = 20)</th>
<th>Group IV (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>35 (8.9)</td>
<td>34 (8.8)</td>
<td>35 (7.8)</td>
<td>37 (6.5)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>12/8</td>
<td>9/11</td>
<td>13/7</td>
<td>11/9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 (3.9)</td>
<td>70 (5.2)</td>
<td>73 (5.09)</td>
<td>74 (3.9)</td>
</tr>
<tr>
<td>ASA status (I/II)</td>
<td>15/5</td>
<td>14/6</td>
<td>16/4</td>
<td>13/7</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>72 (8.8)</td>
<td>71 (7.1)</td>
<td>69 (5.8)</td>
<td>74 (9.2)</td>
</tr>
</tbody>
</table>

Mean arterial pressure: As shown in Table 3, there was no significant difference among the four Groups at baseline as well as all through the study period as regards MAP. Mean arterial pressure showed non significant decrease as a result of administration of general anesthetics. Significant changes at certain times of the study are marked with *.

Table 2
Heart rate (beats/min) in the four Groups of the study [mean (SD)].

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 20)</th>
<th>Group II (n = 20)</th>
<th>Group III (n = 20)</th>
<th>Group IV (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>75 (4.9)</td>
<td>76 (5.6)</td>
<td>76 (6.4)</td>
<td>77 (2.8)</td>
</tr>
<tr>
<td>Before MR</td>
<td>72 (5.2)</td>
<td>73 (6.3)</td>
<td>71 (5.8)</td>
<td>72 (5.5)</td>
</tr>
<tr>
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<td>73 (7.5)</td>
<td>73 (6.8)</td>
<td>72 (9.0)</td>
<td>73 (5.5)</td>
</tr>
<tr>
<td>3</td>
<td>71 (6.6)</td>
<td>73 (6.7)</td>
<td>71 (6.5)*</td>
<td>71 (4.9)*</td>
</tr>
<tr>
<td>5</td>
<td>72 (6.3)</td>
<td>72 (5.3)</td>
<td>71 (7.3)</td>
<td>71 (3.6)*</td>
</tr>
<tr>
<td>10</td>
<td>71 (6.3)</td>
<td>72 (5.9)</td>
<td>71 (7.9)</td>
<td>72 (5.3)*</td>
</tr>
<tr>
<td>15</td>
<td>72 (6.3)</td>
<td>73 (5.9)</td>
<td>70 (8.4)*</td>
<td>73 (5.1)</td>
</tr>
<tr>
<td>20</td>
<td>71 (6.3)</td>
<td>72 (8.1)</td>
<td>73 (7.1)</td>
<td>73 (4.8)</td>
</tr>
<tr>
<td>30</td>
<td>71 (6.3)</td>
<td>72 (6.8)</td>
<td>71 (9.1)*</td>
<td>72 (4.4)*</td>
</tr>
<tr>
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<td>71 (6.6)</td>
<td>71 (5.9)</td>
<td>73 (5.0)</td>
</tr>
<tr>
<td>50</td>
<td>72 (7.5)</td>
<td>73 (6.5)</td>
<td>72 (7.8)</td>
<td>72 (5.5)</td>
</tr>
<tr>
<td>60</td>
<td>70 (6.4)</td>
<td>73 (7.0)</td>
<td>71 (7.5)*</td>
<td>73 (5.4)</td>
</tr>
<tr>
<td>70</td>
<td>72 (7.2)</td>
<td>71 (6.0)</td>
<td>71 (8.0)</td>
<td>72 (5.0)*</td>
</tr>
<tr>
<td>80</td>
<td>70 (6.4)</td>
<td>72 (6.4)</td>
<td>72 (6.2)</td>
<td>71 (3.4)*</td>
</tr>
<tr>
<td>90</td>
<td>71 (5.1)</td>
<td>74 (6.7)</td>
<td>71 (8.4)*</td>
<td>71 (5.5)*</td>
</tr>
</tbody>
</table>

* P < 0.05 compared to baseline values before induction of anesthesia.

Table 3
Mean arterial pressure (mmHg) in the four Groups of the study [mean (SD)].

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 20)</th>
<th>Group II (n = 20)</th>
<th>Group III (n = 20)</th>
<th>Group IV (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>89 (5.3)</td>
<td>87 (4.2)</td>
<td>86 (4.7)</td>
<td>89 (6.0)</td>
</tr>
<tr>
<td>Before MR</td>
<td>84 (8.4)</td>
<td>82 (8.5)</td>
<td>80 (6.2)</td>
<td>83 (7.9)</td>
</tr>
<tr>
<td>1</td>
<td>84 (6.5)</td>
<td>81 (5.9)</td>
<td>79 (6.4)*</td>
<td>81 (7.3)*</td>
</tr>
<tr>
<td>3</td>
<td>82 (7.5)*</td>
<td>81 (7.6)*</td>
<td>79 (5.4)*</td>
<td>81 (7.4)*</td>
</tr>
<tr>
<td>5</td>
<td>84 (8.4)</td>
<td>82 (8.1)</td>
<td>80 (6.2)</td>
<td>82 (7.3)*</td>
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<tr>
<td>10</td>
<td>83 (9.5)*</td>
<td>80 (4.1)*</td>
<td>81 (6.3)</td>
<td>84 (7.3)</td>
</tr>
<tr>
<td>15</td>
<td>84 (6.3)</td>
<td>78 (6.9)*</td>
<td>83 (5.5)</td>
<td>84 (6.9)</td>
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<td>20</td>
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<td>80 (6.8)*</td>
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<td>30</td>
<td>82 (7.7)*</td>
<td>79 (6.2)*</td>
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<td>85 (8.6)</td>
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<td>79 (7.4)*</td>
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<td>60</td>
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<td>81 (7.8)*</td>
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<tr>
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<tr>
<td>90</td>
<td>82 (8.2)*</td>
<td>77 (7.4)*</td>
<td>79 (7.6)*</td>
<td>84 (8.6)</td>
</tr>
</tbody>
</table>

* P < 0.05 compared to baseline values before induction of anesthesia.
Cardiac index (CI): As shown in Table 4, there was no significant difference among the four Groups at baseline as well as all through the study period as regards CI. CI showed non significant decrease as a result of administration of general anesthetics in all Groups. Significant changes at certain times of the study are marked with *.

<p>| Table 4 |
| Stroke index (L/min/m²) in the four Groups of the study [mean (SD)] |</p>
<table>
<thead>
<tr>
<th>Group I (n = 20)</th>
<th>Group II (n = 20)</th>
<th>Group III (n = 20)</th>
<th>Group IV (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3.4 (0.34)</td>
<td>3.5 (0.38)</td>
<td>3.4 (0.29)</td>
</tr>
<tr>
<td>Before MR</td>
<td>3.1 (0.45)</td>
<td>3.3 (0.40)</td>
<td>3.2 (0.35)</td>
</tr>
<tr>
<td>1</td>
<td>3.1 (0.38)</td>
<td>3.3 (0.37)</td>
<td>3.2 (0.33)</td>
</tr>
<tr>
<td>3</td>
<td>3.2 (0.32)</td>
<td>3.3 (0.45)</td>
<td>3.2 (0.37)</td>
</tr>
<tr>
<td>5</td>
<td>3.2 (0.38)</td>
<td>3.2 (0.35)</td>
<td>3.2 (0.37)</td>
</tr>
<tr>
<td>10</td>
<td>3.2 (0.48)</td>
<td>3.2 (0.49)</td>
<td>3.3 (0.36)</td>
</tr>
<tr>
<td>15</td>
<td>3.1 (0.37)</td>
<td>3.2 (0.39)</td>
<td>3.2 (0.34)</td>
</tr>
<tr>
<td>20</td>
<td>3.0 (0.32)</td>
<td>3.1 (0.45)</td>
<td>3.2 (0.46)</td>
</tr>
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<td>3.1 (0.35)</td>
<td>3.2 (0.37)</td>
<td>3.1 (0.32)</td>
</tr>
<tr>
<td>40</td>
<td>3.0 (0.40)</td>
<td>3.1 (0.49)</td>
<td>3.1 (0.37)</td>
</tr>
<tr>
<td>50</td>
<td>3.1 (0.39)</td>
<td>3.2 (0.40)</td>
<td>3.2 (0.34)</td>
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<td>3.1 (0.37)</td>
<td>3.1 (0.38)</td>
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<tr>
<td>70</td>
<td>3.0 (0.30)</td>
<td>3.3 (0.40)</td>
<td>3.2 (0.37)</td>
</tr>
<tr>
<td>80</td>
<td>3.0 (0.37)</td>
<td>3.2 (0.36)</td>
<td>3.1 (0.37)</td>
</tr>
<tr>
<td>90</td>
<td>3.0 (0.38)</td>
<td>3.2 (0.28)</td>
<td>3.2 (0.40)</td>
</tr>
</tbody>
</table>

* P < 0.05 compared to baseline values before induction of anesthesia.

Stroke index (SI): As shown in Table 5, there was no significant difference among the four Groups at baseline as well as all through the study period. Stroke index showed non significant decrease after administration of general anesthetics in all Groups. Significant changes at certain times of the study are marked with *.

<p>| Table 5 |
| Stroke index (ml/m²) in the four Groups of the study [mean (SD)] |</p>
<table>
<thead>
<tr>
<th>Group I (n = 20)</th>
<th>Group II (n = 20)</th>
<th>Group III (n = 20)</th>
<th>Group IV (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>52 (6.8)</td>
<td>53 (5.7)</td>
<td>52 (5.1)</td>
</tr>
<tr>
<td>Before MR</td>
<td>47 (8.9)</td>
<td>49 (7.2)</td>
<td>51 (7.0)</td>
</tr>
<tr>
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<td>50 (7.8)</td>
<td>52 (7.2)</td>
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<td>50 (6.9)</td>
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<tr>
<td>70</td>
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<tr>
<td>80</td>
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<td>49 (6.8)</td>
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</tr>
<tr>
<td>90</td>
<td>47 (7.1)</td>
<td>48 (5.4)</td>
<td>51 (6.9)</td>
</tr>
</tbody>
</table>

* P < 0.05 compared to baseline values before induction of anesthesia.

Neuromuscular Monitoring

Depression of $T_1$ of the train-of-four: Administration of muscle relaxants resulted in a variable degree of depression of the $T_1$ twitch of the train-of-four stimulation in the four Groups of the study. To reach the end-point of at least 95% depression of the $T_1$ twitch, all patients required at least two increments of muscle relaxants. Most patients required a third increment, while a few patients required a fourth increment. The mean depression (as percent of baseline) resulting from administration of increments of muscle relaxants are shown in Table 6. No patient in group II required a fourth increment of muscle relaxant.

Cumulative dose-response curves: Figures 3 through 6 represent the cumulative dose-response curves in the four Groups of the study. The thin lines represent the 95% confidence intervals of the regression line. The narrow confidence intervals imply low inter-individual variability in the response to muscle relaxants. It can be shown from the cumulative dose-response curves that a plateau is reached as the dose approaches the ED$_{95}$. From the cumulative dose-
response curves, the ED$_{50}$ and the ED$_{95}$ were calculated in each of the four Groups. The values of ED$_{50}$, ED$_{95}$, the ED$_{95}$/ED$_{50}$ ratio and the slope of the regression curve in the four Groups are shown in Table 3-9, together with their 95% confidence intervals. Values of ED$_{50}$ and ED$_{95}$ in the sevoflurane Groups were significantly lower than those in the propofol Groups for each muscle relaxant.

Table 6

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>First increment</td>
<td>27 (9.2)</td>
<td>36 (4.4)</td>
<td>14 (4.8)</td>
<td>13 (4.3)</td>
</tr>
<tr>
<td>Second increment</td>
<td>90 (7.2)</td>
<td>93 (2.0)</td>
<td>78 (6.8)</td>
<td>78 (3.9)</td>
</tr>
<tr>
<td>Third increment</td>
<td>97 (1.8)</td>
<td>98 (1.8)</td>
<td>95 (3.1)</td>
<td>90 (3.2)</td>
</tr>
<tr>
<td>Fourth increment</td>
<td>100 (0.0)</td>
<td>100 (1.2)</td>
<td>97 (1.8)</td>
<td>97 (1.8)</td>
</tr>
</tbody>
</table>

Fig. 3

Cumulative dose-response curve for rocuronium in patients anesthetized with sevoflurane. Horizontal bars represent the individual observations. The thick solid line represents the best-fit regression line. The upper and the lower thin solid lines represent the 95% confidence limits of the regression line.

Fig. 4

Cumulative dose-response curve for cisatracurium in patients anesthetized with sevoflurane. Horizontal bars represent the individual observations. The thick solid line represents the best-fit regression line. The upper and the lower thin solid lines represent the 95% confidence limits of the regression line.
However, the slope of the curve and the ED$_{95}$/ED$_{50}$ ratio were comparable among the Groups (Table 7). The cumulative dose-response curve was shifted to the left with sevoflurane anesthesia as compared to propofol anesthesia for each of the muscle relaxants (Fig. 7 & 8). The slope of the curve was not much affected by changing the anesthetic.

**Table 7:**

Values of ED$_{50}$, ED$_{95}$, eED95/ED50 ratio and the slope of the regression curve in the four Group of the study.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED$_{50}$ (µg/kg)</td>
<td>Mean</td>
<td>124</td>
<td>17</td>
<td>150*</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>119.9 to 128.0</td>
<td>16.8 to 17.2</td>
<td>146.8 to 153.9</td>
</tr>
<tr>
<td>ED$_{95}$ (µg/kg)</td>
<td>Mean</td>
<td>238</td>
<td>32</td>
<td>295*</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>215.1 to 267.1</td>
<td>30.5 to 34.2</td>
<td>276.1 to 316.2</td>
</tr>
<tr>
<td>ED$<em>{95}$/ED$</em>{50}$</td>
<td>Mean</td>
<td>1.92</td>
<td>1.90</td>
<td>1.96</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>1.68 to 2.23</td>
<td>1.77 to 2.04</td>
<td>1.79 to 2.15</td>
</tr>
<tr>
<td>Slope</td>
<td>Mean</td>
<td>4.519</td>
<td>4.600</td>
<td>4.376</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>4.002 to 5.035</td>
<td>4.293 to 4.907</td>
<td>4.088 to 4.665</td>
</tr>
</tbody>
</table>

* * P < 0.01 compared with group I. † P < 0.01 compared with group II.
Recovery from muscle relaxation: Time to recovery of T₁ to 25% of baseline (T₂₅%) was not significantly different with the different anesthetics or muscle relaxants; while time to recovery of T₁ to 75% of baseline (T₇₅%), the recovery index (the difference between T₇₅% and T₂₅%) and time required for return of TOF ratio to 0.7 (TOF₀.₇) were significantly prolonged by the use of sevoflurane compared with propofol, and were significantly longer with cisatracurium than rocuronium (Table 8).

 Recorded Side Effects

Three patients in the propofol with rocuronium Group elicited pain on drugs injection and postoperative phlebitis. Also we report two cases of postoperative nausea and vomiting in the sevoflurane Groups, one in each Group.

### Table 8

<table>
<thead>
<tr>
<th>Group</th>
<th>Recovery Criteria [mean (SD)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T₂₅% (min)</td>
</tr>
<tr>
<td>Group I (n = 20)</td>
<td>18 (4.8)</td>
</tr>
<tr>
<td>Group II (n = 20)</td>
<td>19 (4.5)</td>
</tr>
<tr>
<td>Group III (n = 20)</td>
<td>15 (3.3)</td>
</tr>
<tr>
<td>Group IV (n = 20)</td>
<td>16 (6.3)</td>
</tr>
</tbody>
</table>

T₂₅% = time to recovery of T₁ to 25% of baseline; T₇₅% = time to recovery of T₁ to 75% of baseline; Recovery index = the difference between T₇₅% and T₂₅%; TOF₀.₇ = time necessary for the TOF ratio to return to 0.7. *P < 0.05, same muscle relaxant, different anesthetic, † P < 0.05, same anesthetic, different muscle relaxant.
Discussion

This comparative study determined the influence of sevoflurane on the dose response relationship of either rocuronium or cisatracurium compared to a TIVA with propofol as well as hemodynamic effects of both relaxants under the two anesthetics. The neuromuscular blocking effect of rocuronium and cisatracurium were enhanced by sevoflurane. The interaction between sevoflurane and both neuromuscular blocking drugs (NMBD) led to increased intensity of block and prolongation of recovery in comparison to TIVA with propofol.

Usually, potentiation of NMBD by volatile anesthetics results predominantly in prolongation of the duration and recovery of neuromuscular block. Recovery was prolonged significantly by the volatile anesthetic sevoflurane under the conditions of the present study. The prolongation of the effect of rocuronium or cisatracurium during sevoflurane anesthesia is probably caused by a faster and more complete equilibrium among the end-tidal, blood, and muscle concentrations of sevoflurane because of its smaller muscle-gas partition coefficient, resulting in slower recovery, as seen in all groups under sevoflurane anesthesia. As regarding the potency (augmentation of depression of T1), we determined the anesthesia-related effects of cisatracurium and rocuronium but not the absolute potency data.

The cumulative dose technique may underestimate the potency of neuromuscular blocking agents. However, administration of both, cisatracurium and rocuronium was standardized and the use sevoflurane or TIVA with propofol was randomized; thus the cumulative pattern of cisatracurium and rocuronium administration would have similar effects in all groups.

In the present study values of ED50 and ED95 in the sevoflurane Groups were significantly lower than those in the propofol Groups for each muscle relaxant. The values of mean ED50 and ED95 of rocuronium were lower during sevoflurane anesthesia than with TIVA. Similarly the values of mean ED50 and ED95 of cisatracurium were lower during sevoflurane anesthesia than with TIVA. However, the slope of the curve and the ED95/ED50 ratio were comparable among the Groups. The cumulative dose-response curve was shifted to the left with sevoflurane anesthesia as compared to propofol anesthesia for each of the muscle relaxants. It was found that degree of potentiation (ratio of ED50 during TIVA/ED50 during volatile anesthesia) was 1.2 for sevoflurane in both types of relaxants.

Using a single-dose technique for rocuronium, Oris et al. reported a lower ED50 during halothane, isoflurane and enflurane anesthesia compared to TIVA using a cumulative dosing technique. Similarly, Lowry et al. demonstrated a significant increase in the apparent potency of rocuronium during anesthesia with 1.5 MAC of sevoflurane compared with propofol anesthesia. The study of Xue et al. estimated the potency of rocuronium during sevoflurane and thiopental-nitrous oxide anesthesia and found values in broad agreement with our results. Thomas et al. investigated the interaction between the cumulative dose requirements of cisatracurium and anesthesia with isoflurane, sevoflurane, desflurane or propofol using closed-loop feedback control. They found that in comparison to propofol, isoflurane, sevoflurane and desflurane reduce the cumulative dose requirements of cisatracurium by 42%, 41% and 60%, respectively to maintain a 90% depression of T1 of TOF. Kopman et al. suggested that drug potency may be more intense under N2O anesthesia compared with total IV anesthesia (TIVA).

Regarding the clinical duration, we found that it was not significantly different with the different anesthetics or muscle relaxants. Lowry et al. demonstrated that the time course of action after a bolus dose of rocuronium 0.6 mg/kg that was studied in patients anesthetized with 66% nitrous oxide in oxygen and 1.5 minimum alveolar anesthetic concentration of sevoflurane or isoflurane, or a propofol infusion did not differ significantly among groups. Similarly Wulf et al. concluded that following equi-effective dosing of rocuronium (T1 > 95%), the clinical duration to 25% T1 recovery during desflurane, isoflurane, sevoflurane and total intravenous anesthesia did not result in significant difference among these groups.

Regarding recovery in the present study, T25% the recovery index and TOF0.7 were significantly prolonged by the use of sevoflurane compared with propofol, and were significantly longer with cisatracurium than rocuronium. Reid et al. demonstrated that recovery from rocuronium induced neuromuscular block was slowed in the presence of potent volatile
agents in comparison to TIVA, and that this effect is more marked in patients receiving sevoflurane. Similarly Bock et al.19 studied recovery characteristics of rocuronium during 1.25 MAC of isoflurane, desflurane, and sevoflurane or propofol anesthesia in 84 patients using electromyography. After 120 min, the cumulative infusion rate of rocuronium required to obtain twitch depression of 90-95%, recovery index was prolonged under isoflurane, sevoflurane and desflurane anesthesia, in comparison to propofol. There were no significant differences between the three potent inhalation anesthetics in relation to recovery characteristics of rocuronium.

Cisatracurium is the only neuromuscular blocker that is both free of histamine-releasing properties and that undergoes organ-independent Hofmann elimination1. Other studies20-21 demonstrated that hemodynamically stable patients receiving a rapidly administered bolus dose of 6-8 x ED95 of cisatracurium did not have hemodynamic changes that would be expected with a histamine-releasing compound. However, with bolus administration of rocuronium, some studies documented an increase in heart rate (HR), pulmonary vascular resistance (PVR), stroke index (SI) and cardiac index (CI), with decreased pulmonary capillary wedge pressure (PCWP), whereas other studies found no hemodynamic changes1.

In our study, propofol and sevoflurane anesthesia induced non statistically significant hypotension and bradycardia in all Groups before administration of the muscle relaxants. There were no evidences of any significant clinical cardiovascular changes (Heart rate, MAP, SI, CI) when comparing post induction values to those after administration of cisatracurium or rocuronium, but there were statistically significant decline in MAP and CI at certain periods in comparison to preinduction values, attributed to the interaction between the relaxant used and maintenance agents. Heart rate in sevoflurane groups did not change significantly from baseline all through the study period, whereas some readings of heart rate in the propofol Groups were significantly lower than their baseline. SI in the propofol Groups remained comparable to baseline all through the study period whereas, SI decreased significantly relative to its baseline in the sevoflurane Groups at some points of study. However, these points of decline in all previous hemodynamic parameters, although statistically significant, but are clinically not significant and required no medications to treat adverse hemodynamic events.

Researches22 found no clinical significant hemodynamic changes after rocuronium administration, but differed from others23 that showed that a dose of 0.9 mg/kg rocuronium (3x ED95) caused some cardiovascular effects (10-15% increase in mean arterial pressure and 5-10% increase in heart rate). These effects although statistically significant, are not likely to be clinically important, however, our study showed absence of statistically significant difference before and after administration of rocuronium due to the small dose equaling ED95 that was given in increments.

Naguib et al.24 found that administration of rocuronium 0.6 mg.kg-1 caused no significant changes in plasma histamine concentrations or in hemodynamic state at any time. Mark et al.25 found that the hemodynamic profile of a 0.6 mg.kg-1 bolus of rocuronium was acceptable for patients with coronary artery disease, and changes that occurred would not promote increases in myocardial oxygen demand or further decreases in oxygen supply. Although CVP and MPAP decreased significantly, rocuronium had no effect on PCWP, SVR, MAP, or CI. Overall, these results indicate that clinical doses of rocuronium are not associated with hemodynamic instability in ASA class 3 and 4 patients undergoing cardiac surgery.

NMB AGENTS & HEMODINAMIC EFFECTS

Cisatracurium is the only neuromuscular blocker that is both free of histamine-releasing properties and that undergoes organ-independent Hofmann elimination1. Other studies20-21 demonstrated that hemodynamically stable patients receiving a rapidly administered bolus dose of 6-8 x ED95 of cisatracurium did not have hemodynamic changes that would be expected with a histamine-releasing compound. However, with bolus administration of rocuronium, some studies documented an increase in heart rate (HR), pulmonary vascular resistance (PVR), stroke index (SI) and cardiac index (CI), with decreased pulmonary capillary wedge pressure (PCWP), whereas other studies found no hemodynamic changes1.

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in a subparalysing dose, 50-100% of patients report discomfort. Also in our study, we reported two cases of postoperative nausea and vomiting in the sevoflurane Groups. In most meta-analyses, propofol was associated with a lower frequency of PONV when used for total intravenous anesthesia in the absence of N₂O. In one meta-analysis, the rate of PONV was lower with the use of propofol when compared with sevoflurane.

From the previous clinical study, the effects of rocuronium and cisatracurium are enhanced by sevoflurane, in comparison to TIVA with propofol anesthesia, and there recovery is slower. Particular attention should be paid to monitoring of neuromuscular block during sevoflurane anesthesia with careful titration of relaxants’ doses to avoid inadvertent prolongation of recovery. The combination of sevoflurane and cisatracurium resulted in the longest duration of recovery between Groups and recommended for long procedures while the combination of rocuronium and TIVA with propofol resulted in the shortest duration of recovery in comparison to all Groups and recommended for short and day case procedures.

When cardiovascular stability is of importance, the use of rocuronium and cisatracurium are recommended, as well as sevoflurane (producing more stable heart rate than TIVA with propofol).
References


IS I-GEL A NEW REVOLUTION AMONG SUPRAGLOTTIC AIRWAY DEVICES?

- A Comparative Evaluation -

PARUL JINDAL*, ASLAM RIZVI** AND JP SHARMA***

Summary

In an attempt to reduce the pressor responses subsequent to laryngoscopy and intubation in normotensive anesthetized paralysed patients, the hemodynamic effects of three supraglottic devices were compared: I-gel, SLIPA, and LMA. The I-gel produced the least hemodynamic changes.

Keywords: LMA, I-gel, SLIPA, Hemodynamic changes.

Introduction

Discovery of endotracheal intubation has not only made administration and maintenance of anesthesia easy, but has also helped in saving several lives. Endotracheal intubation is usually carried out under direct vision made possible by direct laryngoscopy, which in healthy patient, may not lead to serious complications.

Laryngoscopic stimulation of oropharyngolaryngeal structures may be an important factor in the hemodynamic stress response associated with tracheal intubation\(^1\). The sudden rise in blood pressure may cause left ventricular failure, myocardial ischemia or cerebral hemorrhage in the presence of coronary or cerebral atheroma or hypertension. In these conditions it can even become life threatening\(^3\).

Attempts to prevent the pressor response to laryngoscopy and intubation are being made. By using alternative guiding devices such as fibreoptic scope\(^4\), light wand\(^5\) or laryngeal mask airway\(^6\) (LMA), the incidence pressor response may be reduced\(^7\).

In recent years, the I-gel, another supraglottic airway device with some distinctive features, has been devised that sets it apart from other competitors\(^8\). The I-gel is competing to be the easiest and simplest device.

The aim and objectives of the present study is to evaluate and compare the hemodynamic changes during insertion of supraglottic devices LMA, SLIPA or I-gel and to report on the technic of airway instrumentation that is less likely to produce hemodynamic changes in patients undergoing elective surgery.

From Dept of Anaesthesiology, Intensive Care and Pain Management, Himalayan Institute of Medical Sciences, Dehradun (Uttarakhand).

* MD, Assistant Professor.
** MD, Resident.
*** MD, Professor & Head.

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Materials and Methods

The study was conducted in the Department of Anaesthesiology & ICU, HIMS, Dehradun from October 1, 2007 to March 31, 2008. Following approval of the Hospital Committee and the fully informed consent of patients, a prospective study was conducted on 75 patients of either sex, 20-70 years, ASA I and II, scheduled to undergo elective surgical procedures under general anesthesia. Exclusion criteria consisted of patients with ASA III, IV, blood pressure ≥150/100 mmHg, history of sore throat within the previous 10 days, full stomach, patients scheduled for head, neck surgery and patients with potential difficult airway, MP grade IV.

After a detailed history, general and systemic examinations and airway assessment (using MP classification), opening a sealed envelop, the 75 patients were divided into three equal groups (25 each) to receive either one of three supraglottic devices: I-gel (Group I), SLIPA (Group II) or LMA (Group III).

All patients were kept fasting for 8 hours before surgery and all received diazepam tab. 10 mg at night and 5 mg at 6 am in the morning of surgery.

After confirming consent and fasting status, an iv line was established with 18G cannula and ringer lactate was started. All the monitors were placed and baseline reading of HR, BP, SpO₂, ECG were noted. The patient was in supine position and head was placed on a pillow 7 cm in height.

Following, preoxygenation with 100% oxygen, patients were induced with propofol 1.5-2.5 mg/kg slowly and vecuronium 0.1 mg/kg facilitate intubation. All three supraglottic devices were introduced using the standard techniques by a single anesthesiologist who is noted to possess considerable experience in all three techniques (approximate number of uses, I-gel >150; SLIPA >150; and LMA >200).

Maintenance of anesthesia was done with 66% N₂O in oxygen, muscle relaxant vecuronium 0.015 mg/kg and morphine 0.1 mg/kg. Surgeons were requested not to clean, drape or position patient till 5 minutes after placement of supraglottic devices so as to avoid any stimuli likely to interfere with the findings.

The following data were collected by an blinded observer:

(a) number of intubation attempts
(b) intubation time (time from insertion of the intubating device into the mouth, to time of confirmation by mechanical ventilation)
(c) mucosal trauma (blood detected on the intubation device after use)
(d) lip or dental injury
(e) episodes of hypoxia during intubation (SpO₂ <95%)
(f) serial heart rate, arterial pressure, SpO₂ and ECG recording were done at the time of insertion, 1, 3 and 5 minutes following insertion thereafter at the time of removal and then 1 min after removal.

At end of surgery neuromuscular block was reversed with neostigmine 50 µg/kg and gentle assisted ventilation was done to allow patient to breathe spontaneously considering the extubation criteria. When reflexes were restored and the patient was able to open mouth on command, the devices were removed. Oral suctioning was done and the airway patency and respiratory depth were confirmed.

Statistical analysis was done using two sample ‘t’ test and by chi-square test.

Results

There were no differences in demographic and airway assessment data among the three groups. The number of intubation attempts was similar among groups, but intubation time was significantly longer in the LMA group (Table 1).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients’ Characteristics, Airway Assessment, and Intubation Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I (I-gel)</td>
</tr>
<tr>
<td>Age: Mean ± SD</td>
<td>38.52 ± 8.89</td>
</tr>
<tr>
<td>Range</td>
<td>22-53</td>
</tr>
<tr>
<td>Sex</td>
<td>Female: 13:12</td>
</tr>
<tr>
<td>ASA Grade I:II</td>
<td>19:06</td>
</tr>
<tr>
<td>MP Grade I:II</td>
<td>13:12</td>
</tr>
<tr>
<td>No. of Attempts I:II</td>
<td>24:1 (96%; 4%)</td>
</tr>
<tr>
<td>Duration of intubation Mean ± SD</td>
<td>3.48 ± 1.41</td>
</tr>
</tbody>
</table>
The Hemodynamic changes

Heart Rate

No significant change in heart rate in group (I-gel) was observed. In group II (SLIPA) there were significant changes during removal and 1 min after removal when compared to baseline. On comparing group I to group II there was no significant change in heart rate at any time. On comparing group II (SLIPA) with group III (LMA), there were significant changes at the time of insertion and 1 min after insertion (Fig 1).

Systolic Blood Pressure

In all three groups, there was significant difference in systolic blood pressure from baseline till 5 min after insertion and highly significant difference at the time of removal in group I. On comparing group I and II and group II with group III there was significant difference at 1, 3, 5 min after insertion and at removal (Fig. 2).

Diastolic Blood Pressure

In Group I, significant difference in diastolic blood pressure (DBP) was seen from 1 min after insertion to 5 min after insertion. Group I & II showed no significant difference in DBP at 3 & 5 minutes after insertion. On comparing Group I & III and Group II & III there was significant difference from insertion to 5 min after insertion (Fig. 3).

Mean Arterial Pressure

In Group I there was significant difference in MAP from baseline. On comparing Group I & II and Group I & III, there was significant difference in MAP at 3 and 5 minutes after insertion (Fig. 4).
Table 2
Comparison various hemodynamic parameters among all groups

<table>
<thead>
<tr>
<th></th>
<th>I-gel (Group I)</th>
<th>SLIPA (Group II)</th>
<th>LMA (Group III)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>2.4% ↓ at I-0</td>
<td>2.4% ↓ at I-0</td>
<td>11.2% ↑ at I-0</td>
</tr>
<tr>
<td></td>
<td>9.5% ↓ at I-5</td>
<td>10% ↓ at I-5</td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>12.2% ↓ at I-0</td>
<td>8.27% ↓ at I-0</td>
<td>12.5% ↑ at I-0</td>
</tr>
<tr>
<td>DBP</td>
<td>16.7% ↓ at I-5</td>
<td>7.31% ↓ at I-5</td>
<td>20% ↑ at I-5</td>
</tr>
<tr>
<td>MAP</td>
<td>10.5% ↓ at I-0</td>
<td>3.44% ↓ at I-0</td>
<td>19.3% ↑ at I-0</td>
</tr>
<tr>
<td></td>
<td>18.5% ↓ at I-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPP</td>
<td>13.7% ↓ at I-0</td>
<td>1.3% ↓ at I-0</td>
<td>3.4% ↓ at I-5</td>
</tr>
<tr>
<td></td>
<td>25% ↓ at I-5</td>
<td></td>
<td></td>
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</table>

At time of insertion, there was no fall in saturation, dental and mucosal trauma or ECG changes, in any of the groups.

Discussion
The I-gel is a new single-use, noninflatable supraglottic airway for use in anesthesia during spontaneous or intermittent positive pressure ventilation. The I-gel airway an anatomically designed mask made of a gel-like thermoplastic elastomer.
I-gel is available in three sizes size 3, 4, 5. An endotracheal tube (CETT) can be passed through the device. When correctly inserted, the tip of the I-gel will be located into the upper esophageal opening, providing a conduit via the gastric channel to the esophagus and stomach. This then allows for suctioning, passing of a nasogastric tube and can facilitate venting.

The maximum size of cuffed ETT and nasogastric tube that can be passed through each size of I-gel is as follows:

| Size 3 I-gel | Maximum size of CETT 6.0 mm |
| Size 4 I-gel | Maximum size of CETT 7.0 mm |
| Size 5 I-gel | Maximum size of CETT 8.0 mm |
- 12G nasogastric tube
- 14G nasogastric tube

In our study, it was observed that I-gel produced less hemodynamic changes than SLIPA which is also a non-inflatable supraglottic device. This difference could be because SLIPA, is made of moulded plastic (polypropylene) that does not conform to anatomic structures.

The tensile properties of the I-gel bowl, along with its shape and the ridge at its proximal end, contribute to the stability of the device upon insertion. Upon sliding beneath the pharyngo-epiglottic folds it becomes narrower and longer, creating an outward force against the tissues. The ridge at the proximal bowl catches the base of the tongue, also keeping the device from moving upwards out of position (and the tip from moving out of the upper esophagus).

I-gel does not have any epiglottic/aperture bars like some other supraglottic devices. I-gel has an artificial epiglottis called the ‘epiglottis blocker’ which prevents epiglottis from down-folding. But in case epiglottis does down-fold, the airway channel exits so deeply into the bowl of the cuff that there is no danger of the epiglottis interfering with the fresh gas flow.

In a study on 100 patient by Gabbot DA et al it was observed that the seal pressures by I-gel were good. Peak airway pressures above 30 cm H₂O were possible in the vast majority of patients (mean and median 32 cm H₂O). The mean and median leak on sustained pressure (with the circle gas flows of 4 L min⁻¹ and the APL valve closed) was 24 cm H₂O. They compared this finding with the previous findings of 18-21 cm H₂O for the cLMA and 29 cm H₂O for the Proseal LMA. They also observed that the seal pressure appeared to improve over time in a number of patients and postulated that this might be due to the thermoplastic properties of the gel cuff which may form a more efficient seal around the larynx after warming to body temperature.

It has been mentioned that insertion of the I-gel does not require any maneuver but in our cases we had to depress the tongue by a finger for easy insertion.
impulses to the vasomotor centre which in turn activate sympahtoadrenal system to release catecholamine resulting in increase of increased cardiac output, rather than increased systemic vascular resistance. The cardiovascular response is maximum during the stimulation of epipharynx whereas those arising from the stimulation of tracheobronchial tree are least marked. During removal of LMA the hemodynamic response is probably triggered by pharyngeal stimulation during reverse rotation of the cuff.

There are limitations to our study. First, insertions were done in patients with normal airway (MP grade, I, II) and normotensive patients. Our results may not apply to patients with difficult airways and hypertensive patients. Second, our results are specific to the anesthetic administered and might not apply for other anesthesia regimes such as the use of large-dose narcotics.

### References


### Conclusion

**I-gel** effectively conforms to the perilaryngeal anatomy despite the lack of an inflatable cuff, it **consistently achieves proper positioning** for supraglottic ventilation and causes **less hemodynamic changes** as compared to other supraglottic airway devices.

### Acknowledgements

We are grateful to Mr. David Chapman, Ariway Manager of Intersurgical Ltd. (Wokingham, Berkshire UK) who provided free samples of the device. The company however was neither involved in data collection and analysis nor in manuscript preparation. We are also grateful to Mr. Pradeep Khanduja of CSI enterprises Pvt Ltd (Intersurgical) for his kind support.
JAW THRUST AS A PREDICTOR OF INSERTION CONDITIONS FOR THE PROSEAL LARYNGEAL MASK AIRWAY

RUSSELL TOWNSEND*, JOSEPH BRIMACOMBE**, CHRISTIAN KELLER***, VOLKER WENZEL **** AND HOLGER HERFF*****

Abstract

We test the hypothesis that the response to jaw thrust is an effective predictor of insertion conditions for the ProSeal laryngeal mask airway (ProSeal LMA). One hundred and sixty patients (ASA grade 1-3, aged >18 yr) were studied. Five anesthetists blinded to the response to jaw thrust participated in the study, each performed >30 insertions. Induction of anesthesia was with propofol titrated to loss of lash reflex and apnea. A standard amount of jaw thrust was applied and any motor response noted by three observers. The ProSeal LMA was inserted using the standard digital technique. Insertion conditions were considered optimal if there was no motor or upper airway reflex response to insertion. There was no response to jaw thrust in 86% (137/160) of patients and insertion was optimal in 76% (121/160) of patients. A response to jaw thrust predicted suboptimal insertion conditions in 74% (17/23) and a lack of response predicted optimal insertion conditions in 84% (115/137). The accuracy, sensitivity and specificity were 0.82, 0.95 and 0.44, respectively. We conclude that jaw thrust is a reliable predictor of insertion conditions for the ProSeal LMA with the digital insertion technique after induction of anesthesia with propofol. We suggest that clinicians learn how to apply the correct amount of jaw thrust and perform this test routinely.

Keywords: ProSeal laryngeal mask airway; clinical test; jaw thrust; complications.

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Disclosure: this project was supported solely by Department resources. Drs Brimacombe and Keller have worked as consultants for the laryngeal mask company which manufactures the ProSeal laryngeal mask airway.
Introduction

Failure to achieve an adequate depth of anesthesia is perhaps the commonest cause of problems during insertion of extraglottic airway devices in non-paralysed patients. Such problems vary in severity from gagging and coughing to laryngospasm and aspiration. Clearly, a reliable, routinely performed clinical test for depth of anesthesia would help obviate such problems. Potential tests include, loss of lash reflex, jaw relaxation, apnea, ease of face mask ventilation, dropping a weighted syringe, loss of verbal contact, bispectral index and the motor response to jaw thrust. There have only been three studies investigating this issue: two showed that dropping a weighted syringe was unreliable1,2 and one that loss of verbal contact was unreliable3.

However, Drage and colleagues found that the motor response to jaw thrust was a reliable indicator for insertion of the classic laryngeal mask airway following induction of anesthesia with propofol3.

The ProSeal laryngeal mask airway (ProSeal LMA) is a improvement of the classic LMA with a modified cuff to increase the seal and a drain tube to provide a channel for regurgitated fluid, prevention of gastric insufflation and insertion of a gastric tube4,5. We test the hypothesis that the motor response to jaw thrust is an effective predictor of insertion conditions for the ProSeal LMA.

Materials and Methods

After Ethics Committee approval and written informed consent, we studied 160 consecutive patients, (ASA 1-3, aged >18 yr) scheduled for elective surgery with the ProSeal LMA as the airway device. Patients were excluded if they had a known difficult airway, jaw pathology or mouth opening less than 5 cm, were at risk of aspiration (unfasted, gastro-esophageal reflux) or had a body mass index greater than 35 kg.m⁻².

Patients were not premedicated. A standard anesthesia protocol was followed and routine monitoring was applied. Anesthesia was conducted in the supine position with the patient’s head on a standard pillow, 7 cm in height. The patient was pre-oxygenated for 3 minutes. Fentanyl 0.5-1.5 µg.kg⁻¹ i.v was administered and then propofol titrated at approximately 100 mg.min⁻¹ until loss of lash reflex and apnea. The lungs were manually inflated via a face mask using sevoflurane 5% in oxygen 100% for 30 sec. A Guedel airway was not used. The propofol contained lignocaine 1 mg.ml⁻¹ to reduce pain on injection.

Jaw thrust was applied by a single operator who had been trained to apply a standard amount of force. The technique involved placing the three middle fingers of each hand behind the angle of the jaw and lifting it anteriorly for 5 seconds using a total of 500g of force. Training involved learning the force required to lift a 500g weight using the middle three fingers of both hands. Any motor or upper airway reflex response was noted by three observers.

The anesthetist, who was blinded to the response to jaw thrust by facing away from the patient during jaw thrust, inserted the ProSeal LMA using the standard digital technique. This involved an assistant opening the mouth, placing the fully deflated cuff flat against the hard palate and pressing the device into and pushing it along the palatopharyngeal curve. A size 4 was used for females and a size 5 for males. Once inserted, the cuff was inflated with air, the proximal tube connected to the anesthesia breathing system and manual ventilation commenced.

A maximum of two attempts were allowed to obtain an effective airway. An attempt was defined as removal of the device from the mouth. An effective airway was defined as two consecutive breaths with an expired tidal volume ≥6 ml/kg. Ease of insertion was scored by the three observers and was graded as:

1) optimal-no motor response or upper airway reflex activation to insertion

2) suboptimal-motor response or upper airway reflex activation to insertion.

The study end-point was a response to insertion or effective ventilation if there was no response to insertion. After the study end-point, the patients was managed according to the preference of the clinician.

All insertions were done by five anesthetists (>6 month training) who were proficient with the ProSeal LMA (>50 uses). Each anesthetist performed >30 insertions. Sample size was based upon a projected difference of 15% for optimal ProSeal LMA insertion conditions, a type I error of 0.05 and a power of 0.90,
and was based on a 87% incidence of optimal insertions conditions from a previous study⁴.

Results

The mean (range) age and weight of patients were 47 (18-88) yr and 76 (39-125) kg. There were 78 females and 82 males. The mean ± sd dose of fentanyl and propofol were 1.45 ± 0.23 µg.kg⁻¹ and 2.53 ± 0.62 mg.kg⁻¹, respectively. There were no interobserver variations in observations. There were no differences in performance among anesthetists. The results are presented in Table 1. There was no response to jaw thrust in 86% (137/160) of patients and insertion was optimal in 76% (121/160) of patients. The response to jaw thrust predicted suboptimal insertion conditions in 74% (17/23; 95% CI 54-93%) and a lack of response predicted optimal insertion conditions in 84% (115/137; 95% CI 78-90%). The accuracy, sensitivity and specificity were 0.82, 0.95 and 0.44, respectively. An effective airway was obtained in 94% (114/121) of patients in whom there was no response to insertion.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Optimal conditions</th>
<th>Suboptimal conditions</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No motor response</td>
<td>115</td>
<td>22</td>
<td>137</td>
</tr>
<tr>
<td>to jaw thrust</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor response to</td>
<td>6</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>jaw thrust</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>121</td>
<td>39</td>
<td>160</td>
</tr>
</tbody>
</table>

Discussion

We found that the response to jaw thrust predicted optimal and suboptimal insertion conditions for the ProSeal LMA in 84 and 74% of patients, respectively. This supports the findings of Drage and colleagues³, who showed that it predicted optimal and suboptimal insertion conditions for the classic LMA in 87 and 80% of patients, respectively, using a similar dose of propofol and a similar insertion technique.

Jaw thrust does not predict the probability of insertion success; it only predicts the probability of patients defense reactions on insertion attempt of a ProSeal LMA. Nevertheless, these defense reactions could not only make insertion more difficult, they may even endanger the patient by regurgitation or they may result in injuries of the upper airway while inserting the ProSeal LMA. Therefore, it could be useful for clinicians to apply the correct amount of jaw thrust before induction of a ProSeal LMA to avoid these unpleasant and potentially dangerous defense reactions. Our study suggests that the response to jaw thrust is sufficiently reliable for routine use when digital insertion and propofol are employed with a ProSeal LMA.

An effective airway was only obtained in 94% of patients despite optimal insertion conditions. This is similar to the established success rate for insertion of the ProSeal LMA using the digital technique⁴,⁵. The most common causes of failure are an inability to insertion the ProSeal LMA into the pharynx and malposition once in the pharynx⁶. Much higher success rates can be obtained using guided techniques which prevent impaction at the back of the mouth and ensure correct positioning⁷.

Our study has several limitations. First, our findings may not apply to other insertion techniques (such as the laryngoscope-guided technique) or other laryngeal mask airway devices (such as the intubating LMA), as the level of stimulation may be different. However, there is indirect evidence that the level of stimulation from other insertion techniques is similar for the ProSeal LMA⁷; and Drage and colleagues showed that the response to jaw thrust is a reliable indicator for classic LMA insertion. Second, our findings may not apply to other induction agents, particularly those that are less effective at obtunding upper airway reflexes, such as thiopentone⁸. Third, we did not determine the optimal level of jaw thrust and our findings may not apply if different level of jaw thrust are used. The optimal amount of jaw thrust would be that with the highest predictive value without morbidity. Finally, we did not formally assess any airway morbidity associated with jaw thrust. Perhaps jaw thrust increases the frequency of jaw ache, as occurs during face mask anesthesia⁹.

We conclude that jaw thrust is a reliable predictor of insertion conditions for the ProSeal LMA with the digital insertion technique after induction of anesthesia with propofol. We suggest that clinicians learn how to apply the correct amount of jaw thrust and perform this test routinely.
References


REMIFENTANIL-PROPOFOL VS DEXMEDETOMIDINE-PROPOFOL

- Anesthesia for Supratentorial Craniotomy -

NAMIGAR TURGUT*, AYGEN TURKMAN*, ACHMET ALI*, and AYSEL ALTAN*

Abstract

The aim of the present study was to compare the perioperative hemodynamics, propofol consumption and recovery profiles of remifentanil and dexmedetomidine when used with air-oxygen and propofol, in order to evaluate a postoperative analgesia strategy and explore undesirable side-effects (nausea, vomiting, shivering).

In a prospective randomized double-blind study 50 ASA-I-III patients scheduled for supratentorial craniotomy, were allocated into two equal Groups. Group D patients (n = 25), received i.v. dexmedetomidine 1 µg kg\(^{-1}\) as preinduction over a 15-min period and 0.2-1 µg kg\(^{-1}\)hr\(^{-1}\) by continuous i.v. infusion during the operation period. Group R patients (n = 25), received remifentanil 1 µg kg\(^{-1}\) as induction i.v. over a 15-min period and 0.05-1 µg kg\(^{-1}\)min\(^{-1}\) as maintenance. The propofol infusion was started at a rate of 10 mg kg\(^{-1}\)h\(^{-1}\) and titrated to maintain BIS in the range 40-50.

Propofol doses for induction and maintenance of anesthesia was lower with dexmedetomidine (respectively p < 0.05, p < 0.01). The time for BIS to reach 50 was significantly shorter in Group D (p < 0.01). Comparison of the parameters of recovery revealed; exubation time (p < 0.01); response to verbal commands (p < 0.05) and time for orientation (p < 0.05) were longer with Group D. With respect to Post Anesthesia Care Unit (PACU) discharge time, dexmedetomidine patients required longer time when compared to remifentanil patients to achieve their first normal neurological score (33 min vs 31 min). The earliest opioid administration was at 38 min. in the dexmedetomidine group and 33 min. in the remifentanil group. Propofol-remifentanil and propofol-dexmedetomidine are both suitable for elective supratentorial craniotomy and provide similar intraoperative hemodynamic responses and postoperative adverse events. Propofol-remifentanil allows earlier cognitive recovery; however, it leads to earlier demand for postoperative analgesics. Undesirable side-effects were similar in two Groups.

Keywords: Dexmedetomidine, remifentanil, propofol, neurosurgery.
Introduction

Because of its rapid onset of action and ultra-short duration, the effect of remifentanil hydrochloride does not increase with prolonged administration. Therefore, it is useful in settings, such as intracranial surgery, when rapid drug titration and recovery from anesthesia would be advantageous. Remifentanil may thus have benefits through enhancing timely and complete neurological assessments of patients shortly after the completion of surgery. It is generally known that a good anesthetic agent provides hemodynamic stability without any side effects.

Dexmedetomidine on the other hand, is the pharmacologically active dextroisomer of medetomidine that displays specific and selective α₂-adrenoceptor agonism. Activation of the receptors in the brain and spinal cord inhibits neuronal firing and causes hypotension, bradycardia, sedation, and analgesia. Presynaptic activation of α₂-adrenoceptors in the central nervous system (CNS) inhibits sympathetic activity, possibly leading to a decrease in blood pressure and heart rate.

The aims of the present study were:

1. To compare the perioperative hemodynamics, propofol consumption, and recovery profiles of remifentanil and dexmedetomidine when used with air-oxygen and propofol
2. To evaluate a postoperative analgesia strategy of administering iv tramadol in two groups at the time of craniotomy closure
3. To assess undesirable side-effects: postoperative nausea and vomiting (PONV) and shivering.

Materials and Methods

The study was approved by the local Ethical Committee of the Ministry of Health, Okmeydani Research and Teaching Hospital and an informed consent was obtained from each patient.

In a prospective, randomized, double-blind study, 50 ASA I-III, 18-80 yrs patients (mean 55.04 ± 11.39), scheduled for supratentorial craniotomy with a maximum anticipated duration of 300 minutes, were allocated into two equal groups. Group D received Dexmedetomidine-Propofol and Group R received Remifentanil-propofol. The allocation was done by a computer-generated codes based on a two-way randomization and which were kept in sequentially numbered envelops and opened 3 hours before operation.

Eligible patients had no incapacitating severe systemic disease, and only those in whom immediate postoperative extubation was planned, were included. Exclusion criteria consisted of body weight more than 130% of ideal body weight, uncontrolled hypertension with blood pressure higher than 140/90 mmHg, severe respiratory disease such as bronchial asthma, ischemic cardiac findings at ECG during preoperative visit or cardiac conducting defects (e.g., second-degree atrioventricular block, left bundle branch block). Patients were also excluded if they had any of the following neurological conditions: cerebral aneurysms, intracranial arteriovenous malformations, posterior fossa tumors, and symptoms of uncontrolled increased intracranial pressure (ICP), risk of impending cerebral herniation. Also excluded were patients requiring procedures performed in the sitting or prone position.

Before induction the routine monitoring of ECG and pulse oximetry (Datex-Ohmeda S/5 Compact Critical Care Monitor) were started. The Bispectral Index (BIS) electrodes were placed on the forehead and were connected to an A-2000 BIS monitoring system (Aspect Medical Systems, BIS XP, Framingham, MA, USA).

Group D patients (25) received i.v. dexmedetomidine 1 µg kg⁻¹ as preinduction over a 15-min period before induction of anesthesia and 0.2-1 µg kg⁻¹ hr⁻¹ by continuous i.v. infusion during the operative period. Group R patients (25) received remifentanil 1 µg kg⁻¹ as induction iv over a 15-min period and 0.05-1 µg kg⁻¹ min⁻¹ as maintenance.

The infusion of dexmedetomidine or remifentanil was started before induction and adjusted to keep the mean arterial blood pressure at −20% to +10% from the preoperative value.

After preoxygenation for at least 2 min, anesthesia was induced with propofol in increments of 20 mg every 15s until the BIS reached a predetermined value of 50 (1-2.5 mg kg⁻¹). After induction with propofol, neuromuscular blockade was induced using cisatracurium in a bolus dose of 0.2 mg kg⁻¹ followed by continuous intravenous infusion to maintain 90%
suppression of the single twitch response. Anesthesia was maintained with air (50%), oxygen (50%), and propofol. Depth of anesthesia was monitored by using a BIS-system, a range between 40 and 50 was thought to be adequate. Propofol maintenance doses were 50-150 µg kg⁻¹ min⁻¹.

Patients were ventilated mechanically with an oxygen/air mixture to maintain an adequate oxygenation and a P₅₀ level between 30 and 35 mmHg (Datex-Ohmeda S/5 Avance). Approximately 30 min. before the end of the surgery, the cisatracurium infusion was discontinued. After that, the patients were allowed to recover spontaneously until the return of T₁ = 25%. A combination of neostigmine 0.04 mg kg⁻¹ and atropine 0.02 mg kg⁻¹ were then administered to antagonize residual neuromuscular blockade. Tramadol of 1 mg kg⁻¹ i.v. was given before the craniotomy closure.

At the end of surgery, the fresh gas inflow rate was changed to 6 L min⁻¹ of oxygen and the following times were recorded:

1 – Time to extubation (spontaneous breathing with a minimum of 8 mL kg⁻¹ body weight, ability to sustain a 5-s head lift, and adequate negative inspiratory force [-40 cm H₂O], sustained hand grip and, sustained arm lift).

2 – Time to response to verbal commands (starting from the time of discontinuation of anesthetic administration, a blinded investigator asked each patient at 1-min intervals, to open his or her eyes, squeeze the investigator’s hand).

3 – Orientation time (for the patient to tell his name, birthday and the place he or she is in).

Apart from these, all patients were evaluated with the Aldrete Post Anesthesia Recovery Scoring System (PACU time).

Hemodynamics were monitored for 120 min. after surgery; at the time of postoperative first analgesic requirement, and undesirable side-effects (PONV), shivering, hypotension, and bradycardia were noted, whenever they occurred.

Statistical Analysis

For evaluation of the study findings, SPSS (Statistical Package for Social Sciences) for Windows 10.0 program was utilized for statistical analysis. Study data was evaluated according to Student t test for the comparison between groups. For the comparisons in groups, the paired sample t test was used. Chi-square test and Fisher’s exact test were used for comparison of the qualification data. The results were taken into consideration in 95% confidence interval and the level of significance was set at \( p < 0.05 \).

Results

The two groups, D and R, were similar in terms of age, weight, height, duration of surgery (\( p > 0.05 \)) Propofol doses for induction of anesthesia (\( p < 0.05 \)) and the maintenance of anesthesia (\( p < 0.01 \)) was lower with Dexmedetomidine (Table 1).

The time for BIS to reach 50 was significantly shorter in Group D (\( p < 0.01 \)). At the end of anesthesia, recovery time for BIS to reach 80 was significantly shorter for Group R with respect to Group D (\( p < 0.01 \)).

### Table 1

Demographic Data

<table>
<thead>
<tr>
<th></th>
<th>Group D (n = 25)</th>
<th>Group R (n = 25)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.52 ± 12.54</td>
<td>53.56 ± 10.14</td>
<td>0.364</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.12 ± 6.72</td>
<td>166.80 ± 4.83</td>
<td>0.315</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.00 ± 11.27</td>
<td>70.00 ± 6.45</td>
<td>0.702</td>
</tr>
<tr>
<td>Propofol doses for induction (mg kg⁻¹)</td>
<td>1.65 ± 0.17</td>
<td>1.74 ± 0.08</td>
<td>0.020*</td>
</tr>
<tr>
<td>Propofol doses for maintenance (mg kg⁻¹ h⁻¹)</td>
<td>6.14 ± 0.71</td>
<td>7.51 ± 0.45</td>
<td>0.001**</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>216.08 ± 52.01</td>
<td>229.40 ± 37.06</td>
<td>0.302</td>
</tr>
<tr>
<td>Perioperative Dexmedetomidine usage (µg kg⁻¹ hr⁻¹)</td>
<td>0.213 ± 0.0106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perioperative Remifentanil usage (µg kg⁻¹ min⁻¹)</td>
<td>0.052 ± 0.002</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD, number (%) or median (range).
When comparing the groups with respect to the parameters of recovery; extubation time (p < 0.01), response to verbal commands (p < 0.05) and the time for orientation (p < 0.05) were longer in Group D.

With respect to PACU discharge time; dexmedetomidine patients required a longer time compared to remifentanil patients to achieve their first normal neurological score (33 min vs 31 min).

Remifentanil patients required supplemental analgesia earlier than dexmedetomidine group, median time 33 vs 38 min (Table 2).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Induction and recovery period for BIS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group D (n = 25)</td>
</tr>
<tr>
<td>BIS &lt; 50 (sec)</td>
<td>83.32 ± 13.17</td>
</tr>
<tr>
<td>BIS &gt; 80 (sec)</td>
<td>120.12 ± 15.93</td>
</tr>
<tr>
<td>Extubation time (min)</td>
<td>12.72 ± 2.56</td>
</tr>
<tr>
<td>Response to verbal commands (min)</td>
<td>6.48 ± 2.02</td>
</tr>
<tr>
<td>Time for orientation (min)</td>
<td>12.52 ± 3.01</td>
</tr>
<tr>
<td>PACU Discharge Time (min)</td>
<td>33.60 ± 4.44</td>
</tr>
<tr>
<td>Time for postoperative analgesic requirement (min)</td>
<td>38.04 ± 3.98</td>
</tr>
<tr>
<td>PCA (Patient controlled analgesia) Tramadol Quantity (mg kg⁻¹ sa⁻¹)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Data are the mean (± SD) p values were determined by comparing dexmedetomidine and remifentanil groups. Significant difference within groups (* p < 0.05, ** p < 0.01, *** p < 0.001).

The preoperative value of intraoperative MAP (prior to the administration of drug), was similar in both groups (p > 0.05). Nevertheless, comparing to the values before extubation; the MAP in Group D were significantly higher than those in Group R (p < 0.01) two hours later after extubation (Table 3). When each group was evaluated independently, MAP in two groups was observed to decrease significantly with respect to the values before and after infusion (p < 0.01). On the contrary, MAP was observed to increase significantly after intubation; after pinned head-holder; after skin incision; after dura opening and after extubation with respect to the values before (p < 0.01). The increases observed in MAP levels at 20th min and at 2nd hour postoperatively were not statistically significant with respect to those observed before extubation (p > 0.05), (Table 3).

Heart rate (HR) levels in Group D before incision were found statistically lower than those in Group R (p < 0.05). HR values in dexmedetomidine group were significantly lower than the values of the preoperative period at the 3rd hour of the operation; during skin closure, after extubation (p < 0.01), and before extubation (p < 0.05).

When each group was evaluated independently, the decrease observed in HR level after infusion was found statistically highly significant when compared to the HR levels in the beginning in both Group D and Group R (p < 0.01). On the contrary, a highly significant increase was observed after intubation, after pinned head-holder, after skin incision and after dura opening with respect to the values before in both group (p < 0.01). The increase in HR levels observed in Group D after extubation compared to the HR level before extubation; at 20th minute and at 2nd hour postoperatively was found statistically highly significant (p < 0.01). Similarly, the increase in heart rate in Group R was found statistically highly significant (p < 0.01); the increase at postoperative 20th min was also significant (p < 0.05). Nevertheless, there was no statistically significant change in heart rate at postoperative 2nd hour when compared to the values before extubation (p > 0.05), (Table 4).
### Table 3
Mean arterial blood pressure (mmHg)

<table>
<thead>
<tr>
<th></th>
<th>Group D (n = 25)</th>
<th>Group R (n = 25)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>At the beginning</td>
<td>100.08 ± 9.48</td>
<td>95.44 ± 11.00</td>
<td>0.117</td>
</tr>
<tr>
<td>After</td>
<td>88.68 ± 10.93</td>
<td>87.56 ± 9.52</td>
<td>0.701</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>79.52 ± 15.85</td>
<td>79.52 ± 14.14</td>
<td>1.000</td>
</tr>
<tr>
<td>After</td>
<td>91.08 ± 15.16</td>
<td>96.64 ± 13.85</td>
<td>0.182</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Pinned-head holder</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>77.88 ± 12.52</td>
<td>76.95 ± 6.93</td>
<td>0.780</td>
</tr>
<tr>
<td>After</td>
<td>90.70 ± 14.05</td>
<td>88.22 ± 6.83</td>
<td>0.508</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Skin incision</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>78.24 ± 9.05</td>
<td>76.76 ± 6.96</td>
<td>0.520</td>
</tr>
<tr>
<td>After</td>
<td>84.96 ± 10.59</td>
<td>81.32 ± 7.16</td>
<td>0.161</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Dura Opening</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>76.52 ± 9.54</td>
<td>76.87 ± 6.68</td>
<td>0.889</td>
</tr>
<tr>
<td>After</td>
<td>82.38 ± 7.81</td>
<td>80.61 ± 6.55</td>
<td>0.418</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Intraoperative Period (120 min)</td>
<td>65.12 ± 5.13</td>
<td>67.36 ± 4.60</td>
<td>0.084</td>
</tr>
<tr>
<td>Intraoperative Period (180 min)</td>
<td>63.33 ± 4.37</td>
<td>67.52 ± 4.22</td>
<td>0.601</td>
</tr>
<tr>
<td>Skin closing</td>
<td>64.12 ± 5.81</td>
<td>70.84 ± 5.12</td>
<td>0.319</td>
</tr>
<tr>
<td>Before Exthubation</td>
<td>87.56 ± 8.64</td>
<td>84.96 ± 7.07</td>
<td>0.250</td>
</tr>
<tr>
<td>After Exthubation</td>
<td>97.12 ± 10.18</td>
<td>101.52 ± 10.61</td>
<td>0.141</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>After Exthubation (20 min)</td>
<td>89.08 ± 10.15</td>
<td>85.80 ± 7.09</td>
<td>0.192</td>
</tr>
<tr>
<td>P</td>
<td>0.466</td>
<td>0.606</td>
<td></td>
</tr>
<tr>
<td>After Exthubation (120 min)</td>
<td>92.04 ± 8.71</td>
<td>85.08 ± 7.88</td>
<td>0.005**</td>
</tr>
<tr>
<td>P</td>
<td>0.087</td>
<td>0.942</td>
<td></td>
</tr>
</tbody>
</table>

Result are means ± SD p values were determined by comparing dexmedetomidine and remifentanil groups. Significant difference within groups (** p < 0.01). When the p values groups evaluated as independent from each other (** p < 0.01).

### Table 4
Heart Rate (Beat/min)

<table>
<thead>
<tr>
<th></th>
<th>Group D (n = 25)</th>
<th>Group R (n = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>At the beginning</td>
<td>80.20 ± 5.76</td>
<td>77.32 ± 7.25</td>
<td>0.127</td>
</tr>
<tr>
<td>After</td>
<td>71.92 ± 8.62</td>
<td>70.00 ± 6.36</td>
<td>0.375</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>67.44 ± 5.79</td>
<td>65.40 ± 5.95</td>
<td>0.225</td>
</tr>
<tr>
<td>After</td>
<td>77.48 ± 6.12</td>
<td>81.32 ± 8.52</td>
<td>0.074</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Pinned-head holder</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>68.59 ± 5.07</td>
<td>71.84 ± 5.56</td>
<td>0.077</td>
</tr>
<tr>
<td>After</td>
<td>82.82 ± 7.95</td>
<td>83.04 ± 5.96</td>
<td>0.921</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Skin incision</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>66.76 ± 6.42</td>
<td>70.60 ± 5.07</td>
<td>0.020*</td>
</tr>
<tr>
<td>After</td>
<td>70.84 ± 5.93</td>
<td>75.40 ± 5.17</td>
<td>0.006**</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Dura Opening</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Before</td>
<td>67.62 ± 7.23</td>
<td>70.00 ± 4.22</td>
<td>0.185</td>
</tr>
<tr>
<td>After</td>
<td>70.71 ± 8.12</td>
<td>73.30 ± 4.74</td>
<td>0.199</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Intraoperative Period (120 min)</td>
<td>65.12 ± 5.13</td>
<td>67.36 ± 4.60</td>
<td>0.115</td>
</tr>
<tr>
<td>Intraoperative Period (180 min)</td>
<td>63.33 ± 4.37</td>
<td>67.52 ± 4.22</td>
<td>0.002**</td>
</tr>
<tr>
<td>Skin closing</td>
<td>64.12 ± 5.81</td>
<td>70.84 ± 5.12</td>
<td>0.001**</td>
</tr>
<tr>
<td>Before Exthubation</td>
<td>70.24 ± 5.82</td>
<td>74.72 ± 5.92</td>
<td>0.010*</td>
</tr>
<tr>
<td>After Exthubation</td>
<td>78.04 ± 5.94</td>
<td>91.84 ± 10.19</td>
<td>0.001**</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>After Exthubation (20 min)</td>
<td>78.68 ± 8.87</td>
<td>77.76 ± 4.46</td>
<td>0.645</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>After Exthubation (120 min)</td>
<td>77.84 ± 7.57</td>
<td>77.04 ± 5.12</td>
<td>0.664</td>
</tr>
<tr>
<td>P</td>
<td>0.001**</td>
<td>0.114</td>
<td></td>
</tr>
</tbody>
</table>

Result are means ± SD p values were determined by comparing dexmedetomidine and remifentanil groups. Significant difference within groups (** p < 0.01, * p < 0.05). When the p values groups evaluated as independent from each other (* p < 0.05, ** p < 0.01).
There was no statistically significant difference for nausea, vomiting, shivering and bradycardia in Group D and Group R (p > 0.05) (Table 5).

**Table 5**

<table>
<thead>
<tr>
<th></th>
<th>Group D (n = 25)</th>
<th>Group R (n = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>3 (12.0%)</td>
<td>7 (28.0%)</td>
<td>0.157</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (4.0%)</td>
<td>3 (12.0%)</td>
<td>0.609</td>
</tr>
<tr>
<td>Shivering</td>
<td>7 (28%)</td>
<td>13 (52.0%)</td>
<td>0.083</td>
</tr>
<tr>
<td>Bradycardia (atropine administered)</td>
<td>5 (20.0%)</td>
<td>1 (4.0%)</td>
<td>0.189</td>
</tr>
</tbody>
</table>

**Discussion**

In nonemergent intracranial surgery, fast recovery from anesthesia is especially important for detecting early complications and for performing the neurological examination\(^1\). The results of the current study demonstrate that an ultra-short acting opioid, such as remifentanil, is an effective and safe alternative to fentanyl. It is advantageous to the patient undergoing supratentorial craniotomy to emerge and recover from anesthesia quickly, as this allows prompt neurological assessment and determination of the need for urgent intervention\(^1\).

Despite the potential advantages of total intravenous anesthesia in titratability, rapid return of consciousness and reduced respiratory complications, making it suitable for planned extubation at the end of neurosurgery, the postoperative complications of shivering, postoperative nausea and vomiting, and hypertension were still high\(^1\).

The propofol-remifentanil regimen has been successfully used in various surgical settings, but a comprehensive comparison of propofol-dexmedetomidine and propofol-remifentanil anesthesia in patients undergoing craniotomy for supratentorial intracranial surgery, has not yet been done.

It has been reported that Dexmedetomidine has anesthetic and analgesic effects in addition to its sedative effects, appearing at i.v. 0.5-2 µg kg\(^{-1}\) dose intervals\(^1\). Our study showed that when dexmedetomidine was used perioperatively for BIS 40-50, the doses of propofol for induction and maintenance were significantly reduced and the time for intubation was significantly shorter. It is predictable that the induction dose of propofol would be lower in Group D than in Group R, because dexmedetomidine is a sedative but remifentanil is not.

Because of the ventilatory depressing effects of fentanyl, Feld JM et al.\(^1\) studied various alternative methods for analgesia in bariatric surgery. In their study comparing dexmedetomidine to fentanyl, they reported that dexmedetomidine provided both stable perioperative hemodynamics and postoperative analgesia, thus reducing the use of supplementary morphine. Similarly, Tanskenen PE et al.\(^1\) reported that dexmedetomidine provided good perioperative hemodynamic stability compared to fentanyl in patients undergoing brain tumor surgery and that it also reduced intraoperative opioid requirements. Dexmedetomidine could be convenient as an adjuvant anesthetic in neurosurgical anesthesia. It prevents the tachycardic response to intubation and the hypertensive response to extubation.

In our study, remifentanil and dexmedetomidine were similar in overall efficacy. In the two groups, no hemodynamic and cardiovascular side effects were seen perioperatively. This finding is supported by a similar study by Bauer et al.\(^1\), though the time to extubation was about 4 times longer in the present study (10 vs 47 min).

The major reported problem with dexmedetomidine is its hemodynamic effects, as the drug often causes hypotension, hypertension, and bradycardia\(^1\). In our study, although bradycardia was seen more in Group D patients similar to other studies, this finding was not statistically significant\(^2\). Also, hypotension and hypertension, was not observed in our groups. This could be attributed to the greater depth of anesthesia in the dexmedetomidine group either because the doses of the drug chosen were not exactly equipotent, or because they differ in their potentiation of propofol, or because remifentanil has a lower capability for causing hypotension.

Our study findings are similar to those of Djian et al\(^1\). Other studies of this type of surgery have also demonstrated a longer time to extubation than we found when remifentanil was used. In the study by Bauer et
al\textsuperscript{12}, the time period was 47 minutes, while it was 13 +/- 5 minutes in the study by Bilotta et al\textsuperscript{24}. Gelb\textsuperscript{25}, however, recorded the time period as 8 minutes. In the study by Gerlach et al\textsuperscript{26}, patients in the remifentanil/propofol group were extubated earlier (6.4 min). In our study, extubation time was longer and recovery was slower in Group D (12 vs 10 min). These differences possibly reflect differences in anesthetic protocols between the various studies.

The most commonly encountered complications in the early postoperative period in the recovery room in extubated patients after elective neurosurgical procedures using propofol-remifentanil anesthesia were, shivering, nausea, vomiting, and postoperative hypertension\textsuperscript{14}.

As for emergence characteristics, our study showed an advantage for remifentanil. With respect to PACU discharge time, dexmedetomidine patients required longer time compared to remifentanil patients to achieve their first normal neurological score (33 min vs 31 min). In the study by Gelb et al.\textsuperscript{25} the remifentanil group PACU time was 26 minutes. Statistically significant differences between the groups were also found at times when the patients responded to verbal commands.

Previous studies with remifentanil identified pain and the need for early analgesia in the PACU, because of problems inherent in such an active drug\textsuperscript{27}. In recent years, however, alpha\textsubscript{2} agonists have found wider applications, particularly in the fields of anesthesia and pain management. It has been noted that these agents can enhance the analgesia provided by traditional analgesics, such as opioids, and may result in opioid-sparing effects\textsuperscript{28,29,30}.

Another important aim of the present study was the evaluation of the use of tramadol 1 mg kg\textsuperscript{-1} i.v. at bone flap replacement for transitional analgesia. This proved to be effective in that early recovery but superior quality was still found in the dexmedetomidine group without early pain requiring urgent treatment.

Similar to the studies by Gelb et al.\textsuperscript{25} and Gerlach et al\textsuperscript{26}, our study showed that remifentanil group required supplemental analgesia earlier than dexmedetomidine group (The earliest opioid administration was at 38 min. for the dexmedetomidine group and at 33 min for the remifentanil group).

Although respiratory depression due to opioids have been reported in different anesthetic combinations\textsuperscript{31,32,33}, dexmedetomidine, the highly selective alpha\textsubscript{2} adrenoreceptor agonist, has sedative and analgesic effects without causing postoperative respiratory depression\textsuperscript{18,19}. 0.5 to 1.0 µg kg\textsuperscript{-1} dexmedetomidine over 20 minutes followed by an infusion at rates of 0.01 to 1.0 µg kg\textsuperscript{-1} h\textsuperscript{-1} was used in awake craniotomy and enabled the performance of the neurological examination\textsuperscript{34,35}.

The analgesic profile of dexmedetomidine has not been fully characterized in humans\textsuperscript{36}. However, the anxiolysis, blood pressure stabilization, analgesia, anesthetic sparing effects, and sedation without respiratory depression or significant cognitive impairment effects of dexmedetomidine, are known. Cormack et al.\textsuperscript{37} suggests that both of these alpha\textsubscript{2}-agonists are useful adjuncts for the management of the neurosurgical patient during surgery and in the intensive care unit.

Conclusion

In conclusion, propofol-remifentanil and propofol-dexmedetomidine are both suitable for elective supratentorial craniotomy and provide similar intraoperative hemodynamic responses and postoperative adverse events. Propofol-remifentanil allows earlier cognitive recovery; however, it leads to a higher demand for postoperative analgesics.
References


PREVENTION OF PROPOFOL PAIN:
A COMPARATIVE STUDY

NITIN SETHI*, LAKSHMI JAYARAMAN**,
MAMTA SETHI***, SHIKHA SHARMA****
AND JAYASHREE SOOD*****

Abstract

A common drawback of propofol is pain on injection and lignocaine is commonly mixed with propofol to reduce the incidence and severity of this pain. In this study we sought to draw a comparison between the effectiveness of propofol medium chain and long chain triglyceride (MCT/LCT) alone, propofol medium chain and long chain triglyceride (MCT/LCT) premixed with lignocaine, and propofol long chain triglyceride (LCT) premixed with lignocaine, in preventing propofol pain on injection. 300 patients were randomly divided into three equal groups. Group A received propofol-MCT/LCT premixed with normal saline, Group B received propofol-MCT/LCT premixed with 20 mg lignocaine and Group C received propofol-LCT premixed with 20 mg lignocaine. The incidence of pain in Group A was 63% compared to 15% in Group B ($X^2 = 48.242$, $p<0.001$), whereas in Group C the incidence of pain was 24% compared to 63% in Group A ($X^2 = 30.247$, $p<0.001$). There was no significant difference in incidence of pain between Groups B and C ($X^2 = 2.5$, $p = 0.11$). To conclude, propofol MCT/LCT alone provides no advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine and propofol LCT premixed with lignocaine. Also, there is no significant difference in pain on injection between propofol LCT and propofol MCT/LCT as soon as lignocaine is added.

Keywords: lignocaine, propofol, pain on injection.
Introduction

Propofol is a popular intravenous anesthetic agent providing smooth induction and rapid recovery from anesthesia. However, pain on injection is a major disadvantage with a reported incidence of approximately 70% when a standard formulation of propofol is administered with no intervention to reduce pain.1

Several strategies have been applied to alleviate pain, such as previous administration of opioids or metoclopramide and adaptation of the temperature of the emulsion. The most frequently used method to reduce pain is the administration of lignocaine, either before propofol injection, with or without a tourniquet or added to the propofol emulsion as a premixture.2,3,4 The mechanism of pain relief can be two fold; first by reduction of propofol in the aqueous phase and second by lignocaine acting as a stabiliser in the kinin cascade.5

Injection pain has been attributed to the amount of free propofol in the aqueous phase of the emulsion. In 1997, Doenicke et al6 advocated a reformulated lipid emulsion of propofol to alleviate injection pain. This reformulation of propofol contains both medium chain triglycerides (MCT) and long chain triglycerides (LCT) in equal proportions in contrast to usual LCT formulation. The amount of free propofol in a MCT/LCT emulsion is assumed to be less compared with propofol LCT thus causing less pain on injection. However, recent studies have suggested that propofol MCT/LCT emulsion when used alone causes more pain on injection, as compared to propofol LCT with lignocaine.7,8,9

The aim of the present study was to determine whether propofol in a reformulated MCT/LCT emulsion without further addition, was more effective in preventing pain on injection as compared to propofol MCT/LCT with lignocaine and more frequently used standard LCT propofol with a premixture of lignocaine.

Materials and Methods

Following approval by the Institutional Ethics Committee and written informed consent, 300 ASA I-III patients, aged 18-65 years, scheduled for elective surgery under general anesthesia, were recruited into this prospective randomized double blind study. Sample size was determined by performing a power analysis which showed that a minimum of 200 patients will be required for the study. Exclusion criteria consisted of patients with ischemic heart disease and neurological problems, pregnant or lactating patients, those who were taking any analgesics before surgery, or those with known hypersensitivity to propofol or to any of the constituents of the emulsion (soy-bean oil, MCT, glycerol, egg lecithin, sodium oleate or water for injection).

The drugs used were propofol-LCT (Propofol™, Claris Lifesciences, India), lignocaine hydrochloride 2% (Xylocard®, AstraZeneca, India) and propofol-MCT/LCT (Propofol®-Lipuro, B Braun Ltd, Melsungen, Germany).

The patients were assigned to 3 groups (100 each), using computer generated randomization. Group A received propofol-MCT/LCT premixed with normal saline (1 ml of normal saline added to 19 ml propofol-lipuro). Group B received propofol-MCT/LCT premixed with lignocaine (1 ml of 2% lignocaine added to 19 ml propofol-lipuro). Group C received propofol-LCT premixed with lignocaine (1 ml of 2% lignocaine added to 19 ml propofol). The investigators and patients were blinded to the study preparation being used.

Patients received no premedication. On arrival at the operating theatre, routine monitoring was applied and a 20G cannula was inserted into a suitable vein on the dorsum of non-dominant hand. A blinded investigator injected 5 ml of the propofol solution at a constant rate over 15 secs and patients were asked to grade any associated pain or discomfort using a four-point verbal rating scale that had been previously described to them (Table 1). Once the assessment of injection pain had been made, induction of anesthesia continued according to the anesthesiologist’s routine practice.

<table>
<thead>
<tr>
<th>Pain Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No pain or discomfort at all.</td>
</tr>
<tr>
<td>1</td>
<td>Sensation of mild discomfort only.</td>
</tr>
<tr>
<td>2</td>
<td>Sensation of moderately severe pain.</td>
</tr>
<tr>
<td>3</td>
<td>Sensation of severe pain and/or grimacing or withdrawal of limb.</td>
</tr>
</tbody>
</table>
Statistics

Statistical analysis was conducted using SPSS version 11.5. Descriptive statistics such as mean, range and standard deviation have been used to summarize the baseline clinical and demographic profile of the patient. Categorical data was analyzed using Chi-square test and Fisher’s exact test. Parametric data was analyzed using analysis of variance (ANOVA) with post hoc analysis (least square difference).

Results

All the three groups were comparable with respect to age, weight and male: female ratio (Table 2).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Demographic data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A (n = 100)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.02 ± 14.12</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.6 ± 9.46</td>
</tr>
<tr>
<td>Male: Female</td>
<td>59: 41</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD

MCT = medium-chain triglycerides; LCT = long chain triglycerides.

Group A = propofol MCT/LCT mixed with normal saline; Group B = propofol MCT/LCT mixed with lignocaine; Group C = propofol LCT mixed with lignocaine.

Patients in Group A had significant pain compared to patients in Groups B and C. In Group A the incidence of pain was 63% compared to 15% in Group B (X² = 48.242, p<0.001), whereas in Group C the incidence of pain was 24% compared to 63% in Group A (X² = 30.247, p<0.001) (Table 3). There was no significant difference in incidence of pain between Groups B and C (X² = 2.5, p = 0.11).

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Incidence of pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A (n = 100)</td>
</tr>
<tr>
<td>No pain</td>
<td>37</td>
</tr>
<tr>
<td>Pain</td>
<td>63</td>
</tr>
</tbody>
</table>

X² = 58.021, p = <0.001

MCT = medium-chain triglycerides; LCT = long chain triglycerides.

Group A = propofol MCT/LCT mixed with normal saline; Group B = propofol MCT/LCT mixed with lignocaine; Group C = propofol LCT mixed with lignocaine.

There was significant difference in incidence of severity of pain between Groups A and B and Groups A and C. There was no difference in severity of pain between Groups B and C (Table 4).

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Incidence of severity of pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score</td>
<td>A (n = 100)</td>
</tr>
<tr>
<td>0 = no pain or discomfort</td>
<td>37</td>
</tr>
<tr>
<td>1 = mild discomfort</td>
<td>23</td>
</tr>
<tr>
<td>2 = moderately painful</td>
<td>32</td>
</tr>
<tr>
<td>3 = severely painful</td>
<td>8</td>
</tr>
</tbody>
</table>

X² = 61.338, p = <0.001

MCT = medium-chain triglycerides; LCT = long chain triglycerides.

Group A = propofol MCT/LCT mixed with normal saline; Group B = propofol MCT/LCT mixed with lignocaine; Group C = propofol LCT mixed with lignocaine.

Discussion

In this study patients receiving propofol MCT/LCT premixed with lignocaine, and propofol LCT premixed with lignocaine, had significantly less pain on injection than LCT/MCT formulations of propofol.

Several mechanisms of pain on injection have been suggested, but investigations have shown that the free concentration of propofol in the aqueous phase may be the most important factor. Emulsions of MCT/LCT, although maintaining similar pharmacological properties as standard propofol have smaller propofol concentrations in the aqueous phase.

Rau et al. reported that 37.8% of patients receiving propofol MCT/LCT were painfree and of the patients who had pain none graded it as severe. Kam et al. have reported a similar incidence of pain on injection, 38% in patients receiving propofol MCT/LCT compared to 36% in patients receiving propofol LCT. Larsen et al. have shown a lower incidence of pain on injection in patients receiving propofol MCT/LCT (37%) compared to patients receiving propofol LCT (64%). Yew et al. have reported an incidence of 24% in patients receiving propofol LCT premixed with lignocaine and propofol MCT/LCT emulsion.

In our study, the incidence of pain with propofol MCT/LCT was 63%. Schaub et al. have reported a 47%
incidence of pain with propofol MCT/LCT compared to 24% in patients receiving propofol LCT with lignocaine pretreatment. Nyman et al.\(^8\) in their study in pediatric patients reported 33.3% patients having pain free propofol injection in the propofol MCT/LCT group compared to 61% patients having pain free propofol injection in the propofol LCT premixed with lignocaine group. Adam et al.\(^9\) reported that patients receiving propofol MCT/LCT had a higher verbal analogue scale (VAS) as compared to patients receiving propofol LCT with lignocaine.

We found that mixing propofol MCT/LCT with lignocaine was effective in significantly reducing the incidence of pain from 63% in propofol MCT/LCT to 15% in propofol MCT/LCT with lignocaine.

Yew et al.\(^14\) have reported a decrease in pain on injection from 24% to 4% in patients receiving propofol MCT/LCT mixed with lignocaine. Kunitz et al.\(^16\) have also suggested that addition of lignocaine to propofol MCT/LCT seems to have an additive effect to reduce propofol injection pain.

In our study, the incidence of pain with propofol LCT premixed with lignocaine was 24% which is in accordance with reported incidence in other studies\(^1,15\). We did not use propofol LCT without lignocaine as it was not ethically justified and studies have shown that propofol LCT used alone increases incidence of pain.

In conclusion, propofol MCT/LCT alone does not provide any advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine and propofol LCT premixed with lignocaine. Further studies need to be done to establish the role of this new propofol MCT/LCT emulsion on propofol injection pain.

References

LOW DOSE INTRAVENOUS MIDAZOLAM FOR PREVENTION OF PONV, IN LOWER ABDOMINAL SURGERY

- Preoperative vs Intraoperative Administration -

MOHAMMAD REZA SAFAVI* AND AZIM HONARMAND**

Abstract

Background: The aim of the present study was to compare anti-emetic efficacy of low dose midazolam premedication (35 µg/kg) 15 minutes before induction of anesthesia with midazolam (35 µg/kg) administered intravenously 30 min before conclusion of surgery, in patients undergoing lower abdominal surgery under general anesthesia.

Methods: Sixty patients were assigned to one of three equal groups: Group MP (n = 20), which received intravenous midazolam 35 µg/kg in a volume of 3 ml 15 minutes before induction of anesthesia and 3 ml normal saline 30 minutes before extubation. Group MI (n = 20), which received 3 ml normal saline 15 minutes before induction of anesthesia and intravenous midazolam 35 µg/kg in a volume of 3 ml 30 minutes before extubation. Group NS (n = 20), which received 3 ml normal saline 15 minutes before induction of anesthesia plus 3 ml normal saline 30 minutes before extubation. Assessments of the occurrence of postoperative nausea and vomiting (PONV) were made at regular intervals for the first 24h.

Results: Incidence of PONV was significantly lower in Group MI compared with Group NS and Group MP at 6, 12, 18, and 24 hours after operation (P < 0.05). The time for the first episode of PONV was significantly higher in Group MI compared with Group NS and Group MP (P < 0.05).

Conclusion: Our results indicated that midazolam 35 µg/kg (2 mg) given intravenously 30 minutes before the end of surgery was more effective in decreasing the incidence of PONV than midazolam premedication 35 µg/kg.

Keywords: Midazolam, postoperative nausea and vomiting, antiemetics, anesthetics.

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Introduction

PONV is the most frequent side effect following anesthesia\(^1\), occurring in about 30% of unselected inpatients and up to 70% of “high-risk inpatients during the 24 h after emergence\(^2\). Although PONV is almost always self-limiting and non-fatal\(^3\), it can cause significant morbidity, including dehydration, electrolyte imbalance, suture tension and dehiscence, venous hypertension and bleeding, esophageal rupture, and life threatening airway compromise, although the more severe complications are rare\(^4,5\). Each vomiting episode delays discharge from the recovery room by about 20 min\(^6\).

A number of treatments have been introduced to reduce PONV, such as 5-HT3 antagonists, dopamine receptor antagonists, and antihistamine drugs. However, each of these treatments is associated with critical limiting factors, namely cost with 5-HT3 antagonists, extrapyramidal symptoms with dopamine receptor antagonists and excessive sedation, and tachycardia with antihistamine drugs\(^7-9\). In several studies, benzodiazepines have been demonstrated to improve comfort and decrease anxiety in patients. In particular, lorazepam has been reported to be capable of reducing the severity and the duration of nausea and vomiting\(^10\). However, its slow onset and long duration of action can result in sedation and undesirable anxiolytic effects that last longer than necessary.

Midazolam is a short-acting benzodiazepine with a rapid onset of action, which is used for induction of general anesthesia and preoperative sedation. In recent years, midazolam has been reported to be effective for prophylaxis of PONV by bolus administration before or after induction of anesthesia or postoperative continuous infusion\(^11-16\). Heidari et al\(^12\) showed that prophylactic intravenous midazolam premedication 75 microg/kg reduced the incidence and severity of PONV in adult patients subjected to cholecystectomy under general anesthesia. Lee and colleagues\(^17\) compared the prophylactic anti-emetic efficacy of midazolam and ondansetron in patients scheduled for minor gynecological or urological procedures and showed that midazolam 2 mg (35 µg/kg) were administered intravenously 30 min before the end of surgery, was as effective as ondansetron in treating PONV.

In Heidari et al study\(^12\), the dosage of midazolam premedication was 75 µg/kg, and it effectively reduced the incidence of nausea and vomiting up till six hours after surgery. However, it is not known whether lower dosage (35 µg/kg) of midazolam premedication has similar effect. It is also not clear of the premedicant effect of midazolam in comparison to intraoperative midazolam on PONV. In randomized double-blind placebo-controlled study we compared the effectiveness of intravenous midazolam premedication 35 microg/kg as an anti-emetic with midazolam 35 µg/kg administered intravenously 30 min before the end of surgery, in patients undergoing lower abdominal surgery under general anesthesia. Our hypothesis was that intraoperative midazolam administration before conclusion of surgery was more effective than premedicant midazolam for the prevention of PONV.

Materials and Methods

Following approval of the University Research Committee and obtaining informed consents from all subjects, 80 ASA I or II patients, aged 18-60 years, scheduled for lower abdominal procedures planned to last 1-2 h were eligible to participate in this study. Patients who had gastrointestinal disorders, histories of PONV after a previous surgery, renal or liver dysfunction, history of motion sickness, had received any opioid, steroid, or antiemetic medication in the 24 h before surgery, and those who were pregnant or menstruating, were excluded.

Before induction, patients were instructed on the use of the visual analogue scale (VAS) for pain assessment. Monitoring included continuous ECG, non-invasive blood pressure, pulse oximetry and end-tidal carbon dioxide.

Patients were randomly allocated to one of three equal groups:

Group MP (n = 20), received intravenous midazolam premedication 35 µg/kg in a volume of 3 ml, 15 minutes before induction of anesthesia

Group MI (n = 20) received intravenous midazolam 35 µg/kg in a volume of 3 ml 30 minutes before extubation at the end of surgery

Group NS (n = 20), received 3 ml normal saline 15 minutes before induction of anesthesia plus 3 ml normal saline 30 minutes before extubation at the end of surgery.

To achieve adequacy of blinding, all patients in
Group MP received 3 ml normal saline 30 minutes before extubation at the end of surgery, and the patients in Group MI received 3 ml normal saline 15 minutes before induction of anesthesia. The estimated doses of all drugs were diluted in equal volume (3 mL). The dosage of midazolam was formulated on the basis of an earlier report\textsuperscript{17}. The randomized process and the identity of the study drugs were blinded to the anesthesiologists during surgery and the investigators who collected the postoperative data.

No premedication was given. Patients in the three groups underwent a standardized anesthesia protocol which included induction with thiopental (5 mg/kg) and fentanyl (2 µg/kg). Atracurium was used as a muscle relaxant. After tracheal intubation, anesthesia was maintained with a 50% nitrous oxide/oxygen mixture along with isoflurane in a concentration of 0.8%-1.2%. Ventilation was adjusted to produce normocapnia. At the end of surgery, reversal of residual neuromuscular blockade was accomplished using i.v. atropine 20 µg/kg and neostigmine 40 µg/kg. Assessments of patients recovery were made by a blinded observer, including the times from discontinuation of anesthesia until the time to achieve a modified Aldrete score of 10\textsuperscript{8}.

Sedation was assessed during the first 5, 15, 30, 60 and 120 min in the PACU by a physician using the five-point Observer’s Assessment of Alertness/Sedation (OAA/S) scale (where 1 = awake/alert and 5 = deep sleep)\textsuperscript{19}. All assessments were carried out by a physician who had no knowledge of the treatment patients had received. The discharge criteria in the post anaesthesia care unit (PACU) consisted of: an awake and alert patient, stable vital signs, no severe pain, and no persistent nausea and vomiting.

PONV assessment was started at extubation and was carried out hourly for the first 4 h and thereafter every 4 h until the first 24 h. PONV was evaluated by the following variables: incidences of nausea and vomiting, requirements of rescue antiemetics, and complete responses. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit, and vomiting was defined as the forceful expulsion of gastric contents from the mouth. For the purpose of data collection, retching (same as vomiting but without expulsion of gastric contents) was considered vomiting. Nausea was recorded according to the following scale: 0 none; 1 mild (patient able to eat); 2 moderate (oral intake significantly decreased); and 3 severe (no significant oral intake necessitating i.v. fluid)\textsuperscript{20}. The absence of nausea was defined as complete protection from nausea. An emetic episode was defined as a single vomit or retch, or any number of continuous vomiting episodes or retches (one emetic episode should be separated from another by an absence of vomiting or retching for at least 1 min). The absence of emetic episodes was defined as complete protection from vomiting. Rescue medication (metoclopramide 10 mg) was given intravenously if patient was nauseous for more than 15 min or experienced retching or vomiting during the observation periods. The treatment was repeated if necessary.

For the first 24 h after anesthesia, the levels of pain and sedation experienced by the patients were recorded by a physician who had no knowledge of the treatment patients had received. Pain intensity score was measured with a visual analog scale (VAS) from 0 (no pain) to 10 (the worst possible pain). If patients asked for analgesic or experienced pain with a VAS more than 3, meperidine 1 mg/kg was administered intravenously.

Sample size was predetermined with a power analysis based on the assumption that:

1) the total incidence of nausea and vomiting in the saline group would be 60%\textsuperscript{21};
2) a 40% reduction (from 60% to 20%) in the total incidence of PONV in the treatment group would be of clinical relevance;
3) $\alpha = 0.05$, $\beta = 0.2$. The analysis showed that 20 patients per group would be sufficient. Statistical analyses were performed with SPSS version 15.0 (SPSS, Chicago, IL).

Data are presented as mean ± SD, median or number (%). Patient demographics, duration of surgery or anesthesia, PACU discharge eligibility, first nausea or vomiting time, rescue opioids and metoclopramide dosage were analyzed by using one-way ANOVA, and multiple comparison between pairs was done by the Bonferroni’s test. VAS scores were compared among groups by two-way analysis of variance for repeated measures. Between-group differences in the numbers of patients needing rescue antiemetic were analyzed using the chi-square test. Fisher’s exact test was used.
Discussion

This is the first clinical trial testing of the efficacy of midazolam as an antiemetic when administered as a premedicant as compared to its i.v. administration intraoperatively in patients at intermediate risk for PONV. This study demonstrated that intravenous administration of midazolam 35 µg/kg, 30 min before the end of surgery was more effective than intravenous midazolam premedication 35 µg/kg in patients undergoing lower abdominal surgery under general anesthesia.

The causes of PONV are of multifactorial origins: age, gender, history of previous PONV, motion sickness, type of surgery and anesthetic technique, pain, and use of opioid8.

Results

The three groups were comparable with respect to demographic characteristics, duration of surgery or anesthesia, the median sedation level at arrival to PACU, the postoperative pain scores (VAS) in the different time intervals, PACU discharge eligibility time, and requirement for rescue pain medication (Table 1).

The was no statistically significant difference between the three groups for SAP, DAP, MAP, HR, or SpO2 at any time. The incidence of PONV and requirements for rescue anti-emetics during different observatory periods are presented in Table 2.

Incidence of PONV was significantly lower in Group MI when compared to Group NS and Group MP (P < 0.05). The metoclopramide dosage and numbers of patients needed rescue anti-emetic was significantly lower in Group MI or Group MP compared with group NS during 24 hours after operation (P < 0.05) (Table 2). None of the patients who had PONV required more than 1 dose of rescue medication.
In our study since the three groups were similar in patient characteristics, type of surgery, anesthetics administered, pain intensity, and analgesic used after surgery, therefore, the incidence of PONV can be attributed to the study of the drug under consideration.

We found that 3% of the patients in the MI group reported PONV in the first 24 h postoperatively, which was significantly less than group MP (24%). Also in patients who received midazolam premedication showed a higher incidence of PONV than those who received midazolam 30 minutes before conclusion of surgery in the first 2 h. This study, however, was not sufficiently powered to detect such differences. More patients were needed to detect the same relative reduction in nausea. Also, rescue antiemetic, metoclopramide dosage and numbers of patients needing rescue antiemetic was higher in MP group than MI group during 24 hours after surgery. However, due to probably small sample size, this difference was not statistically significant.

Based on our data, the incidence of PONV was significantly lower in group MI than in group MP or group NS at 12, 18, and 24 hours after surgery. In contrast, there was no significant difference between group MP and group NS in this regard. Heidari et al. investigated the effect of intravenous midazolam premedication on the incidence and severity of PONV in a sample of adult patients undergoing anesthesia for cholecystectomy, and showed that severity of nausea was significantly lowered in midazolam group during the first six hours after recovery period compared with placebo group. Our finding is in agreement with this study.

Several investigations have indicated that midazolam may have anti-emetic properties. Splinter et al. observed that administering midazolam 0.05 mg.kg after induction of anesthesia has antiemetic effects that are similar to the same dose of droperidol in children undergoing strabismus surgery. Bauer et al. found that pre-operative intravenous midazolam 0.04 mg.kg is an effective way to reduce the frequency of PONV and increase patient satisfaction. Unlugenc et al. demonstrated that midazolam used in subhypnotic dose was as effective as ondansetron in treating PONV without untoward sedative effects. The prophylactic

### Table 2

<p>| Severity of PONV, incidence of requiring rescue anti-emetics, first postoperative nausea or vomiting, metoclopramide dosage and numbers of patients needed rescue antiemetic during different observatory periods among three groups. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Group MP (0/1/2/3)</th>
<th>Group MI (0/1/2/3)</th>
<th>Group NS (0/1/2/3)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 h</td>
<td>15/3/2/0*</td>
<td>18/2/0/0*</td>
<td>8/8/4/0</td>
<td>0.013</td>
</tr>
<tr>
<td>6 h</td>
<td>15/4/1/0</td>
<td>1/9/1/0/0*</td>
<td>10/2/0/0*</td>
<td>0.005</td>
</tr>
<tr>
<td>12 h</td>
<td>15/5/0/0</td>
<td>20/0/0/0*†</td>
<td>9/10/1/0</td>
<td>0.003</td>
</tr>
<tr>
<td>18 h</td>
<td>15/5/0/0</td>
<td>20/0/0/0*†</td>
<td>9/11/0/0</td>
<td>0.000</td>
</tr>
<tr>
<td>24 h</td>
<td>16/4/0/0</td>
<td>20/0/0/0*†</td>
<td>10/10/0/0</td>
<td>0.001</td>
</tr>
<tr>
<td>Rescue anti-emetics</td>
<td>8 (40)*</td>
<td>4 (20)*</td>
<td>15 (75)</td>
<td>0.002</td>
</tr>
<tr>
<td>First nausea or vomiting time (hr)</td>
<td>1.36 ± 0.2</td>
<td>3.1 ± 0.2*†</td>
<td>0.90 ± 0.2</td>
<td>0.000</td>
</tr>
<tr>
<td>Metoclopramide dosage (mg)</td>
<td>6.5 ± 2.1*</td>
<td>2.0 ± 0.9*</td>
<td>13.5 ± 2.3</td>
<td>0.000</td>
</tr>
<tr>
<td>Numbers of patients needing rescue antiemetic (%)</td>
<td>8 (29.6)*</td>
<td>4 (14.8)*</td>
<td>15 (55.6)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values are number (%) of patients with each grade of PONV in each group or mean ± SEM. Group MP = midazolam premedication; Group MI = midazolam intraoperative; Group NS = normal saline; PONV = postoperative nausea vomiting. PONV was graded as: 0 none; 1 mild (patient able to eat); 2 moderate (oral intake significantly decreased); and 3 severe (no significant oral intake necessitating i.v. fluid). * P < 0.05 vs. Group NS. † P < 0.05 vs. Group MP.
administration of midazolam was also reported to be effective in reducing vomiting after tonsillectomy in children. Midazolam is an effective antiemetic in patients having chemotherapy.

The mechanism of action of midazolam has not been fully understood. It is thought that midazolam decreases dopamine input at the chemoreceptor trigger zone (CRTZ) and decreases adenosine re-uptake. This leads to an adenosine-mediated reduction in synthesis, release, and postsynaptic action of dopamine at the CRTZ. It may also decrease dopaminergic neuronal activity and 5-HT3 release by binding to the gamma-aminobutyric acid (GABA) receptor.

In our study, we reported a significant (P = 0.002) lower use of rescue antiemetics (20%) in the MI group when compared with the NS (75%) group. This is consistent to the study by Lee et al., who reported a 23% use of rescue antiemetics in their midazolam group.

Clinical practitioners may be cautious of using hypnotic agents for anti-emetic purposes because of the risk of delayed recovery. The sedation scores recorded in our trial have clearly demonstrated that the patients in three study groups had similar scores and laid to rest the speculation that the patients in the midazolam group were failing to report nausea because they were more sedated than the patients who received ondansetron. Moreover, midazolam has been stated to be a sedative in a larger dose range than that used in our trial.

We also observed that midazolam as a premedicant or intraoperative bolus administration did not prolong the duration of anesthesia, increase the degree of sedation, increase the postoperative stay in the PACU, or alter the postoperative pain scores. Also, administration of midazolam preoperatively did not significantly affect perioperative vital signs, a finding that is consistent with previous studies.

Lerman has suggested that PONV is approximately two to three times more frequent in women than in men. In our study, PONV was predominant in women (49% vs. 35% in men). In common with most other studies on PONV, we found that PONV was associated significantly with the female sex. This overwhelming incidence of PONV in women suggests that women should be a target population to receive antiemetics after lower abdominal surgery.

There are few limitations in our trial. First, plasma levels of midazolam were not measured. Second, meperidine was used for pain relief in the postoperative period. Meperidine being an opioid could per se cause PONV, and it was used in three study groups.

In conclusion, the results of this study indicated that patients undergoing lower abdominal surgery under general anesthesia, midazolam 35 µg/kg (2 mg) given intravenously 30 minutes before the end of surgery was more effective than midazolam premedication 35 µg/kg, in decreasing the incidence of PONV without increasing recovery time and the level of sedation. Further prospective randomized studies with varying doses of midazolam to evaluate its antiemetic properties are needed before drawing any firm conclusions.
References


THE ANALGESIC EFFECTS OF ROPIVACAINE IN ILIOINGUINAL-ILIOHYPOGASTRIC NERVE BLOCK IN CHILDREN

- Concentration or Volume? -

MEHDI TRIFA*, ZIED CHAABANE, SOFIANE DRIKI, BESSIM SEBAI, ADEL MISSAOUI, AMJED FEKH HASSEN AND SONIA BEN KHALIFA

Abstract and Objectives: The aim of the present study was to compare the analgesic effects of ripovacaine when used as high concentration/small volume, versus its use as high volume/low concentration, in ilioinguinal-iliohypogastric nerve block in children.

Methods: This is a prospective single-blind randomized study consisting of 72 children ASA I & II, 3-9 years of age, scheduled for outpatient elective surgery. Children were randomly assigned into two equal groups (36 each), to receive ropivacaine 0.8 mg.kg⁻¹, for ilioinguinal-iliohypogastric block, either as:

1 mg.ml⁻¹ (0.8 ml.kg⁻¹) G1 group, or
2 mg.ml⁻¹ (0.4 ml.kg⁻¹) G2 group

The postoperative pain was assessed using the Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS), at the end of surgery (H0), at one (H1), tow (H2), four (H4) and six (H6) postoperative hours. Parents were requested to record their child’s pain every 6 hours during the first 24 postoperative hours, using the postoperative pain measurement for Parent Scale.

Results: CHEOPS score H0 was significantly lower in G2 as compared to G1 group (p = 0.03). Only 2 children in G2 as compared to 8 children in G1 group, required i.v. paracetamol administration after surgery (p = 0.04). In group G1, two children required paracetamol at home and three developed a postoperative transitory femoral nerve block (p = 0.23).

Conclusions: Ropivacaine when used with high concentration/small volume is more efficient than when used a high volume/low concentration, for ilioinguinal-iliohypogastric nerve block in children.

Keywords: ilioinguinal block, ropivacaine, children.
Introduction

Ilioinguinal-iliohypogastric (IL/IH) nerve block has been shown to produce adequate safe analgesia following peritoneo-vaginal canal surgery in children\(^1\). Ropivacaine, a regional analgesic agent, is known to be a safer substitute, with lesser central nervous system effects and cardiac toxicity than bupivacaine\(^2,3\).

Several concentrations of ropivacaine have been used in IL/IH nerve block in children: 0.75\(^4\), 0.5\(^5\) and 0.2\(^6,7\). The appropriate concentration, however, is yet to be determined. To our knowledge no published study had compared the analgesic effects of ropivacaine when used in two different concentrations in the IL/IH nerve block in children. Therefore the purpose of the present study was to compare the analgesic effects of ropivacaine when used with high concentration/small volume, to its effects when used as high volume/low concentration, for IL/IH nerve block.

Materials and Methods

Following approval of the local Ethics Committee and obtaining the parent’s informed consent, 72 ASA I-II children, 3-9 years of age, scheduled for outpatient elective surgery (unilateral hernia, hydrocelectomy, orchidopexy), were included in a prospective single-blind study. Children with a significant risk of pulmonary aspiration, malignant hyperthermia, known neurological or psychiatric pathology, or with any history of allergy to ropivacaine, were excluded. Children in which the IL/IH nerve block had failed, were also excluded.

All children were premedicated with oral hydroxyzine 2 mg.kg\(^{-1}\), 2 hours before induction of anesthesia. Anesthesia was induced with sevoflurane 6% and maintained with isoflurane in N\(_2\)O/O\(_2\). No other anesthetic or analgesic agents were given during surgery.

Children were then randomly allocated (using a random-number table) to receive ropivacaine 0.8 mg.kg\(^{-1}\), either as 1 mg/ml\(^{-1}\) (0.8 ml.kg\(^{-1}\))-G1 group, or as 2 mg.ml\(^{-1}\) (0.4 ml.kg\(^{-1}\))-G2 group.

The peripheral block in all children was established by the insertion of a short PLEXUFIX 24G beveled needle, using Dalen’s technique\(^1\). The intraoperative data was collected by another anesthetist who was not present in the OR during induction.

A painful stimulus was applied on the surgical site 10 min after the IL/IH nerve block. If the child reacted by an increase of the mean arterial pressure (MAP) and/or heart rate (HR) 20% above baseline values, the surgeon was asked to delay skin incision. If the signs of insufficient anesthesia persisted after another 5 min, the nerve block was declared failed, alfentanil 20 µg.kg\(^{-1}\) was administered and child was excluded from the study.

In the Recovery Unit, pain was assessed using the Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS) which utilizes behavioral changes (facial expressions, body movements, intensity of crying), as indices of response to nociceptive stimuli.

Data was recorded at the end of surgery (H0), two (H2), four (H4) and six (H6) postoperative hours. If the CHEOPS score was higher than 7, children received paracetamol 15 mg.kg\(^{-1}\). Pain was assessed 60 min later and nalbuphine 0.2 mg.kg\(^{-1}\) was administered if the CHEOPS remained higher than 7.

Before leaving the Hospital, parents were instructed to evaluate their children’s pain every 6 hours, during the first 24 postoperative hours, using the postoperative pain measurement for parents (PPMP). The PPMP includes 15 items of routine behavioral change\(^8,9\). Parents were directed to medicate their child with oral paracetamol, if PPMP ≥6. Parents were contacted the following day to collect the PPMP scores, and the number of paracetamol required at home. They were also asked if they had been satisfied with the analgesic care of their children.

The study results were compared using Student t-test and Chi square test. A p value of <5% was considered statistically significant.

Results

Seventy-five ASA I children were originally included in the study. Three children (G1 = 2, G2 = 1)
were excluded because of failure of block. Therefore data of 72 children (G1 = G2 = 36) were analyzed.

There were no statistical differences between the two groups with regard to demographics, types and duration of surgery, anesthesia and preoperative HR and MAP (Table 1, Fig. 1).

Table 1
Patient characteristics data, surgical and anesthetic details

<table>
<thead>
<tr>
<th></th>
<th>G1 (n = 36)</th>
<th>G2 (n = 36)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6 ± 2</td>
<td>6 ± 2</td>
<td>0.54</td>
</tr>
<tr>
<td>Sex male (%)</td>
<td>33 (92%)</td>
<td>32 (89%)</td>
<td>1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>21.6 ± 4.5</td>
<td>23.3 ± 6.7</td>
<td>0.22</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>21</td>
<td>23</td>
<td>0.17</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>33</td>
<td>33</td>
<td>0.87</td>
</tr>
<tr>
<td>Preoperative HR/min</td>
<td>101 ± 12</td>
<td>98 ± 15</td>
<td>0.43</td>
</tr>
<tr>
<td>Preoperative MAP (mmHg)</td>
<td>69 ± 10</td>
<td>69 ± 9</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Data are mean ± SD except for number (%) of patients.

Intraoperative analgesia

Skin incision was delayed (accelerated HR) in 8 (G1) and 5 (G2) children (p = 0.36).

Intraoperative HR

At skin incision, the intraoperative HR was significantly lower in the G2 as compared to the G1 group (p = 0.03), at 10 min (p = 0.027), at 20 min (p = 0.008) and 30 min (p = 0.003) (Fig. 2). There was no statistical difference between the two groups with regard to the intraoperative MAP.

Postoperative analgesia

CHEOPS at H0 was significantly lower in G2 as compared to the G1 group (p = 0.03) (Fig. 3).

Mean CHEOPS score obtained every hour for two hours then every two hours for four hours in the recovery unit. * p <0.05 in comparison among groups.

Eight children (22%) in G1 required supplementary analgesia (paracetamol) after surgery (p = 0.04), compared to two children (6%) in the G2 group.

Eight children in G1 had received paracetamol at H0, whereas two children in G2 group had received paracetamol at H2 and at H6.

Tow children, both in the G1 group required paracetamol at home.

All parents were satisfied with the analgesic care of their children.
Discussion

Ropivacaine 0.8 mg.kg\(^{-1}\) in two different concentrations were used in this study: 0.1% (0.8 ml.kg\(^{-1}\)-G1) and 0.2% (0.4 ml.kg\(^{-1}\)-G2).

The G2 children had a better analgesic profile than those of G1, as evidenced by the lower postoperative pain score at the end of surgery and the amount of analgesic consumption.

The block had failed in 3 children among those originally enrolled. So our success rate was 96%, similar to that of Dalens’s ≥95%\(^{1}\), but higher than that of Lim’s (76%). This variety of results could be explained by the varying definitions of “failure of the block”.

The intra operative HR was significantly lower in G2 as compared to G1. Thus ropivacaine 0.1% seems to be less efficient than 0.2%.

Results show that increasing the volume of local anesthetic could hamper the surgical procedure. Others found that the importance of volume consists in favouring dissection of the aponeurotic planes.

Three patients in the G1 group had developed postoperative transient femoral nerve palsy due to the diffusion of the analgesic solution below the inguinal ligament to the femoral nerve. This side effect had been described in adults\(^{11,12}\) as well as in children\(^{13-16}\). Erez et al\(^{13}\) had observed 6 femoral nerve blocks in a total of 2624 IL/IH nerve blocks using a mixture of bupivacaine 0.5% and lidocaine 0.5%. Lip et al\(^{17}\) reported an incidence of 8.8%, using 0.25 ml.kg\(^{-1}\) of bupivacaine 0.25%.

The appropriate dose of ropivacaine has been variable. Dalens et al in 2001\(^{3}\) report the use of 3 mg.kg\(^{-1}\). Our use of the 0.8 mg.kg\(^{-1}\) ropivacaine dose has proven to be satisfactory. Only 12 children had required complementary analgesia for an observation period of 24 hours. The paracetamol was sufficient to calm the pain in all cases.

Ivan et al\(^{6}\) had successfully used the same dose of ropivacaine together with clonidine 2 µg.kg\(^{-1}\) for IL/IH nerve block in children. On the other hand, Shimoda et al\(^{18}\) used three concentrations of ropivacaine: 1.875, .9375 and .5625 mg.kg\(^{-1}\) in nerve blocks in children for inguinal hemiorrhaphy and found that the postoperative pain scores were significantly higher in the third concentration.

Conclusions

Our study showed that ropivacaine, when used with high concentration/small volume in IL/IH nerve block, is more efficient than with high volume/low concentration. The dose of 0.8 mg.kg\(^{-1}\) ropivacaine seems to be appropriate and is recommended for IL/IH nerve blocks in children.

Acknowledgements

The authors wish to thank Fethi Ben Mohamed and M’hamed Fakhfekh for their English review of the manuscript.
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EVALUATION OF PEDIATRIC CPR
COURSE ON KNOWLEDGE
OF PEDIATRIC RESIDENTS

- Before and After ACLS Course -

Alireza Ebrahim Soltani*, Zahid Hussain Khan****, Shahriar Arbabi*, Babak Hossini*****,
Hedaiatollah Nahvi** and Asghar Agamohammadi***

Abstract

An evaluation was conducted on the knowledge gained by pediatric residents on CPR, before and after a PALS (Pediatric Advanced Cardiac Life Support) course. Following an examination of all pediatric residents at Tehran University of Medical Sciences, they were divided into two groups: non-trained (Group 1) and a group scheduled to undergone training (Group 2). A course on ACLS was conducted. Examination were performed before and after the ACLS course.

The mean of the examination prior to the course in Group 1 and 2 was low, reflecting no significant differences between the Groups. Examination after the ACLS course showed a statistically significant improvement in Group 2 (P ≤ 0.05). It is concluded that knowledge of pediatric residents was low before ACLS course and enhanced after the course.

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Introduction

Guidelines for training in resuscitation have been written in both Australia and United Kingdom, and an Advanced Life Support Group has been formed with the aim of improving emergency care of patients\(^1\,^2\).

In children, the initial care of the critically ill is often made by pediatric residents, whose knowledge of both the cognitive and practical skills are much needed in the management of such children. The effective resuscitation of those patients may optimize their outcome\(^3\). The American Heart Association (AHA), the Pediatric Advanced Life Support course (PALS) is required in 99% of US pediatric residency programs.

Knowledge of CPR is highly crucial for all medical trainees. The AHA has divided the CPR courses into two categories: Basic Life Support (BLS) and the Advanced Cardiac Life Support (ACLS).

Pediatric CPR is different from adult CPR. Pediatric skills in airway management, drug information, cardiac massage and vascular access abilities, are of paramount importance.

We believe that pediatric residents lack sufficient knowledge in CPR. Advanced resuscitation course offers both cognitive knowledge and practical skills. The objectives of the present study was to evaluate the standing knowledge of pediatric residents in CPR, and evaluate this knowledge after those residents receive a PALS course.

Materials and Methods

Pediatric residents from three hospitals affiliated to Tehran University of Medical Sciences (Imam Khomeini General Hospital, Children Medical Center, Bahrami Children Hospital), participated in an examination where their knowledge in airway management, vascular access and proper pharmacological use of drugs, were assessed. A total of forty four pediatric residents (14 females, 30 males) with an average 32.3 years participated.

Prior to examination, the pediatric residents filled-out a questionnaire + experience in CPR, intubation and any PALS course attended, if any (Table 1).

All information necessary to answer the questions on resuscitation was included in the course. Instructors, other than the researchers, were unaware of the contents of the survey. Acceptable answers had to be consistent with guidelines of the AHA and the Advanced Life Support Group\(^5\,^7\).

Resuscitation knowledge prior to the PALS course was first tested, and later followed by second test after the PALS course. Analysis was done by SPSS 11.5 software.

Results

The majority of the pediatric residents failed to pass the PALS course. Most of them (81.8%) were married with a mean age of 32.23 ± 2.8. Eight (18.2%) pediatric residents had previously passed an adult CPR course. All the group had a median of 22.89 ± 1.9 months experience of work in emergency department.

The mean score of results of the first examination (prior to ACLS) in Group 1 were 5.27, 4.27 and 3.55

| Table 1 |
|-------------------|-------------------|-----------------|
| Demographic characteristics of untrained (Group 1) trained (Group 2) resident | Group 1 (untrained) | Group 2 (trained) | sum |
| Gender | | | |
| female | 8 (36.4%) | 6 (27.3%) | 14 (31.8%) |
| Male | 14 (63.6%) | 16 (72.7%) | 30 (68.2%) |
| Marriage | | | |
| Single | 3 (13.6%) | 5 (22.7%) | 8 (18.2%) |
| Married | 19 (86.4%) | 17 (77.3%) | 36 (81.8%) |
| Age (mean) | | | |
| | 32.14 ± 2.7 | 32.32 ± 2.9 | 32.23 ± 2.8 |
| Previous adult CPR | Yes | 18 (81.8%) | 18 (81.8%) | 36 (81.8%) |
| Course | No | 4 (18.2%) | 4 (18.2%) | 8 (18.2%) |
| Mean of work in emergency department (month) | | | |
| | 19.4 ± 19.9 | 20.6 ± 25.8 | 19.8 ± 22.8 |
| Previous CPR experience | | | |
| | 19.4 ± 25.6 | 27.9 ± 20.1 | 24.1 ± 22.6 |
The objective of this study was to pinpoint the pitfalls and professional deficiencies of the pediatric residents in the subcategories of pediatric CPR (airway management and appropriate drugs used and vascular access). Our results revealed that pediatric residents who participated in this study lacked the necessary and optimal knowledge in airway management, pharmacological action of drugs and maintenance of circulatory support.

The outcome of our results showed that pediatric residents had a poor performance in the pretest (before PALS course) (Table 2) but showed a statistically significant improvement after the post test (after PALS course) was conducted (Table 3). A similar study conducted in USA also showed similar results with the only difference that the study was carried out among participants who were not physicians. Two other studies conducted by Lin Ij et al and Waismann et al10 in two different centers arrived at conclusions similar to that depicted in our study.

In another study in USA, only half of the 427 certified pediatricians displayed a sense of satisfaction after completion of the course which mainly assessed the skill performance of the participants. Our study, although designed similarly, did not take into consideration or measured the resuscitation skills of the candidates. However, the participants did show significant improvement in their knowledge of resuscitation after a PALS course, a project we were aiming at.

Our study confirms the significance of instituting a short term PALS course in order to improve the knowledge of the participants in the basic elements of CPR. Others however, have advocated the continuation of such courses in CPR at regular and short intervals in an attempt to achieve the desired outcome.

It is important to state that although 81% of residents participated in an adult ALS course prior to participating in the present PALS course (Table 1), they still lacked the necessary knowledge in conducting pediatric CPR, and did not show better results compared to those participants who participated in this course for the first time, and had no formal training in ACLS at all.

We emphasize that a PALS course is strongly needed and recommended for all those who deal with
pediatric emergencies specially those undergoing residency training. Quan et al, is also of the same opinion that a PALS course is highly effective in improving the knowledge of pediatric residents. This also gives the opportunity to emergency physicians and others interested in undergoing such courses.

Though prior experience in an emergency setting cannot guaranty that such physicians would be able to conduct a pediatric CPR properly and adequately, Dourojaiye et al emphasize the need for such a course for emergency physicians as well.

It is felt that the PALS course is of immense importance not only for the health worker but also for qualified consultant physicians, as both have shown a relatively poor performance in conducting ventilation and properly performing the other requirement of PALS.

Variables such as sex age and marital status does not affect the quality of training as shown in our study as well (Table 1, 2).

In conclusion, we recommend that conducting short and effective courses of PALS should be preferably included in the training curriculum of pediatric residents. This also gives the opportunity to emergency physicians and others interested in undergoing such courses.

We also concur that PALS courses are imperative and highly important in the improvement of the knowledge and skills of the participants. Such courses should preferably be conducted at frequent and short term intervals so that participants do not lose their professional knowledge and competency with the passage of time. This aspect has been elucidated by Wolfram RW et al who argue that three quarters of the subjects failed to achieve a passing score on the retest after a passage of 21 months from their last PALS examination.

**Acknowledgements**

Thanks to all the candidates and instructors on the pediatric life-support course specially the Vice Chancellor of Research of Tehran University of Medical Science.

**References**

CAN PREOPERATIVE ANESTHESIA CONSULTATION CLINIC HELP TO REDUCE OPERATING ROOM CANCELLATION RATE OF CARDIAC SURGERY ON THE DAY OF SURGERY?

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Abstract

Background: Many surgical procedures are delayed or cancelled due to inadequate preoperative assessment and preparation. Case cancellations can be decreased by improved preoperative patient evaluation, improved communication between physician and patient, and modified schedule design. Because of importance of the high cost associated with operating room cancellations; healthcare providers have exerted efforts to decrease case cancellations on the day of surgery. The aim of this study was to evaluate the role of “pre-anesthesia consultation clinic” in reducing operating room cancellation.

Methods: We prospectively studied cancellation rate in 1716 scheduled cases for open heart surgery during a 4 months period in a teaching hospital. Of the 1716 patients, 866 cases were scheduled for operation before establishment of pre-anesthesia consultation clinic (Group 1) and 850 cases were scheduled after establishment of those clinics (Group 2). The data collected included patient age, ASA physical status and date of the preoperative assessment.

Results: Of the 1716 patients studied, 15.03% of cases were cancelled in the two groups. Cancellation rate in Group 1 was 146 (16.8%) and cancellation rate in Group 2 was 113 (13.29%). This difference was statistically significant (p = 0.046). The most common cause of cancellation in the two groups was incomplete medical work-up (32%) [group 1 (19.8%) more than group 2 (12.6%)].

Conclusion: Since the most common cause of cancellation in the two groups was incomplete medical work-up, then visitation of patients to the pre-anesthesia consultation clinic would minimize cancellation rate on the day of surgery.

Keywords: pre-anesthesia evaluation, cancellation rate, consultation clinic, cardiac surgery.

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Introduction

One of the ultimate goals of preoperative medical assessment of patients is to increase the quality and decrease the cost of perioperative care \(^1\). Timing of the pre-anesthesia assessment may influence the cancellation rate on the day of surgery. These cancellations may lead to patients dissatisfactions, increase costs and prolong stay of patients in hospital \(^1\).

There are investigations that confirm positive effects of pre-anesthesia consultation clinic on the cancellation rate of surgery \(^1,2,3\). Among these studies Conway in 1992 \(^4\) and Badner in 1998 \(^5\) reported that with ideal functioning of the pre-anesthesia consultation clinic, delay and cancellations could potentially be reduced. Lacqua in 1994 \(^6\) reported that case cancellations can be decreased by improved preoperative patient evaluation, improved communication between physician and patient and modified schedule design. Fisher in 1996 showed that almost 90% of operating room cancellation is day of surgery cancellations. These cancellations increase turn over time of operating room and so increase costs. Against these result John B. Pollard in 1999 \(^7\) reported that operating room cancellation rate of patients are evaluated within 24h of surgery is similar those patients are seen 2-30 days before surgery.

Because of controversies about influence of timing of the pre-anesthesia assessment on the cancellation rate on the day of surgery, we decided to compare the effect of establishment of “pre-anesthesia consultation clinic” on cancellation rate in cardiac surgery.

Methods and Materials

We prospectively reviewed cancellation rate of 1716 scheduled patients for open heart surgery during a 4 months period in Shahid Rajaii Heart Center (Tehran-Iran) between May 1, 2007 and August 31, 2007. Of 1716 patients, 866 cases were scheduled for open heart surgery in May & June before the establishment of pre-anesthesia consultation clinic (Group 1 or pre-clinic group), and 850 cases were scheduled in July & August after establishment of pre-anesthesia consultation clinic (Group 2 or post-clinic group). All patients in Group 1 were visited on the day before surgery, and in Group 2, we asked surgeons and cardiologists to refer patients to the pre-anesthesia consultation clinic.

All patients were referred to us with their medical record including: history and physical examination, primary essential laboratory tests, chest X-ray and signed operation consent form. Patients were evaluated by cardiac anesthesiologists and their assistants. The data for patients included age, sex, ASA physical status, date of preoperative assessment, scheduled date of surgery, and the actual date of surgery, were entered in the hospital database. Additional laboratory tests or consultations were obtained as needed. A patient was classified as cancelled case, if the patient’s name was on the published operating room schedule but did not have surgery performed on the day scheduled.

Results were analyzed with SPSSv. 12.0 statistical software (SPSS Inc. Chicago, IL). Statistical analysis between categorical variables was done by using Chi-square test, and comparing continuous variables between the two study groups was done by using “independent samples t-test”. The statistically significance level considered \(p \leq 0.05\).

Results

1716 patients scheduled for open heart surgery were divided into two groups who were similar in gender, age, operation type and ASA physical status (Table 1).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients’ background characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
<td>523/343</td>
</tr>
<tr>
<td>Age (year)</td>
<td>59 ± 19</td>
</tr>
<tr>
<td>ASA class III-IV</td>
<td>303 (34.9%)</td>
</tr>
<tr>
<td>Operation type (CABG/Valve)</td>
<td>589/277</td>
</tr>
<tr>
<td>Timing of preoperative evaluation (1 day/3-10 days before Op.)</td>
<td>866/0</td>
</tr>
</tbody>
</table>

ASA = American Society of Anesthesiologists physical status.
CABG = Coronary bypass grafting surgery.
All of 866 patients in Group 1 (100%) and 527/850 (61.9%) of patients in Group 2 received their preoperative evaluation within 24h of surgery. Only 323/850 (38.1%) of patients in Group 2 were referred to the pre-anesthesia consultation clinic after admission by the surgeon (3-10 days before surgery). The frequency of cancellations in all of patients (before and after establishment of consultation clinic) was 259/1716 (15.1%): 146/866 (16.8%) of cases in Group 1 and 113/850 (13.29%) of cases in Group 2 (Fig. 1). There was statistically significant difference ($P = 0.046$) between the two groups.

**Table 2**

<table>
<thead>
<tr>
<th>Causes of operation cancellation before (Group 1) and after (Group 2) establishment of pre-anesthesia consultation clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancelled cases</td>
</tr>
<tr>
<td>Incomplete medical work-up</td>
</tr>
<tr>
<td>Acute patient illness</td>
</tr>
<tr>
<td>Insufficient OR time</td>
</tr>
<tr>
<td>Surgeon’s decision</td>
</tr>
<tr>
<td>Patient’s decision</td>
</tr>
<tr>
<td>ICU admission problem</td>
</tr>
<tr>
<td>Other causes</td>
</tr>
</tbody>
</table>

The most important causes of cancellations in all patients included: incomplete medical work-up (32%, 83/259), acute patient illness (23%, 60/259), ICU problem in patient admission (18%, 47/259), surgeon’s decision (12%, 31/259), patient’s decision (7%, 18/259), insufficient operating room time (4%, 10/259) and other causes (4%, 10/259). Comparison of the two groups for causes of cancellation showed that the most important cause of cancellation in the two groups was incomplete medical work-up (Table 2).

**Discussion**

Cancellation of an elective operation results in waste of operating room time and additional hospital expense$^{8,9}$. The most important causes of these cancellations are: insufficient OR time, surgeon’s discretion (included urgent or emergent surgery preempting elective surgery of illness of surgeon), incomplete medical work-up, acute patient illness, patient decision and ICU problems$^9$.

Some of these causes are preventable e.g. incomplete medical work-up is a preventable cause. If patients are completely evaluated preoperatively, cancellation rate of operating room on the day of surgery is reduced. For this reason, timing of the pre-anesthesia assessment may reduce cancellation rate on the day of surgery$^{10,11}$.

Other benefits of early preoperative assessment consent of: lower anxiety levels, lower analgesic requirements, greater satisfaction with surgical experience, decreased frequency of problems on postoperative follow-up$^{12-14}$. It has been demonstrated that the knowledge gained by patients taught four to eight days before surgery was greater than those who were taught the day before surgery$^4$.

At our Hospital, it was assumed that incomplete medical work-up was a preventable major cause of cancellations. In this study we found that patients who visited within 24 hours of surgery have higher (35%) cancellation rate in Group 1 than those visited 3-10 days before surgery (28% in group 2) (Table 2).

In total, establishment of pre-anesthesia consultation clinic has effective role in total rate of surgery cancellation in our study (Fig. 1). The reason in that timing of the pre-anesthesia assessment would allow enough time for further testing and further medical evaluation of patients when necessary. This may be true in some settings, such as in our Hospital. In some other centers administrative problems have been found to be the single most important source of cancellation. A review of operating room cancellations at a community hospital revealed that 43% of their cancellations were a result of administrative reasons$^{15}$. Similar results were reported in an academic setting, in which 45% of operating room cancellations were
attributed to a single administrative reason (shortage of OR time)\(^6\). For hospitals like ours, with high rate of medical cancellations, early visiting the patients in pre-anesthesia consultation clinic is important.

References

CRITICAL INCIDENT MONITORING
IN A TEACHING HOSPITAL

- The Third Report 2003-2008 -

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Abstract

Several factors have been incriminated in the etiologies of critical incidents: shortages in organizing rules, anesthesia technique, patient environment, human factor, team work and communication. This is the third follow up report describing our performance during the last five years (2003-2008). The possible incriminating causes were identified with the objective of avoiding such eventualities and consequently providing a better patient outcome.

Patients & Methods: The computerized database and the medical records of critical incidents reports in our Department during the period of 2003-2008 were reviewed on case-by-case basis. Seventy reported incidents were discussed in the Department’s Morbidity & Mortality Meetings (MMM). Incidents were classified as per possible incriminating causes: pulmonary, cardiovascular, central nervous system, metabolic, inadvertent drug injection, communicating failure, equipment failure and miscellaneous causes.

Results: Most of the critical incidents reports occurred during maintenance of anesthesia, followed next by during induction and next by same operative day later in the ward. The majority of cases were respiratory events (29 cases), followed by communication failure (12 cases), failure of equipment (9 cases) and inadvertent drug injection (4 cases).

Conclusions: Respiratory events, human errors, team communication and equipment failures, continue to be the leading causes of critical incidents. Critical incidents are apt to occur so long as the human factor is involved. Vigilance in operational efficiency and the scrutiny in drug administration, supervision and training should be closely monitored in order to minimize critical incident reports.

Keywords: Critical incident, General anesthesia, Complications.

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Introduction

Critical incident is defined as any untoward and preventable mishap that is associated with the administration of general or regional anesthesia, and which leads to, or could have led to, an undesirable patient outcome. Staender et al1 have reported that death is definitely no longer an incident, it is a complication, or in the language of error-psychologists, an accident.

Several factors have been reported as possible etiologies of critical incidents: shortcomings in organization rules, anesthesia technique, patient environment, human factor, team work and communication, all of which are preventable.

In 19982 we published our first report on critical incidents covering the period 1991-1997, and 143 incidents were reported. The possible causes given then which led to critical incidents were: human error, lack of communication, anesthetic technique, patient condition factor and equipment failure.

Our second report3 covering the period 1998-2002 included 71 incidents and the possible reasons for those incidents were: human factor, team communication, patient condition and technical problems.

The present third report covering the period 2003-2008 is a follow-up of our performance in this field during the last five years and identifying the possible incriminating factors leading to such an eventuality, the main objective being better patient outcome.

Patients and Materials

The computerized data base and the medical records of critical incidents reported to our Department during the period of August 2003-May 2008 were reviewed on case-by-case basis.

The adopted Department’s Incident Form includes:

- Free text description where the narrator describes the incident as it occurred.
- A section on the classification of the incident and its possible etiology.
- Reports of any communication failures.
- The prescription, preparation and administration of drugs. The incident was classified as to whether the incident was aborted before or discovered after it had been inadvertently injected.
- Time and location of the incident.

Seventy incidents reported were discussed in the monthly Morbidity & Mortality Meetings (MMM). After thorough discussions the incidents were categorized as per the possible incriminating cause into: pulmonary, cardiovascular, central nervous system, metabolic, inadvertent drug injection, communication failure, equipment failure and miscellaneous. Incidents were also classified by their actual or potential seriousness as low, moderate or major life threatening. Recommendations were subsequently collected aiming at avoiding repetitions of such incidents, the objective being offering a better patient outcome.

Results

All 70 critical incidents reported were given general anesthesia and had varying ASA classification. Most of the incidents occurred during maintenance of anesthesia, followed next during induction, and next on same operative day later in the ward.

Incidents and frequency were classified as: (Table 1)

<table>
<thead>
<tr>
<th>Reasons</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>29</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>3</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>5</td>
</tr>
<tr>
<td>Metabolic</td>
<td>3</td>
</tr>
<tr>
<td>Communication failure</td>
<td>12</td>
</tr>
<tr>
<td>Equipment failure</td>
<td>9</td>
</tr>
<tr>
<td>Inadvertent drug injection</td>
<td>4</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
</tr>
</tbody>
</table>

- Respiratory events were the majority (29 cases).
- Communication failures (12 cases).
- Failure of equipment (9 cases).
- Inadvertent drug injection (4 cases).
- Cardiovascular events (5 cases).
- Miscellaneous (5 cases).

Of the respiratory events, there were 7 trauma cases of aspiration pneumonitis, were endotracheal intubation was performed in the Emergency Department requiring
prolonged intubation in the surgical intensive care unit (SICU). There was one case of fatal air embolism and two cases of postoperative pulmonary embolism and one case of severe intraoperative hypoxia during thoracotomy in a pediatric patient.

Failures of equipment consisted of failure of anesthesia machine, failure of patient controlled analgesia (PCA) pump and one rare case where the stomach was perforated during introduction of nasogastric tube. The drugs contemplated for inadvertent injections were insulin, bupivacaine and potassium.

In the cardiovascular events, one case of intraoperative cardiac arrest occurred due to severe hypotension during knee replacement surgery, which was resuscitated successfully with no postoperative sequelae.

Under miscellaneous events is listed a corneal abrasion, prolonged surgical hours and unavailability of blood transfusion.

**Discussion**

In the first published report covering the period 1991-1997, 143 critical incidents were analyzed and the following leading possible reasons were identified: human errors, lack of communication, anesthetic techniques, patient condition and equipment failure. In the second published report of 71 incidents for 1998-2002, the following leading causes of incidents were recognized: human error, team communication, patient condition and technical problems. In this third report for 2003-2008, the same reasons that led to the incidents of the previous two reports, have repeated themselves.

It is apparent that human error and communication failures are common reasons in the three reports. Human error is defined as failure of planned action to be completed as planned. Human error can be classified into active and latent. Active error refers to an event occurring immediately before an incident. Latent error refers to problems occurring within the system that cause accidents to occur under situations resulting from inappropriate decisions made by a careless staff e.g. an anesthetic drug trolley loaded with an incorrect drug.

In a retrospective review and analysis of all critical incidents at Birmingham Children Hospital, showed that human factors occur in 42.5% of in-theatre incidents in pediatric anesthesia. Similarly, analysis of the first 2000 incidents in Australia providing data on all aspects of anesthetic error, 79% were due to human error. In our present Third Report, the most common problems were related to respiratory issues (41%), human factors (communication failure and inadvertent drug injection) (23%) and equipment failure (13%). This is in accordance with two recently published reports on critical incidents where the most common problems were related to respiratory events.

In a recent study on incidents reported to UK National Safety Agency, 12,084 submitted were associated with medications, most commonly morphine, gentamycin and noradrenaline. In our Third Report, one case of inadvertent potassium was given i.v. instead of sodium bicarbonate because of the similarities of the two vials and lack of a double check procedure. The patient developed near fatal cardiac arrhythmia and was successfully resuscitated with no further sequelae. At the time a decision was taken to remove all potassium vials out of the operating rooms and make it only available at submission of a prescription order.

Equipment failure still presents an ongoing problem and inspite of machine upgrading by company authorities, the problem still exists.

**Conclusion**

Respiratory events, human errors, team work and equipment failure are continuing to be the leading causes of critical incidents. We believe that critical incidents will still occur so long as the human factor is involved. Therefore vigilance in checking the anesthesia machine and its maintenance and double checking the administered drugs, better supervision and training, are essential to minimize the frequency of critical incidents and thus provide better patient outcome.
References

CASE REPORTS

MANAGEMENT OF A2B BLOOD GROUP IN A PATIENT FOR HYPOTHERMIC CARIOPULMONARY BYPASS SURGERY

- A Case Report -

RASOUL AZARFARI and AZIN ALIZADEH ASL

Abstract

A2 is one of the rare subgroups in the ABO blood group system. Because of the weak antigenic power of A2 subgroup, the hemolytic reaction is not severe under normothermic situations. Under hypothermic conditions, however, such as in cardiac surgery under hypothermic cardiopulmonary bypass (CPB), lethal hemolytic reaction may occur.

Autologous blood transfusion helps the anesthesiologist to avoid banked blood and thus avoid unwanted transfusion reactions. The following case report is a 59 yrs old man with an “A2B” negative blood group who underwent CABG under hypothermic CPB (28C, using cold cardioplegia 4C). Following induction, the anesthesiologist drew three units of patient’s own blood (1200cc) and replaced it with the same volume of colloid solution (Acute Normovolemic Hemodilution-ANH). The collected autologous blood was then re-transfused at the end of surgery.

With the use of the ANH technique, the patient was successfully managed during hypothermic CPB without the risk of a hemolytic reaction.

Keywords: A2B blood group, cardiac surgery, hypothermia, transfusion, anesthesia.

Introduction

Much of the blood given to patients during the perioperative period is administered by the anesthesiologist1. Anesthesiologists, therefore, must have an up-to-date knowledge of transfusion medicine.

There are different blood subgroups among different races and countries (Table 1) that can be clinically important2. From these varying blood subgroups, A2B is one of the rare subgroups of ABO blood group system. Because of the weak antigenic power of A2 subgroups, hemolytic reaction is not severe under normothermic situations. But under hypothermic conditions, such as in cardiac surgery under hypothermic CPB, lethal hemolytic reaction may occur3.
The CPB lasted 93 min and the operation 5 hrs. Patient was then taken to the ICU. In the ICU, blood drainage from chest and mediastinal tubes was estimated to be 1000 ml in 24 hours causing a Hct decreases to 27% (preop. Hct was 47%), for which one unit of homologous A2B blood was transfused. Patient’s trachea was extubated four hours after admission to the ICU. In 48 hours, patient was transferred to the ward and was discharged home on the 7th day, without any complications.

Discussion

ABO blood group system includes different genotypes and phenotypes of A, B and O antigens due to different gene mutations. 44.6% of all blood groups are A which includes two subgroups: A1 and A2 with a respective prevalence of 80% and 20%2. The A2 antigen has a weaker antigenic power than the A1, is not observed in macroscopic agglutination, and is just observed in microscopic studies hence its name “weak A”2.

Prevalence of A2B blood group is 0.9%-1% in the general population2-5. Considering 15% prevalence of Rh negative, the prevalence of A2B negative, is about 0.1%.

A2 and A2B individuals have anti A1 in their serum. Approximately 0.4% of A2 and 25% of A2B individuals have anti A1 in the serum6.

ABO system is of special significance in kidney transplantation7-13. A blood group with its subgroups of unknown weaker antigen is diagnosed as blood group O and causes no problem while receiving blood. However, when subgroup A2, as blood group O, is transfused to another individual with O blood group, causes hemolytic intravascular reaction, because of the presence of anti A1 in the serum.

Because of the weaker antigenic power of A2, hemolytic reaction is not severe or lethal under normothermic situations. However, severe reaction may occur due to presence of anti A1 at lower temperatures (≈ 25°C). It follows that severe reaction may be observed in patients undergoing CABG under hypothermic CABG14.

It is of great importance that anesthesiologists should be well aware that blood subgroups can be

<table>
<thead>
<tr>
<th>Blood group</th>
<th>O</th>
<th>A1</th>
<th>A2</th>
<th>B</th>
<th>A1B</th>
<th>A2B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>44%</td>
<td>33%</td>
<td>10%</td>
<td>9%</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Black people</td>
<td>49%</td>
<td>19%</td>
<td>8%</td>
<td>20%</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Asian</td>
<td>43%</td>
<td>27%</td>
<td>Rare</td>
<td>25%</td>
<td>5%</td>
<td>Rare</td>
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We report a patient with A2B blood group who underwent CABG surgery under hypothermic CPB and was successfully managed using the ANH technique, without hemolytic reaction.

Case Report

The patient is a 59 yrs old man, candidate for CABG due to severe stenosis of three coronary vessels. He had undergone ear surgery 45 years previously without need for transfusion. His blood group was reported to be “B negative” at that time, but in the present operation, blood group was reported to be “AB negative”. Because of these contradictory reports, complimentary laboratory tests (agglutination by monoclonal anti-A) was requested. Patient’s blood was reported to be “A2B negative”. The consultant hematologist recommended reserving three units of blood: A2B group or O group if A2B group was not available.

Following induction by sufentanil, midazolam and atracurium, and in accordance to patient’s Hematocrit (Hct) of 47% (Table 2), three units of autologous blood were collected, and the patient’s blood volume was replaced by the same volume of colloid solution using the Acute Autonomous Hemodilution (ANH) technique. After sternotomy, patient underwent bypass grafting of three vessels under hypothermic CPB (28°C and receiving cold cardioplegia). The previously collected autologous blood units were then re-transfused at the end of operation.

<table>
<thead>
<tr>
<th>Laboratory hematologic findings of the patient</th>
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<tbody>
<tr>
<td>White blood cell (WBC) count/ml³</td>
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<tr>
<td>Hemoglobin (Hb) g/dl</td>
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<td>Hematocrit (Hct)</td>
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<td>Platelet count/ml³</td>
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causes of mistakes in blood transfusion centers. By reporting A2B negative, unless A2B negative blood is available, for patients when in need, the O negative transfusion is recommended.

Because of the lower prevalence of the A2B negative subgroup, the preoperative collection of autologous blood and the use of the ANH technique seems to be an effective method to avoid transfusion reactions. In our case, this kind of management under hypothermic CPB (28°C and 4°C cardioplegia), CABG surgery was performed successfully without hemolytic reaction. In ICU, patient received just one unit of A2B negative blood in the postoperative period.

In conclusion, it is recommended that differences in blood group reporting should be considered seriously. Samples should be referred to competent hematologist and a transfusion center, for definitive reporting. In case of rare blood subgroups, blood conservation strategies utilizing autologous transfusion together with the ANH technique, are the recommended ways to avoid transfusion reactions.

References

MEASUREMENT OF CARDIAC OUTPUT IN VENTRICULAR RUPTURE FOLLOWING ACUTE MYOCARDIAL INFARCTION

- Pulmonary Artery Catheter vs Transpulmonary Thermodilution -
- A Case Report -

Schwarzkopf Konrad*, Simon Stefan, Preussler Niels-Peter and Hütter Lars

Abstract

We compared the cardiac output measured by the transpulmonary aortic single indicator thermodilution method with that by the pulmonary artery catheterization in a patient with ventricular septal rupture after acute myocardial infarction. Though the former cardiac output was lower than the latter, in the presence of the ventricular septal rupture, the cardiac outputs were equal after the rupture was closed. This indicates that, while the cardiac output measured by the pulmonary artery catheter is influenced by the ventricular left-to-right shunt, transpulmonary aortic thermodilution method measures the true cardiac output of the left heart, which is responsible for organ perfusion.

Keywords: Hemodynamic monitoring, pulmonary artery catheter, transpulmonary aortic single indicator thermodilution method, ventricular septal rupture.

Introduction

Ventricular septal rupture complicating an acute myocardial infarction has a high mortality rate up to 90% in medically treated patients. Pulmonary arterial catheterization (PAC) is often used for hemodynamic monitoring of these patients during transportation to a specialized hospital for definitive surgical intervention. A major problem with the PAC in the presence of a ventricular septal defect is that PAC may overestimate the cardiac output in this situation, because the measured value contains the left-to-right shunt and the true cardiac output of the left ventricle.

The transpulmonary single indicator thermodilution method (TTM) is a less invasive method to measure the cardiac output compared with PAC.

Following an injection of the cold saline into the venous part of the circulation (e.g. via the internal jugular vein) the resulting change in temperature is measured with a thermodilution catheter typically located in the femoral artery. The cardiac output is calculated based on the Steward-Hamilton equation. An intracardial left-to-right shunt does not disturb the cardiac output measurements using TTM.

We present the case of a patient with ventricular septal rupture where the cardiac outputs derived from PAC and TTM were compared.

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Case Report

A 67-year-old man was admitted to the hospital with epigastric pain for 3 days. On admission, the troponin I level was 22.7 ng/ml and the ECG showed an inferior myocardial infarction. After establishment of mechanical support with an intraaortic balloon pump to treat acute hemodynamic deterioration, coronary angiography, echocardiography and right heart catheterization confirmed the diagnosis of a ventricular septal rupture. The oxygen saturation increased from the right atrium (40%) to the right ventricle (96%).

Before surgery was started, a femoral arterial thermodilution catheter (PV 2015 L 20, Pulsion Medical Systems, Munich, Germany) was inserted in the right femoral artery and connected to a monitor for transpulmonary aortic thermodilution measurement of cardiac output (PiCCO V4.1, Pulsion Medical Systems, Munich, Germany). A 7-French pulmonary artery catheter (Baxter, Irvine, USA) was inserted via the right internal jugular vein and connected to a hemodynamic monitor (Vigilance Monitor, Baxter, Irvine, USA).

Cardiac output measurements were performed in triplicate with 15 ml cold saline (1-5°C) injected through the central venous catheter and averaged. The PAC measured a cardiac output of the right heart of 12.9 l/min, whereas TTM showed a cardiac output of the total heart of 2.95 l/min. Measured by the PAC mixed venous saturation was 86%, mean pulmonary artery pressure was 34 mmHg, pulmonary wedge pressure was 24 mmHg, the central venous pressure was 19 mmHg.

After surgical patch closure of the septal rupture another set of cardiac output measurements by three bolus injections was done. Cardiac output measured by PAC was 6.9 l/min compared with 6.8 l/min cardiac output by TTM. The patient died postoperatively due to multisystem organ failure. The sufficient patch closure was verified on autopsy.

References

FATAL SUBCUTANEOUS EMPHYSEMA SECONDARY TO PULMONARY NOCARDIOSIS IN AN IMMUNOCOMPROMISED PATIENT

- A Case Report -

MUHAMMAD IMRAN* AND HAMEED ULLAH**

We report a case of necrotizing pulmonary nocardiosis complicated by subcutaneous emphysema in a 54 years old male patient receiving immunosuppressive therapy following renal transplant. The subcutaneous emphysema progressed rapidly and despite intervention, the response was poor resulting in fatal cardiorespiratory failure.

Case Report

A 54-year-old male patient was admitted through emergency with recent onset of productive cough with hemoptysis and fever which was gradually increasing since the previous 3 days. He also had a small chest wound just under his right nipple. He had undergone renal transplantation 2 years ago due to chronic renal failure secondary to focal segmental glomerulonephritis and was receiving corticosteroids since then. He also had hypertension and acid-peptic disease for which he was taking medications.

Laboratory investigations revealed leucocytosis with neutrophil predominance, high serum creatinine and blood urea nitrogen and low serum bicarbonate levels. Chest X-ray (CXR) revealed right sided homogenous opacity in mid zone extending to invade the skin just below the nipple. Diagnosis of graft rejection and pneumonia secondary to immunosuppression was made and empiric broad spectrum antimicrobial and antifungal were started. For immunosuppression, cyclosporin and mycophenolate mofetil were initiated and prednisolone continued. Sputum and broncho alveolar lavage (BAL) was sent for culture and acid-fast bacilli (AFB) smear. Microbiology report showed growth of methicillin-resistant staphylococcus aureus (MRSA) and escherichia coli (E. coli), following which antibiotics were changed to those sensitive to the organisms.

Until this time patient was able to maintain acceptable arterial blood gases on oxygen therapy, but on the third day of admission he started to become hypoxic despite supplemental oxygen and developed severe respiratory acidosis. He also developed tachypnea and became drowsy which gradually worsened and therefore was electively intubated and shifted to intensive care unit for mechanical ventilation and further management.

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despite all attempts at cardiopulmonary resuscitation, he could not be revived.

Discussion

The genus *Nocardia* is a member of the order Actinomycetales, found in soil, plants and decomposing organic material. *Nocardia* is divided into several species of which *Nocardia asteroides* accounts for the vast majority of clinical nocardial infection in humans. Immunosuppression is a well established risk factor for nocardiosis as was our patient. A compilation of more than a thousand randomly selected cases from the literature showed that more than 60% of all reported cases of nocardiosis are associated with preexisting immunosuppression, with the most common being corticosteroid treatment and immunosuppressive therapy. The incidence of nocardiosis in renal transplant recipients varies from 2 to 20%. Beaman comprehensively reviewed the published literature and found 140 (21.8%) cases of nocardiosis in organ transplant recipients, of which 81 (58%) were in renal transplant recipients.

Pulmonary disease is the predominant clinical presentation of nocardiosis, with almost 90% of these caused by members of the *N. asteroides* complex. The incidence of pulmonary nocardiosis is increasing due to a higher degree of clinical suspicion and the increasing number of immunosuppressive factors. Characteristically radiological manifestations may include consolidations, irregular nodules, often cavitatory, reticulonodular or diffuse infiltrates, and pleural effusions.

Clinicians should be aware that pulmonary nocardiosis is difficult to diagnose on the basis of clinical and radiological findings. A high level of clinical suspicion is required in patients with risk factors. Growth of *Nocardia* may take from 48 hours to several weeks, but typical colonies are usually seen from 3 to 5 days. In pulmonary nocardiosis, sputum culture is the most frequently used diagnostic test. This patient showed growth of nocardia on second bronchioalveolar lavage approximately fourteen days after his sickness. Successful therapy requires the use of antimicrobial drugs in combination with appropriate treatment.
surgical drainage or debridement. The clinical outcome of therapy for nocardiosis is dependent on the site and extent of disease and underlying host factors. Mortality rates between 20-40% are mentioned in different series and may reach 80-100% in disseminated central nervous system disease.

The association of chest wall subcutaneous emphysema is less common with pulmonary infections and not reported with nocardiosis. Extension of air from respiratory tracts may produce pneumothorax, pneumomediastinum, pneumopericardium, or retroperitoneal collections of air. Subcutaneous emphysema can also extend into the soft tissues of the head and neck upwards and up to legs downwards. Although in most instances subcutaneous emphysema is of little clinical importance, it may be fatal if it leads to upper airway obstruction, acute respiratory failure due to chest wall compression, intracranial hypertension, and circulatory collapse in association with tension pneumomediastinum. It also causes difficulties in the reading of chest radiographs, echocardiography, ultrasound, and electrocardiograms. Prompt diagnosis and treatment is necessary before rapid deterioration may suddenly compromise cardiorespiratory system.

Treatment should not be delayed awaiting further cardiovascular and respiratory compromise. As soon as pneumothorax is suspected, the pleural space should be decompressed. Surprisingly, in our patient mechanical ventilatory parameters were reasonable till the last day when rapid deterioration in subcutaneous emphysema caused a compromise in the delivery of adequate minute ventilation finally resulting in fatal cardiopulmonary failure.

Although the subcutaneous emphysema in nocardiosis is rare, it is important for the clinicians to be aware of this and should intervene early as it may rapidly progress resulting in acute cardio-respiratory failure.

References


ANESTHETIC MANAGEMENT
OF PHEOCHROMOCYTOMA

- A Case Report -

A Turkistani*

Introduction

Pheochromocytoma is pharmacologically volatile, potentially lethal catecholamine-containing tumor of chromaffin tissues. The perioperative course and anesthetic management of patients with catecholamine-secreting pheochromoytoma has typically been reported only in small case series because of the infrequent incidence of these tumors. In this report, we describe a successful management of a case of pheochromocytoma that underwent right adrenalectomy with favorable outcome.

Case Report

A 17 yr-old female patient presented to the Emergency Department complaining of night sweating, headache and lethargy. On physical examination, she had low-grade fever blood pressure 178/105 mmHg, raised jugular venous pressure (JVP) and audible systolic murmur over tricuspid area. Investigations revealed normal routine blood work. The patient was admitted to medical ward. The history was suggestive of pheochromocytoma for which she underwent all investigations. Vanillymandelic acid (VMA) 24-hr urine collection concentration was 76 mcmol/day (normal 5-25 mcmol/day). MRI of the abdomen which showed well defined large rounded mass seen in the left suprarenal gland measuring around 6.6 × 7 cm displacing the left kidney downward. The right suprarenal gland and liver are grossly unremarkable. Echocardiogram showed mild globular LV systolic dysfunction. The diagnosis of pheochromocytoma was made.

Patient was started on oral phenoxybenzamine 10 mg twice daily and oral amlodipine 5 mg once daily. Three days after starting the antihypertensive medications, the blood pressure was controlled and the range of readings were in the range of 118/70 to 132/80 mmHg. She was scheduled to undergo right open adrenalectomy under general anesthesia.

Patient was referred to Anesthesia Department for assessment. On the preoperative visit, supine and standing blood pressure were measured which revealed no postural hypotension. The plan was to increase the oral dose of phenoxybenzamine gradually till start of full alpha-adrenergic blockade with postural hypotension.

Intravenous fluid hydration regimen was started with 1500 ml/day normal saline 0.9%. Five days later, she was reassessed and no postural hypotension was recorded. The dose of phenoxybenzamine was again increased to 40 mg twice daily with continuation on I.V hydration for another two days. At that time she clearly developed postural hypotension; supine blood; pressure range of 115-127/65-78 mmHg and standing blood pressure range of 84-90/48-60

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mmHg. ECG was done and showed sinus tachycardia with heart rate of 115 beats/min with no evidence of PVCs. The hematocrit dropped from 31 prior to 27 following intravenous hydration therapy. At that time the patient was cleared up for surgery.

Premedication was achieved with oral lorazepam 2 mg night before and 2 hr prior to surgery. Phenoxybenzamine was continued as scheduled with no interruption. On the day of surgery in the operation room she was connected to routine non-invasive monitoring: five ECG leads, pulse oximeter and non-invasive blood pressure monitoring. Intravenous and arterial cannulations were performed following i.v. fentanyl 25 mcg under local anesthesia. Right internal jugular venous cannulation was performed after commencement of general anesthesia and after tracheal intubation.

The following drugs were readily available to use in case of emergency, sodium nitroprusside (SNP), phentolamine, noradrenaline and adrenaline infusions. Also level 1 pressure pump was standby in case of rapid volume hydration or blood transfusion required. SNP infusion pump was attached to one of the peripheral i.v. lines ready to be used when needed.

Induction of anesthesia started with i.v. lidocaine 100 mg, phentolamine 2 mg, labetalol 2.5 mg, fentanyl 150 mcg, propofol 120 mg and tracheal intubation was facilitated by i.v. rocuronium 40 mg. At induction of anesthesia the blood pressure was 115/82 mmHg and at tracheal intubation it was 105/70 mmHg. Before skin incision i.v. SNP infusion was started at a rate of 0.5-0.75 µg/kg/min.

During surgery central venous pressure (CVP) increased from 6 to around 12-14 cm H2O with fluid infusion at a rate of 10-15 ml/kg/hr of colloids and crystalloids. The patient tolerated the whole procedure well, with minimal fluctuation of the blood pressure except at the time of ligation of the last blood supply of the tumor where she developed severe hypotension which was successfully managed with i.v. fluids and i.v. phenylephrine 150 mcg in two doses. After completion of surgery and before tracheal extubation epidural catheter was inserted at level of L1-2 for postoperative analgesia. Reversal was given in form of neostegmine 2.5 mg and atropine 1 mg and trachea was extubated.

Patient was transferred fully awake to surgical intensive care unit (SICU) with stable vital signs. She made uneventful recovery and two days later she was discharged to regular surgical ward. Histopathology of the right adrenal gland confirmed the diagnosis of pheochromocytoma.

**Discussion**

Pre-operative assessment of patients with pheochromocytoma is an essential part in management. Although alpha – blockade is not universally considered as absolute necessity, other investigators recommended proper alphal-receptor blockade. In our case, we have used high dose alpha-adrenergic blockade prior to surgery and our target was the development of postural hypotension in order to ensure full blockade.

Roizen et al recommended the following preoperative conditions prior to surgery for pheochromocytoma: (a) blood pressure < 160/90 mmHg for 24 hr before surgery, (b) postural hypotension > 80-45 mmHg, (c) ECG should be free of any ST-T changes for a week and (d) no PVCs more than 1 in five min. In our case we strictly adhered to Roizen’s criteria.

Preoperative alpha-adrenergic blockade is usually achieved by using phenoxybenzamine, although newer generation of selective alpha-blocker have been used which carry several advantages compared to phenoxxbenzamine: they do not produce reflex tachycardia, have shorter half life, so dosage can be adjusted rapidly, such that preoperative and postoperative hypotension should be less. Prazocin and terazocin may be considered.

Preoperative beta-blockade is usually not necessary unless the patient has an epinephrine secreting tumor. This is because cardiac alpha2-receptors are not antagonized by the usual preoperative alpha-adrenergic blockade.

The etiology of hypotension following tumor resection may be due to inadequate intravascular volume replacement, residual effects of preoperative alpha-receptor blockade or hemorrhage. In the present case severe hypotension occurred at ligation...
We used both fluids and phenylephrine during severe hypotension with immediate favorite response.

In conclusion, we believe that early involvement of anesthetist in the management of pheochromocytoma patient is the cornerstone for better outcome. In this case report we confirmed that adherence to Roizen’s criteria can lead to successful perioperative management of such cases.

References


SUPERIOR VENA CAVA SYNDROME:
STILL A MEDICAL DILEMMA

- A Case Report -

PRAGNYADIPTA MISHRA* and RAJINI KAUSALYA**

Implication Statement

Many options are available for treating superior vena cava syndrome. However, the decision of the appropriate plan to be taken can be challenging in critically sick patients with multiple coexisting illnesses, particularly, if it is associated with coagulopathy.

Abstract

Purpose

The purpose of this report is to highlight the dilemma and the associated clinical implications in treating a patient with superior vena cava syndrome (SVCS) with a coexisting coagulopathy.

Clinical Features

This case report describes a post-bone marrow transplant patient who was admitted to our ICU because of bronchiectasis complicated with nosocomial pneumonia. Following the recovery from pneumonia and long ventilatory support, he developed superior vena cava syndrome (SVCS) due to mediastinal lymphadenopathy. The diagnosis was delayed due to associated confounding clinical factors. Due to the rapid deterioration in patient’s condition, the immediate tissue diagnosis of mediastinal lymph nodes and re-canalization of superior vena cava by stenting was not done though it was, our priority. He had many other medical problems as well such as thrombocytopenia, deranged coagulation profile, old cerebral infarction with hemiplegia, seizure disorder and cardiac arrhythmias that complicated the treatment plan.

Ultrasonography (USG) guided biopsy followed by stenting of the SVC was done after discussing the risks and benefits with patient’s relatives. But, he had bleeding from biopsy site due to deranged coagulation profile. He was not given any anticoagulants.

Within 24 hours, the stent was blocked by clot that was diagnosed by the deteriorating clinical features and a repeat CT scan. Then he was given Enoxaparin in therapeutic dose and the clot cleared within a day, possibly partly due to Enoxaparin and partly coagulopathy.

Conclusion

Meticulous care should be practiced in deciding the appropriate treatment of SVCS especially when it is associated with other complicating medical problems particularly coagulopathy.

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Introduction

Superior vena cava syndrome (SVCS) in an uncommon complication of many disease conditions, which include malignancies, hematological disorders, and patients with transvenous pacemakers and central venous catheters.

Most cases are caused by malignancies, and SVC obstruction due to malignancies usually progress rapidly leading to complete obstruction which can cause a patient’s condition to deteriorate rapidly. Also, benign conditions are increasing due to iatrogenic injuries from central venous catheters (CVC) and transvenous pacemakers.

Obstruction due to benign disease may be indolent. SVC obstruction usually presents with swelling of face and upper extremities, conjunctival suffusion, periorbital swelling, proptosis, dyspnea, respiratory distress and pleural effusion and rarely life-threatening complications, one of which is pulmonary embolism (PE).

As symptoms, such as respiratory distress, systemic hypotension, and intracranial hypertension are life-threatening, this condition has to be treated on an emergency basis with definitive strategies, ranging from anticoagulation, medical management to radiological stenting, chemotherapy, radiotherapy, or surgical bypass. We present an interesting case of SVCS in a patient admitted to our ICU.

Case Report

A 20 yr old patient, who had undergone allogenic bone-marrow transplant for acute myeloid leukemia one year earlier, presented to our Emergency Department with breathing difficulty. He was a known case of bronchiectasis with history of exacerbations for which he was admitted many times. He had multiple other complications of bone-marrow transplant such as, liver graft versus host disease (GVHD), hemosiderosis on monthly venesections and Desoferol, 6 month old watershed infarct involving right middle cerebral artery and anterior cerebral artery with hemiparesis, 4 month old chronic subdural hematoma with regular neurosurgical follow ups and past history of seizures on Valproic acid.

Patient was tachypneic, tachycardic and restless.

Chest had rhonchi and crepitations, the oxygen saturation (pulse oximetry) was around 75% on 10 L/min O2 flow by facemask with reservoir bag. Arterial blood gas showed respiratory acidosis due to CO2 retention (pCO2 = 16 kPa).

He was admitted to the ICU and was given a trial of noninvasive ventilation without improvement. His trachea was intubated and started on pressure controlled mechanical ventilation. Patient had a turbulent course in ICU; he developed multiple complications such as nosocomial infection with septic shock, right-sided heart failure, uncontrolled seizures and arrhythmias such as intermittent paroxysmal supraventricular tachycardia (PSVT).

A CVC was inserted in his right internal jugular vein (IJV) to monitor central venous pressure and for giving various intra venous medications. A CT scan of chest done during ICU stay showed significant bronchiectactic changes with bilateral upper lobe fibrosis and his arterial CO2 was always between 10 to 12 kPa. Patient was tracheostomised anticipating prolonged ventilatory support.

Once his respiratory and hemodynamic parameters stabilized, weaning was gradually attempted. His ventilatory requirements came down from a pressure controlled mode to a pressure support mode, but he could not be weaned further. He intermittently complained of headache and pain in the upper chest, which we attributed to hypercarbia and tracheotomy wound. The tracheostomy tube tie was loosened and some analgesics prescribed.

On 26th day of ICU stay, patient developed significant puffiness of face, neck and both upper extremities, along with tachypnea, irritability, drowsiness and oliguria. Initially, the renal impairment was attributed to recurrent sepsis and drug toxicity, as he was on (Amikacin, Amphotericin B, and Cyclosporine). Over a period of two days the swelling became worse in the same region without involving the lower extremities. Form the day of admission his coagulation profile was deranged (INR varying from 1.5 of 1.7) and platelet count was low (40 × 109/L to 80 × 109/L) due to GVHD. He received fresh frozen plasma and platelet concentrates before invasive procedures such as CVC cannulation, tracheostomy, rectal biopsy etc. were done.
Although patient had coagulopathy, SVCS was suspected due to external compression of superior vena cava by mediastinal lymphadenopathy from a relapsed primary malignancy (AML). Initial Doppler ultrasonography (USG) was inconclusive. But, subsequent CT scan confirmed the diagnosis of a superior venacaval obstruction by enlarged mediastinal nodes. A femoral venous catheter was immediately inserted for administration of intravenous medication, but the CVC in the right IJV was retained as advised by the radiologist for potential radiological interventions. A decision was made to perform an USG guided mediastinal lymph node biopsy for tissue diagnosis and SVC stenting in the same sitting. The radiologist performed the mediastinal biopsy and stenting of SVC. There was local bleeding from the biopsy site due to a deranged coagulogram (INR = 1.73, APTT = 73 seconds and platelet count = 79 × 10⁹/L) and high venous pressure in the collateral circulation. Bleeding stopped with local pressure and wound sutured. It was decided not to transfuse any blood products because of fear of thrombosis of the stent. CVC in IJV was withdrawn and fixed just above the stent by the radiologist for possible future use. He was not given any post-stenting anticoagulant due to the deranged coagulogram and possibility of bleeding from biopsy site.

On the next day (day 27 of ICU stay) there was a gross increase in facial, upper limb swelling and diminished air entry at both lung bases. There was no decrease in CVP measured through the CVC in right IJV. Urgent CT scan showed thrombosis of SVC and right subclavian vein along with bilateral pleural effusion. He was started on Enoxaparin in therapeutic dose (40 mg twice daily). Thrombolytic therapy or intravenous Heparin was withheld for fear of possible rebleed from mediastinal biopsy site and also from chronic subdural hematoma and an old cerebral infarct site. Vascular surgeon ruled out the possibility of surgical intervention due to poor general condition of the patient.

He was now complaining of more chest pain. There was a gradual decrease in urine output and increase in blood urea and creatinine, possibly due to contrast induced nephropathy. His lung compliance was deteriorating steadily with a parallel increase in pCO₂ in spite of full ventilatory support. He developed frequent episodes of PSVT and atrial fibrillation. Cardiologist started him on Amiodarone in spite of fibrotic lungs as he was already on Sotalol for PSVT with no response.

There was no improvement in his symptoms after 24 hours of treatment with Enoxaparin. The biopsy of the mediastinal lymph node was reported as crushed tissue. Hence no definitive treatment for the enlarged nodes was possible. Instead it was decided to repeat the CT scan and give local thrombolytic therapy (with Alteplase) through the CVC in the right IJV if found to have persistent thrombosis. Fortunately, the radiologist found the SVC to be patent. So he was continued on Enoxaparin without any further intervention.

Discussion

Superior vena cava syndrome generally occurs due to impairment of normal venous return through superior vena cava by either compression by adjacent tumor mass or lymph nodes, or thrombosis of SVC due to long term indwelling extraneous devices and hypercoagulable states. Even though the diagnosis depends on a high degree of alertness on the part of the treating physician, it can be quite challenging to diagnose SVC syndrome in a critically ill patient like ours.

Our patient had undergone allogenic bone marrow transplant one year earlier for acute myeloid leukemia (AML). There was neither any history of relapse of AML before this admission to ICU nor any signs, symptoms or laboratory reports, which would suggest the same during the current episode of acute illness. The main problem which led to ICU admission and respiratory failure was acute exacerbation of bronchiectasis which was later complicated by severe ventilator associated pneumonia and ARDS. He successfully recovered from all these problems.

On retrospective analysis, though our patient had many signs and symptoms of SVCS, the diagnosis was difficult at an earlier stage due to his various confounding medical factors. He had respiratory distress in the form of inability to wean from ventilatory support. This could have been due to his pathological conditions such as bronchiectasis, lung
fibrosis and poor muscle power. He complained of moderate chest pain in his upper chest, which was attributed to tracheostomy wound and was relieved by analgesics. His coagulation profile was deranged from first day of admission to ICU with low platelet count (40 to 70 × 10^9/L), high INR (1.5 to 2.0) and APTT (45 to 60 seconds) which made thrombosis related to a CVC a remote possibility. Patient was on multiple nephrotoxic drugs; hence the initial low-grade facial swelling was attributed to progressing renal failure. When the swelling progressed in upper limbs without involving lower limbs, patient was investigated as a SVC syndrome.

The treatment options for SVCS depend on the primary pathology and progression on the disease. Any malignant condition has to be treated by radiotherapy or chemotherapy after confirming the tissue diagnosis. If the symptoms progress rapidly leading to respiratory distress, neurological deterioration or hemodynamic instability, immediate intervention may be required in the form of balloon angioplasty, stenting or surgery.

Benign conditions leading to SVCS usually respond to medical treatment in the form of head elevation, anticoagulants, thrombolysis, diuretics and steroids. Nowadays it is increasingly being treated by angioplasty, local thrombolysis and stenting.

USG or CT guided biopsy are time tested methods of tissue diagnosis of mediastinal mass with few contraindications. The absolute contraindications include uncontrollable cough and suspicion of hydatid cyst, whereas relative contraindications include bleeding diatheses, vascular lesions, pulmonary hypertension, uncooperative patient, and advanced emphysema.

In this patient, CT scan revealed mediastinal lymph nodes compressing the SVC and patient’s condition deteriorated rapidly. He developed frequent PSVT and paroxysmal atrial fibrillation (PAF) with hemodynamic instability and desaturation in spite of being treated with sotalol. SVC irritation by compressing lymph node could have been a focus of this atrial arrhythmias. So, mediastinal biopsy was planned for tissue diagnosis and possible chemotherapy to treat the relapsed AML or secondary malignancies.

On retrospective analysis, the decision to do USG guided biopsy along with angioplasty and stenting of SVC was a therapeutic misadventure as it prevented us from giving anticoagulation for maintaining the patency of the stent. But, it was expected that the stent would not clot with a deranged coagulation profile. But next day when the symptoms increased, a repeat CT scan showed thrombosed stent. As this patient had a 6-month-old cerebral infarction and chronic subdural hematoma and was at high risk for intracranial bleed from thrombolysis and intravenous Heparin therapy, only Enoxaparin was started in therapeutic dose. Fortunately, the stent became patent radiologically within 24 hours.

To conclude, patients with rapidly progressing SVCS which requires urgent stenting, diagnostic mediastinal biopsy should not be attempted in the same sitting. In patients with deranged coagulation profile, some anticoagulants should be given after SVC stenting in order to prevent stent thrombosis.
References

MANAGEMENT OF POSTOPERATIVE CHYLOTHORAX IN A PATIENT WITH CARCINOMA OF THYROID AND LYMPHADENOPATHY

- A Case Report -

HIMANSHU KHURANA*, SEEMA MISHRA**, ROOPESH JAIN*, GAURAV NIRVANI GOYAL* AND SUSHMA BHATNAGAR***

Abstract

Chylothorax is a rare but serious complication following neck dissection with an incidence of 0.5% - 2%. Because of the rarity of chylothorax, surgeons are unfamiliar with its early signs which allow a prompt diagnosis and effective management. Most cases reported in the literature are associated with a concurrent external chyle leakage, occurring either during or after surgery. We report a case of chylothorax without concurrent external chyle leakage, which occurred following neck dissection and mediastinal lymphadenopathy, for thyroid cancer.

Introduction

Chyle is the lymphatic fluid enriched with fat and its digestive products, absorbed in the intestines, collected and transported by the thoracic duct into the circulation. Chylothorax is characterized by pleural fluid with a turbid or milky white appearance due to a high lipid content, most common source being from disruption of the thoracic duct. Leakage of chyle and lymph leads to significant loss of essential proteins, immunoglobulins, fat, vitamins, electrolytes and water. While therapeutic thoracentesis provides relief from respiratory symptoms, the nutritional deficiency continues to persist or deteriorate unless definitive therapeutic measures are instituted to stop leakage of chyle into the pleural space.
Case History

A 17 year female weighing 45 kg presented with swelling at the anterior aspect of neck. She was diagnosed as carcinoma of thyroid and posted for total thyroidectomy with bilateral modified neck dissection and superior mediastinal lymphadenectomy under general anesthesia.

Her medical history was unremarkable. All routine investigations were within normal limits. Her cardiovascular and respiratory systems were unremarkable.

The intraoperative course of six hours was uneventful. She was reversed and extubated on the operating table and after observation overnight in the ICU shifted to ward.

Next morning, she developed sudden respiratory distress with facial and neck puffiness and fall of blood saturation of oxygen to 75 to 80% with central cyanosis. Laryngoscopy was done and there was intense oral and tongue edema. An endotracheal tube of 6.0 mm internal diameter could be passed with difficulty. The tube placement was confirmed and connected to an AMBU bag with an oxygen source. At the same time the surgical sutures at side of neck were cut to evacuate around 250 ml of serosanguinous fluid. Pulse rate was 120 per minute and blood pressure 80 mm of Hg systolic with a central venous pressure of 5 cm of water. Respiration was shallow and rapid. Arterial blood gas analysis was a PaO₂ 54 mmHg and PaCO₂ 50 mmHg with a pH of 7.24.

The patient was shifted to the ICU and sedated with morphine and midazolam and connected to the ventilator SIMV mode with a PEEP of 5 and pressure support of 15 cmH₂O. Inj calcium gluconate 10 cc and hydrocortisone 200 mg were given intravenously. Fluid resuscitation was done with 1000 ml of lactated ringer until the central venous pressure increased to 8 cms and systolic blood pressure to 100 mmHg. Arterial blood gases revealed a PaO₂ 96 mmHg and PaCO₂ 40 mmHg with a FIO₂ of 0.5. Chest radiography revealed mediastinal widening with pleural effusion.

An immediate bilateral chest drainage tube was put with an evacuation of chylous fluid. Patient remained hemodynamically stable throughout and after the procedure. There was constant outpour of serous discharge from the surgical site. A tracheostomy was done and octreolide 100 mcg subcutaneously 8 hourly started. By evening the edema and facial puffiness started to decrease.

By the third day, as the patient was hemodynamically stable, it was decided to go for a surgical exploration of the wound. The thoracic duct leak site could not be identified intraoperatively so the procedure was abandoned and wound closed. On the 4th day total parenteral nutrition was started.

Over the next few days the chyle from the chest drains decreased and the facial edema gradually resolved and she could sit up in bed by the seventh day. She was subsequently shifted to the ward and discharged from the hospital on the twelfth day. On follow up she was healthy with no complaints.

Discussion

The accidental damage of thoracic duct, as happened in this case, leads to leakage of chyle into the pleural space which sometimes presents so acutely as to create a life threatening situation. Trauma to the thoracic duct is the commonest cause of chylothorax. Among traumatic chylothoraces, iatrogenic causes constitute the majority². The commonest cause is thoracic surgery, particularly involving dissection of the mediastinum. In the past, the mortality due to chylothorax was in excess of 50%. Currently, the morbidity and mortality have improved due to the more aggressive management strategies adopted.

Introduction of aggressive therapeutic measures to reverse the adverse effects of chyle loss has led to the lowering of mortality rates for post-traumatic chylothorax. Usually, a latency period of 2-7 days exists between the time of injury and clinical evidence of chylothorax if the injury is not a major one. This is because lymph accumulates in the posterior mediastinum until the mediastinal pleura ruptures, usually on the right side at the base of the inferior pulmonary ligament.

The dissection of mediastinal lymph nodes in relation to the thoracic duct can lead to chylothorax. The mode of injury in our case was clearly iatrogenic. Laceration of the thoracic duct during catheterization of the subclavian vein is another possibility to be
considered in this case. Extensive venous thrombosis complicating central venous catheterization has been reported in bilateral chylothorax and chylopericardium.

Large chylothoraces commonly lead to hypovolemia due to a sudden loss of large volume. The rapidity with which decompensation occurs depends on the amount, rate, and duration of chyle loss. In the early stages, the patient may not demonstrate clinical symptoms or signs of loss of chyle but later may exhibit clinical features of severe malnutrition. Hyponatremia, acidosis, and hypocalcemia are the most commonly electrolyte abnormalities and should always be corrected promptly so as to improve outcome.

Conservative management is currently complemented with various drugs that decrease the chyle leakage (somatostatin and analogs such as octreotide, heparin, and etilefrine). Octreotide in particular, because of its easy availability and safety in postoperative patients, has been used extensively to reduce intestinal chyle production and secondarily reduce chyle leak.

With conservative management of chylothoraces, mortality after esophagectomy approaches 50%, whereas with active surgical intervention incidence drops to about 10%. It can be further reduced if full knowledge of the process of chylothorax and its metabolic and nutritional complication are available to the clinician. Conservation management has been reported in various previous articles but we recommend an aggressive surgical therapy especially for post-traumatic or post-surgical chylothorax as first line of approach, supplemented with pharmacological measures with prompt correction of the metabolic and nutritional derangements.

References

LETTER TO THE EDITOR

VISUAL COMPARATIVE COLORIMETRY.  
A PRACTICAL METHOD OF ESTIMATING OPERATIVE BLOOD LOSS

MOHAMED A. DAABISS

To the editor, most anesthesiologists estimate blood loss by rough visual assessment, by noting its effects on cardiovascular parameters, by weighing of swabs, by substraction of fluids used in surgical irrigation from blood in suction reservoir, either by laboratory estimation or by trusting their experiences and instinct. I describe here a simple and practical method of estimating operative blood loss (OBL). It is based on colour comparison of two solutions containing blood using simple equipments readily available in and operating room, without the need to know the patients’ initial Hb or Hct or depend on laboratory results.

Using visual comparative colorimetry (VCC) in a clinical setting is simple. We collect five ml of patient’s blood in a heparinized syringe and use it to prepare a standard 1% solution in water (sample A) (as our pilot study revealed that the optimum concentration of hemoglobin in samples to be compared appears to be about 0.15 gms% i.e. 1% solution). In a large container, a homogenous solution of lost blood is prepared by washing all the soaked swabs. Blood collected in the suction bottle is added to the solution. Sufficient amount of water is then added, so that the final colour of the solution resembles the prepared standard.

Now, 10 ml of this solution is taken by a 10 ml syringe in a test tube. Another test tube is filled with 9 ml plain water. Blood from the original patient sample, suitably diluted to 10% (according to the pilot study) is now loaded in an insulin syringe and added drop by drop into the second test tube (sample B). Both solutions are visually compared against an x-ray view box for colour match. Once a colour match is obtained, the amount of blood required to obtain this result (Vb) is noted.

OBL is then calculated in ml by using a simple mathematical formula:

\[ \text{OBL} = \frac{V_b}{V_c} \times V_d \]

Where \( V_b \) is the volume of blood added to obtain a colour match, \( V_c \) is the volume of the sample (10 ml in this case) and \( V_d \) is the total volume of the prepared homogenous solution (diluents).

Similar samples were sent to the laboratory by a blinded investigator for colour comparison using a spectrophotometer for the naked eye to obtain a colour match.

Results revealed that dilute solution 1-2% gave accurate results; the range of error was much higher in reading by spectrophotometer than in our method, the mean error was 2.3%.

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By using VCC, it is much easier to make an informed decision regarding blood transfusion and avoid unnecessary single unit transfusions. However, the accuracy of the method depends on meticulous preparation of solutions and accurate titrations. Of course the need to observe universal precautions for handling bio-hazardous material cannot be over-emphasized.
Letter to the Editor

SUSPENSION LARYNGOSCOPY USING THE GLIDESCOPE

MUSA MUALLEM* AND ANIS BARAKA**

Suspension laryngoscopy is commonly utilized by the ENT surgeon to facilitate operative procedures on the glottis. The GlideScope is recommended in patients having difficult airway. However, the anesthesiologist often finds himself in need of a third hand to assist him in manipulating the tube, the stylet, and the introducer. In order to achieve tracheal intubation by one operator, suspension laryngoscopy can be achieved by attaching a hook to the end of the GlideScope handle [Fig 1a]. Following laryngoscopy and visualization of the glottis, the handle of the GlideScope with the attached hook is supported on two rods with rings at the upper end, while the lower end is placed on the OR table at the level of the shoulders [Fig 1b]. The three makes a stable Tripod, while maintaining a good view of the glottis.

Fig 1a: Figure shows the hook attached to the handle of the GlideScope

Fig 1b: The Bipod used to suspend the GlideScope

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CORRESPONDENCE

RADIAL ARTERY CANNULATION
AFTER FAILED FIRST ATTEMPT

-A Case Report -

DR RAVINDER PANDEY, DR JYOTSNA PUNJ
AND V DARLONG

In certain clinical situations it becomes imperative not to fail in our first attempt to cannulate the radial artery for invasive monitoring.

We describe a technique for successful arterial cannulation in case we fail to cannulate in our first attempt. If the arterial cannula is removed before second attempt, oozing of arterial blood from first puncture site creates a hematoma, which causes disappearance of arterial pulsations and spasm of artery. This makes an immediate second attempt at arterial cannulation difficult and many times impossible. Previously, displacing the overlying interstitial fluid by applying pressure in edematous patients to make arterial palpation easy and facilitate cannulation has been described. We describe another technique for successful arterial cannulation in case we fail in our first attempt to cannulate.

After puncturing radial artery, if one is not able to negotiate the arterial cannula further, we keep the first cannula with the stillete inside the artery. Arterial pulsations are preserved proximal to the puncture site and thus second arterial cannula is cannulated over this proximal arterial pulsation. After successful arterial cannulation with the second arterial cannula, the first cannula is then removed.

We have tried this technique successfully after a failed first attempt at arterial cannulation in many patients and thus suggest fellow anesthetists to try the same.
Fig. A
First arterial cannula cannot be threaded with formation of hematoma

Fig. B
Second arterial cannula cannulated over proximal pulsations keeping the first cannula with stillete in situ.

Fig. C
First cannula removed

Fig. D
Successful arterial cannulation with second cannula

References
ERRATUM

In Vol. 9, No. 6, October 2008, CONTENTS page 1194:

Two Lung Ventilation Through Single Lumen Tracheal Tube in Thoracoscopic Thymectomy

- A Randomized Clinical Trial of Efficacy and Safety -

........Mihan J. David, Karamollah Toolabi and Ali Aminian

The first author’s name, Mihan J. David, has been misspelled. It should read:

Mihan J. Javid
GUIDELINES FOR AUTHORS

(Adopted mainly from the Uniform Requirements for Manuscripts Submitted to Biomedical Journals of the International Committee of Medical Journal Editors (ICMJE) updated October 2008 (http://www.icmje.org/).

Editors and reviewers spend many hours reading manuscripts, and therefore appreciate receiving manuscripts that are easy to read and edit.

- Preparation of manuscripts:
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  Manuscripts to be submitted to Editor-In-Chief, Department of Anesthesiology, American University of Beirut Medical Center, Beirut, Lebanon e-mail: mej@aub.edu.lb
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- Should follow the title page. It should state the specific purpose of the research or research objective of, or hypotheses tested by, the study or observation. It should state the basic procedures, main findings, principal conclusions and should emphasize important findings.

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Acknowledgements (grants, equipment, drugs etc…), departmental assistance.

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