EFFECTS OF SEVOFLURANE ON POSTOPERATIVE LIVER FUNCTIONS IN MORBIDLY OBESE AS COMPARED TO THE NON-OBESE PATIENTS

SUBHI M AL-GHANEM*, ISLAM M MASSAD**, BASSAM AL-BARAZANGI***, MAHMOUD AL-MUSTAFA****, FAYEZ S DAoud***** and HAMDI Abu-ALI******

Abstract

Objective: To assess the effect of sevoflurane anesthesia on hepatic function in morbidly obese versus non-obese patients undergoing abdominal surgeries.

Methods: We prospectively evaluated the levels of the serum concentration of liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), and total bilirubin (TBil), in 42 morbidly obese and 40 non obese patients who were scheduled for elective abdominal surgery under sevoflurane anesthesia at the Jordan University Hospital, Amman, Jordan. Measurement of liver enzymes was done in the recovery room, and on the first, 3 and 7 days after sevoflurane anesthesia, and the results were compared between the morbidly obese and non obese patients.

Results: ALT, AST, GGT and LDH increased significantly in the morbidly obese than they did in non obese patients. In morbidly obese patients TBil increased gradually peaking 7 days after anesthesia, LDH increased in the recovery room, AST and ALT increased in the recovery room and first day, while GGT increased 7th day after anesthesia. In non obese patients, AST, LDH increased in the recovery. ALP did not change in both groups.

Conclusion: Sevoflurane induces elevation of the serum liver enzymes in morbidly obese patients with variable onsets.

Keywords: Sevoflurane, Liver enzymes, morbid obesity.
Introduction

Postoperative hepatic injury has been reported after exposure to volatile anesthetics especially halothane, and female, obese middle-aged women are more affected than males. The injury is usually seen few days after exposure and is characterized by malaise, fever, jaundice, eosinophilia and marked elevation in serum transaminases which occasionally ends with massive liver necrosis and death.

Sevoflurane is comparatively recent addition to the range of inhalational anesthetics. It has a low blood solubility which results in rapid induction and faster recovery. Although there are reports of sevoflurane-associated liver injury in the literature, sevoflurane is considered less hepatotoxic than the older inhalational agents. Several studies reported the effects of sevoflurane anesthesia on postoperative liver functions in surgical patients, however, there are no reports on the effects of sevoflurane on liver functions in morbidly obese patients. The aim of this study was to compare postoperative serum liver enzymes in morbidly obese and in non-obese patients undergoing elective abdominal surgeries under sevoflurane anesthesia.

Patients and Methods

After Institutional Review Board approval, informed consents were obtained from 82 (40 non-obese and 42 morbidly obese) ASA I or II 16-68 old patients scheduled for the first time elective abdominal surgery at the Jordan University Hospital, Amman, Jordan. Patients who received anesthetics in the last three months, who had received drugs that induce liver enzymes and who had liver diseases, were excluded from the study. Patients who were reoperated or suffered from wound infection were also excluded from the study.

Patients were not premedicated. Anesthesia was induced with propofol 1.5-2.5 mg/kg in a dose sufficient to abolish eyelash reflex and remifentanil 1 µg/kg. The dose of propofol was correlated to the lean body weight. Atracurium 0.5 mg/kg or cisatracurium 0.15 mg/kg were used to facilitate endotracheal intubation. Anesthesia was maintained with 1-3% sevoflurane inspired concentration in air and oxygen with a total fresh gas flow of 6-10 l/min. Intraoperative analgesia was maintained with 0.1-0.2 µg/kg/min of remifentanil. The anesthetic concentration was adjusted to maintain systolic blood pressure ± 20% of the baseline value. Controlled ventilation was adjusted to maintain PaCO₂ between 30-40 mmHg.

All patients were extubated after surgery in the operating room. Prophylactic doses of a third generation cephalosporins antibiotic and Metronidazole were restricted to three grams and 1500 mgs respectively. Patients received prophylactic heparin 5000 IU daily for prevention of deep venous thrombosis. Pethidine was used for post operative analgesia.

Serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT) and total bilirubin (TBil), were measured before, in the post anesthesia recovery room and 1, 3, 7 days after anesthesia, using the antecubital vein for venous blood sampling and the analysis were performed in duplicate.

The MAC. hour exposure to sevoflurane was calculated from the percent anesthetics concentration and the duration of exposure. MAC value of 2% for sevoflurane was used.

All statistical analysis was carried out using Stat graphics Centurion xv (version 15.1.02), (Statpoint, Inc 2006). All values are expressed as means and standard deviations. Multiple sample comparison method was used to study the different variables. The mean for each value was calculated and the standard deviation was also documented. The age, BMI, mean duration of surgery and exposure to sevoflurane (MAC. Hour) were compared between the two groups (obese and non-obese) using the t-test and Fisher’s least significant difference (LSD). For the serum liver enzymes level, the means for the level at pre-surgery, recovery, 1, 3 and 7 days were measured in the two groups. The pre-surgery level of enzymes was compared to the level at recovery, 1, 3 and 7 days after surgery in each group and then compared between the 2 groups using analysis of variance, ANOVA. An asterisk (*) has been placed next to several values, indicating that these values when compared to their pre-surgery values, show statistically significant differences at the 95.0% confidence level. A mark (†) has been placed to show a statistical difference.
between the obese and non-obese patients. A p < 0.05 was considered statistically significant.

Results

There was no difference between the two groups with regard to age, sex and duration of anesthesia (Table 1).

### Table 1
**Demographic Data**

<table>
<thead>
<tr>
<th></th>
<th>Non-obese</th>
<th>Morbidly Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.2 (12.8)</td>
<td>36.8 (12.3)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>5/35</td>
<td>12/30</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.7 (3.4)</td>
<td>46.2 (7.1)</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>139.4 (45.8)</td>
<td>147.2 (49.3)</td>
</tr>
<tr>
<td>Exposure to sevoflurane (MAC hr)</td>
<td>2.59 (0.86)</td>
<td>3.01 (1.4)</td>
</tr>
</tbody>
</table>

Values are mean (SD); BMI: body mass index; MAC: minimal alveolar concentration.

AST, ALT, GGT and LDH increased significantly in the morbidly obese as compared with non morbidly obese patients. In morbidly obese patients, TBil increased gradually peaking 7 days after anesthesia, while GGT increased significantly 7 days after anesthesia (Table 2).

LDH, AST and ALT had their peaks in the post anesthesia recovery room decreasing gradually towards the 7th day. There was no increase in ALP during the study period. In morbidly obese patients, TBil reached 2 mg/dL in one patient, LDH values of 900 to 2110 IU/L were observed in 7 patients and ALT, ALP values of 200 to 660 IU/L were also observed in 4 patients. In non obese patients AST, LDH increased in the recovery period. There was no post operative hepatitis or liver failure.

Discussion

The results of this study showed that when using Sevoflurane, serum concentrations of LDH, GGT, AST and ALT were significantly higher in morbidly obese patients than in the non obese patients. Several studies demonstrated that liver enzymes are elevated after sevoflurane anesthesia. Although several mechanism were postulated to result in this elevation of liver enzymes, none of them alone is responsible for this elevation.

### Table 2
**Serum levels of liver enzymes**

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Pre</th>
<th>Recovery 1</th>
<th>Recovery 3</th>
<th>Recovery 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALP</td>
<td>Non-obese</td>
<td>76.3 (24.1)</td>
<td>71.5 (21.5)</td>
<td>69.0 (22.0)</td>
</tr>
<tr>
<td></td>
<td>Morbidly obese</td>
<td>84.0 (26)</td>
<td>76.1 (22.6)</td>
<td>71.9 (23)</td>
</tr>
<tr>
<td>ALT</td>
<td>Non-obese</td>
<td>22.0 (13.1)</td>
<td>20.7 (10.3)</td>
<td>23.3 (16.5)</td>
</tr>
<tr>
<td></td>
<td>Morbidly obese</td>
<td>27.5 (15)</td>
<td>92.7 (114)**</td>
<td>78.76 (107)**</td>
</tr>
<tr>
<td>AST</td>
<td>Non-obese</td>
<td>21.1 (7.0)</td>
<td>27.2 (17.2)†</td>
<td>25.2 (12.4)</td>
</tr>
<tr>
<td></td>
<td>Morbidly obese</td>
<td>26.2 (13.5)</td>
<td>95.7 (87.7)†</td>
<td>66.8 (82)†</td>
</tr>
<tr>
<td>GGT</td>
<td>Non-obese</td>
<td>21.5 (16.5)</td>
<td>19.9 (15.3)</td>
<td>23.4 (22.9)</td>
</tr>
<tr>
<td></td>
<td>Morbidly obese</td>
<td>28.9 (20)</td>
<td>29.2 (19)</td>
<td>29.3 (22.6)</td>
</tr>
<tr>
<td>LDH</td>
<td>Non-obese</td>
<td>317.3 (97.1)</td>
<td>381.7 (137.8)†</td>
<td>369.3 (137.0)</td>
</tr>
<tr>
<td></td>
<td>Morbidly obese</td>
<td>453.6 (113.0)</td>
<td>661.6 (319.0)†</td>
<td>504.2 (221.0)</td>
</tr>
<tr>
<td>TBil</td>
<td>Non-obese</td>
<td>0.9 (1.6)</td>
<td>0.6 (0.3)</td>
<td>0.8 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Morbidly obese</td>
<td>0.5 (0.2)</td>
<td>0.6 (0.2)</td>
<td>0.7 (0.3)†</td>
</tr>
</tbody>
</table>

Values are mean (SD); *, †: P < 0.05 vs. the control value (pre); †: P < 0.05 non-obese vs. obese; pre: before anesthesia; recovery: post anesthesia recovery room; TBil: total bilirubin; LDH: lactate dehydrogenase; GGT: gamma glutamyl transferase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase.
Factors implicated in liver injury after exposure to inhalational agents include reduction in hepatic blood flow, metabolites of the anesthetics and increase in intracellular calcium\textsuperscript{20-24}. Halothane can reduce hepatic blood flow and can result in hepatic cells injury\textsuperscript{20,21}. In the case of Sevoflurane, there is conflicting evidence whether it reduces hepatic blood flow in humans\textsuperscript{25-27}.

The effects of metabolites of inhalational anesthetics as a mechanism explaining liver injury has been extensively studied especially those of halothane.

Trifluoroacetyl acid (TFA) is a common oxidation metabolite of halothane, enflurane, desflurane and isoflurane and this compound reacts with subcellular hepatic cells proteins and produces new proteins which in certain individuals induces immune response and liver injury\textsuperscript{24}.

Two to 5\% of inhaled sevoflurane in metabolized in humans\textsuperscript{19}. The main metabolite of sevoflurane is hexafluoroisopropanolol (Compound A), this compound does not react with liver cell protein and does not produce liver cell injury\textsuperscript{29,30}. Sevoflurane reacts with CO\textsubscript{2} absorbents and produces compound A, a compound that is nephrotoxic in a dose related manner in rats\textsuperscript{28}. In our study we used fresh gas flow 6-10 L/min were the concentration of compound A is negligible in the anesthesia breathing circuit with the high fresh gas flow used.

The mechanism of sevoflurane-associated hepatic injury seems to be unclear. Four cases of hepatic injury after exposure sevoflurane have been reported in Japan\textsuperscript{11-14}. Toxic metabolites of sevoflurane may explain these injuries since sevoflurane has been found to induce liver enzymes in rats\textsuperscript{30}.

There are no reports about the effects of sevoflurane on intracellular Ca\textsuperscript{++}, whereas halothane and enflurane release intracellular calcium which may increase hepatic cells injury\textsuperscript{23}.

The changes in liver enzymes in this study were statistically significant but were not clinically significant in any patient. Although the effect of other drugs given to patients on the post operative liver enzymes levels cannot be excluded, there is no evidence that these drugs elevate serum liver enzymes\textsuperscript{31}.

In conclusion Sevoflurane anesthesia is associated with a transient increase in liver enzymes in morbidly obese patients. This enzymatic elevation was without the occurrence of postoperative hepatitis or liver failure; and was of statistical but not of clinical significance. The mechanism of action of the increased lever enzymes is not clear.
References:

PATIENT SURVEY OF CONTINUOUS INTERSCALENE ANALGESIA AT HOME AFTER SHOULDER SURGERY

Elie J Chidiac*, Roland Kaddoum**, and Steve A Peterson***

Brief summary statement for table of contents: Patients who went home with continuous interscalene analgesia at home were surveyed for quality of analgesia, catheter site infection, clear fluid leakage, premature catheter dislodgement, shortness of breath, residual neurological symptoms and overall comfort with this method of postoperative pain control.

Abstract

Background: The use of continuous peripheral nerve blocks at home (CPNBH) has improved patients’ perioperative experience. In 30 months, 348 patients were sent home with interscalene CPNBH.

Methods: With the Institutional Review Board (IRB) approval, all patients were surveyed for quality of analgesia and complications. The patients and their caretaker received verbal and written instructions, including care of the catheter and pump, and a list of complications and side effects. All were instructed on catheter removal and were given a contact number, and patients were called once per day.

Results: 172 patients responded to this survey. The majority of patients (76%) had very good postoperative analgesia. There was a 9.3% incidence of leakage of clear fluid, a 5.8% incidence of premature dislodgement, and an 8.7% incidence of shortness of breath. Residual neurological symptoms persisted in 18.6% of responders, all resolving within two months except in one case. A large proportion (40%) required no oral analgesics, and half of the rest required less than 3 pain pills. Most (94.1%) felt comfortable removing the catheters at home by themselves or by a family member/caretaker.

Conclusion: This survey shows that CPNBH results in low pain scores and a low incidence of side effects. Many patients commented positively on their overall impression of their anesthesia care, particularly the level of attention that they received. This highlights the low incidence of those complications and neural injury.

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Introduction

Placement of continuous catheters near peripheral nerves for postoperative pain control has been shown to increase patient satisfaction¹, decrease narcotic requirements and resultant nausea and vomiting², improve quality of sleep³, accelerate the rehabilitation process⁴, and decrease hospital costs⁵. At the Michigan Orthopaedic Specialty Hospital, over 700 patients have been discharged with continuous peripheral nerve blocks at home (CPNBH). The majority have been those undergoing shoulder surgery and receiving a continuous brachial plexus catheter via an interscalene approach. There is one article in the literature, based on a telephone survey reviewing CPNBH from the patients’ perspective, with 131 patients⁶. Of those, only 22 had interscalene catheters. The purpose of this retrospective study was to gather data on a larger patient sample and evaluate the quality of pain control and the frequency of side effects, particularly pulmonary, neurological and infectious complications.

Materials and Methods

With approval from Wayne State University’s Institutional Review Board, all patients were mailed a letter and consent explaining the survey. Two weeks later, all were mailed a questionnaire (Table 1).

<table>
<thead>
<tr>
<th>Survey Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - How well was your pain controlled during the continuous infusion?</td>
</tr>
<tr>
<td>2 - Where there any catheter problems?</td>
</tr>
<tr>
<td>3 - Was there any infection, pus or drainage?</td>
</tr>
<tr>
<td>4 - Did you have any difficulty breathing?</td>
</tr>
<tr>
<td>5 - Did you have any residual numbness or tingling after catheter removal? If yes, for how long?</td>
</tr>
<tr>
<td>6 - How many pain pills did you take while the catheter was in place?</td>
</tr>
<tr>
<td>7 - When was the catheter removed?</td>
</tr>
<tr>
<td>8 - Did you feel comfortable removing the catheter at home?</td>
</tr>
<tr>
<td>9 - Would you recommend this technique?</td>
</tr>
<tr>
<td>10 - Rate your overall satisfaction.</td>
</tr>
</tbody>
</table>

Between March 2003 and August 2005 (30 months), 378 interscalene catheters were inserted for various shoulder procedures (Table 2).

<table>
<thead>
<tr>
<th>Types of surgeries</th>
<th>Total CPNB¹</th>
<th>Survey responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open musculotendinous repairs</td>
<td>86</td>
<td>33</td>
</tr>
<tr>
<td>Shoulder arthroplasties</td>
<td>78</td>
<td>37</td>
</tr>
<tr>
<td>Open shoulder capsular repairs</td>
<td>39</td>
<td>26</td>
</tr>
<tr>
<td>Arthroscopic surgeries</td>
<td>148</td>
<td>65</td>
</tr>
<tr>
<td>Shoulder manipulation under anesthesia</td>
<td>27</td>
<td>11</td>
</tr>
</tbody>
</table>

¹ continuous peripheral nerve blocks.

Most were sent home with CPNBH (Table 3) and 30 were removed prior to discharge (Table 4). All 348 patients who went home with CPNBH were included in this study.

<table>
<thead>
<tr>
<th>Outcome after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home on day-of-surgery with CPNBH¹: 147</td>
</tr>
<tr>
<td>Home on POD#1² with CPNBH: 103</td>
</tr>
<tr>
<td>Home on POD#2³ with CPNBH: 98</td>
</tr>
<tr>
<td>Catheter removed in-hospital prior to discharge: 30</td>
</tr>
</tbody>
</table>

¹ continuous peripheral nerve blocks at home.
² Post operative day one.
³ Post operative day two.

<table>
<thead>
<tr>
<th>Catheters removed prior to discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ineffective pain relief: 9</td>
</tr>
<tr>
<td>Catheter inadvertently dislodged: 2</td>
</tr>
<tr>
<td>Excessive fluid leakage: 4</td>
</tr>
<tr>
<td>No pain with CPNB turned off: 4</td>
</tr>
<tr>
<td>Redness at site: 2</td>
</tr>
<tr>
<td>In-hospital till POD#3⁴, so catheter removed as planned: 3</td>
</tr>
<tr>
<td>Shortness of breath: 4</td>
</tr>
<tr>
<td>Disliked feeling of numb hand: 2</td>
</tr>
</tbody>
</table>

¹ Post operative day three.
² Post operative day one.
³ Post operative day two.
⁴ Post operative day three.

After pre-procedure instructions to the patient in the presence of their family member/caretaker, patients were taken into a ‘block room’. With noninvasive monitoring and after intravenous sedation, all interscalene catheters were placed using the modified lateral approach⁶,⁷. Stimulating catheters (Stimucath®, Arrow International, Reading, PA) were used for all cases. No solution was injected through the needle. All catheters were threaded 4-5 cm beyond the needle tip with continuous stimulation and tunneled subcutaneously toward the midline. Just before securing the catheters, the patient’s family member/caretaker was brought into the ‘block room’,
to observe the taping process and learn about removal of the catheter. These were secured with Mastisol® liquid adhesive (Ferndale Laboratories, Ferndale, MI), SutureStripPlus® flexible wound closure strips (Derma Sciences, Princeton, NJ) and covered with a Tegaderm® (3M Corporation, St. Paul, MN). Catheter hubs were attached to the contralateral chest wall with a StatLock® (Venetec International, San Diego, CA). After a test dose of local anesthetic with epinephrine, all patients received an initial bolus through the catheter, with 40 ml mepivacaine 1.5% with epinephrine 1:400,000.

Prior to discharge, all patients received prescriptions for a nonsteroidal anti-inflammatory medication, an oral opioid and a stool softener. All postoperative home infusions consisted of bupivacaine 0.125%. All disposable home pumps were manufactured by I-Flow (Lake Forest, CA). Before March 2004, all patients were sent home with a pump delivering a fixed rate of 5 ml/hr, except those with adhesive capsulitis of the shoulder who were scheduled for outpatient physical therapy, as they received a pump with 5 ml/hr and patient-controlled boluses of 5 ml with a 60-minute lockout. After that date, patients with open shoulder procedures were sent home with a variable-rate pump capable of delivering a rate of zero to 14 ml/hr, in increments of 2 ml/hr, at the patient’s discretion.

Patients and their caretakers received verbal and written instructions regarding the care of the catheter and pump. This included a list of complications and side effects, emphasizing catheter site infection, local anesthetic toxicity, shortness of breath and hand numbness. All were instructed on catheter removal and were given a contact number for the anesthesiologist-on-call. All patients were called once per day, including the day after catheter removal, with a list of specific questions (Table 5).

### Table 5  
**Daily telephone follow-up**

- What is your pain level?
- Do you have any nausea and/or vomiting?
- Are you too sleepy/too groggy?
- Do you have any shortness of breath?
- Is the catheter site leaking?
- Is there any swelling, redness, or bleeding at the catheter site?
- What part of the limb is numb?
- Is the “dead” feeling bothering you?
- Any other concerns?

**Additional questions after removal at home:**
- Were there any difficulties with catheter removal?
- Did you see the silver-colored spring at the tip of the catheter?

### Results

Thirty catheters were removed prior to discharge, because of the reasons listed in Table 4. Of the 348 patients who went home with CPNBH, 172 responded...
to this survey, for a 49.4% response rate. Table 6 lists their answers.

The majority of patients (76%) had very good postoperative analgesia. There was a 9.3% incidence of leakage of clear fluid at the catheter site. Despite this taping and anchoring technique, the catheters were prematurely dislodged in 5.8% of cases. Fifteen patients (8.7%) had a subjective feeling of shortness of breath. Twelve hours after catheter removal, 32 patients (18.6%) had residual neurological symptoms, including tingling, ‘pins and needles’ and numbness. All resolved within two months, except one case. A large proportion (40%) required no oral analgesics, and half of those who took any breakthrough medications required less than 3 pain pills. Most catheters (86.6%) were removed between POD#2 and POD#4, and most patients (94.1%) felt comfortable removing the catheters at home by themselves or by a family member/caretaker.

Discussion

This survey shows that CPNBH is safe, with low pain scores and a low incidence of side effects. A recent meta-analysis of nineteen randomized controlled trials found that, compared to parenteral opioids, CPNB analgesia results in statistically and clinically significant improvements in pain control and decreases the opioid-related side effects of nausea/vomiting, sedation and pruritus. With improvements in the major anesthetic morbidities of death and hypercoagulable states, there is a new focus on these very issues, also called patient-centered nontraditional outcomes, or ‘minor’ morbidities.

Bupivacaine was chosen over ropivacaine because of cost: At our Institution, there is a ten-fold difference in the cost of 500ml ropivacaine 0.2% versus 500ml bupivacaine 0.125% ($70.00 versus $7.00 respectively). At these concentrations, the argument for using ropivacaine is not its cardiac safety profile, since the blood concentrations achieved with this dilute bupivacaine are safe. Instead, the issue is that of neurologic sequelae: Ropivacaine preferentially blocks sensory fibers over motor fibers and causes less hand numbness with continuous interscalene analgesia. It is less myotoxic than bupivacaine in bolus form. However, it is unclear whether at these concentrations and drip rates, ropivacaine may have resulted in less long-term neurologic sequelae.

This series shows no cases of infection. However, two patients had some redness at the insertion site and had their catheters removed prior to discharge. In the literature, there is a high incidence of catheter colonization, but only a total of five cases of catheter infection after peripheral nerve blocks, four of whom were diabetic.

The disposable home infusion pumps were all from the same manufacturer (I-Flow, Lake Forest, CA). It seems that a fixed rate of 5 ml/hr is adequate for interscalene analgesia. After the rate-variable pump became available, most patients used a setting of 4 or 6 ml/hr. Some chose to decrease the infusion rate in the daytime, accepting mild discomfort but avoiding hand numbness, and they would increase the rate at night, so they can sleep without pain. There is no consensus in the literature on the ideal infusion rate or the need for intermittent boluses. The stimulating catheters may allow for slower rates and therefore may render many of the studies with nonstimulating catheters obsolete.

The incidence of leakage of clear fluid was 9.3%. Adding the four cases of leakage among those 30 patients whose catheters were removed prior to discharge, the incidence increases to 9.9%. This is slightly lower than that reported by others and may be related to the low rate of infusion with stimulating catheters, or the ability to thread a stimulating catheter further from the insertion site, or that tunneling decreases leakage.

The incidence of accidental dislodging of catheters was 5.8% (increases to 5.9% by adding the two that were dislodged while inpatient). This incidence is lower than in previous reports and will probably continue to decrease with the ongoing development of new anchoring techniques and liquid adhesives.

Four catheters (1.05% of 378 patients) were removed before discharge because of shortness of breath, and fifteen patients (8.7%) had a subjective feeling of shortness of breath. Unlike others, no patients developed acute respiratory failure requiring admission to the intensive care unit. There are rare case reports of pulmonary complications after continuous interscalene blocks. These may be related to phrenic nerve paresis. A study using the paresthesia technique
found an incidence of 100% phrenic nerve paresis with single-shot interscalene blocks\textsuperscript{23}. Newer work shows a lower incidence with the nerve stimulator technique and an even lower incidence with injections through a catheter\textsuperscript{24}, perhaps because the latter allows injection at a more distal site\textsuperscript{1}. In the only study of the effects of continuous interscalene analgesia with 0.125\% bupivacaine on pulmonary function, the infusion was stopped after 24 hours, at which point ipsilateral hemidiaphragmatic motility was at 50\% of preoperative values, yet pulmonary function tests (forced vital capacity, forced expiratory volume in one second and peak expiratory flow) were only decreased by 10\%. The author suggested that the loss of diaphragmatic function on one side is compensated by all other respiratory muscles, resulting in this minimal decrease in pulmonary function\textsuperscript{25}. Although there is no study comparing the effects of CPNBH with bupivacaine and ropivacaine on phrenic nerve and pulmonary function, similar results have been found with ropivacaine, along with the same compensatory increased activity of the contralateral hemidiaphragm\textsuperscript{1}.

Ilfeld and Enneking\textsuperscript{19} have pointed out that, in the process of moving this method of pain control from an in-patient to an outpatient setting, one must be mindful of complications, as they may become more difficult to treat at home. This is where the initial use of mepivacaine 1.5\% helps identify those patients where respiratory compromise may become symptomatic. If there is a complaint of subjective feeling of shortness of breath, the block wears off sooner than with a long-acting local anesthetic and the catheter can be removed, thus avoiding a prolonged period of respiratory compromise. There is another patient population who benefits from using mepivacaine: Those undergoing total shoulder arthroplasty, where there is a need to assess the integrity of the brachial plexus after surgery. The block is used to decrease intraoperative anesthetic requirements and wears off early in the postanesthesia recovery room where, after post surgical confirmation of neuromuscular integrity, additional local anesthetics can be given.

Thirty patients (18.5\%) reported residual neurological symptoms after catheter removal, with complete resolution within two months in all except one case. That patient had prolonged numbness in the radial distribution, which resolved completely after 5 months. She had excessive numbness throughout the infusion period and was not reached via telephone until her fourth postoperative day. Typically, at this Institution, patients with excessive hand numbness are instructed to intermittently clamp the pump tubing. As discussed above, it is unclear whether the use of ropivacaine may have decreased this problem. This neural deficit in one patient results in an incidence of 0.26\%, similar to findings by others\textsuperscript{7,15}. Preexisting neurological deficits, perioperative positioning and surgical traction may have contributed to this, in what has been termed the ‘double-crush injury’\textsuperscript{26}.

Ten patients (7.5\%) reported they were “not comfortable” removing the catheter at home, and would have preferred to return to the hospital for this, and two patients did return. This is similar to the results of Ilfeld et al\textsuperscript{5}, where two of their 22 patients (9\%) with interscalene catheters preferred to return for removal.

Fourteen patients were not satisfied with their care. This was not intended to be a ‘satisfaction study’, since that portion of the survey was limited to a single global rating. In general, patient satisfaction is multifactorial and includes emotional, cultural, psychological and cognitive elements, and a more detailed psychometric questionnaire would have been required to measure satisfaction\textsuperscript{27}. Nevertheless, this low rate may reflect the active involvement of the anesthesiologists in the patients’ perioperative care. Many patients commented positively on their overall impression of their anesthesia care, with comments about the level of preoperative attention that they received, the postoperative teaching and the daily follow-up phone calls.

This is a retrospective patient survey and therefore not as reliable as a prospective randomized study. It is an attempt to highlight current practice at this Institution, with the low incidence of those complications that are most worrisome to the anesthesia community: Infection, pulmonary complications and neural injury\textsuperscript{28}. There are no guidelines on CPNBH. For instance, some prefer to wear a sterile gown\textsuperscript{15}, some use non-stimulating catheters\textsuperscript{1}, some prefer ropivacaine\textsuperscript{2}, some coach their patients on catheter removal while simultaneously on the phone with them\textsuperscript{2}; there is no consensus on infusion rate or the need for patient-controlled boluses, or the length of time catheters can be left in place. At this
time, anesthesiologists go by their own Institutional preferences.

In conclusion, this survey reaffirms that CPNBH is safe and has few side effects. It reinforces the need for daily contacts with patients and ties in with the anesthesiologist’s role as the perioperative physician who cares about the patient-centered morbidities of improved postoperative pain, decreased nausea, improved quality of sleep, and improved rehabilitation.

References
EVALUATION OF A BLOOD CONSERVATION STRATEGY IN THE INTENSIVE CARE UNIT: A PROSPECTIVE, RANDOMISED STUDY

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Abstract

**Objective and Methods:** Anemia is a common problem in the ICU population. Most patients are anemic at admission, their hemoglobin concentrations declining further thereafter. The aim of the present study was to evaluate the effect of a combination strategy, involving closed arterial blood gas sampling and the use of pediatric vials for phlebotomy (Group A), on the sampling-induced blood loss and the rate of decline in hemoglobin in adult ICU patients. Combination (Group A) was compared to the current standard technique of arterial line sampling and adult vial phlebotomy (Group B) in a prospective, randomised, ethically-approved trial for the first 72 hours of their ICU stay. Peri-operative, oncology, coagulopathic and uremic patients were excluded. All other ICU patients with arterial cannulae and predicted to stay beyond 3 days, were enrolled.

**Results:** 39 patients entered the study, 20 in Group A, and 19 in Group B. Data collection was complete for all. There was a statistically significant difference in sampling-induced blood loss between the groups over the first 72 hours of treatment (mean +/- standard deviation: 15.16 +/- 5.3 ml Group A vs 45.11 +/- 14 ml Group B, p<0.001). There was a smaller decline in mean hemoglobin level, which was not statistically significant (0.79 +/- 0.6 g/dL vs 1.30 +/- 1.13, p = 0.09).

**Conclusions:** Overall, this strategy reduced measurable blood losses from phlebotomy. In larger trials it might also preserve hemoglobin levels.
blood gas sampling, allowing return of dead-space blood, along with the use of pediatric blood vials) on the volume of blood lost through sampling and also on the progression of anemia, in adult ICU patients. We compared this to the current practice of arterial pressure line sampling, where dead-space blood is discarded, and adult phlebotomy vials are used. We hypothesised that this combination strategy would decrease the volume of blood lost through sampling in critically ill patients and thus reduce the rate of decline in the patients’ hemoglobin levels and, perhaps, their need for transfusion.

Methods and Materials

Approval was obtained from the Ethics and Research Committee of Cork University Hospital to conduct a pilot study in order to evaluate the VAMP system’s efficiency, in a prospective randomised unblinded controlled clinical study. The study was carried out in the Hospital’s ICU from January to March of 2006. Written consent was obtained around the time of admission from appropriate patients (or their next-of-kin). These included those who were expected to require more than 3 days of intensive care. Patients with clinical evidence of bleeding, such as perioperative or trauma patients, or those with upper and lower gastrointestinal blood (ie visible blood in the gastric aspirate or melena) and menstruating female patients were excluded. Also excluded were oncology patients and those requiring renal replacement therapies.

Thirty nine patients were randomised into two groups. (Study group A n = 20) had the VAMP (closed system) used for blood gas sampling, in which dead space blood is returned to the patient and the catheter flushed clear, while group B (the control group n = 19) had standard sampling systems used. The frequency of blood gas analysis and phlebotomy complied with the routine management in ICU (ie once daily, or at the discretion of the ICU physician and nursing staff, in turn guided by the clinical condition of the patient).

Pediatric syringes (1 ml) for blood gas analysis were used in study group A and we used pediatric vials for hematology and biochemistry analysis, which required 0.4 and 1.4 mls respectively, as compared to 2.7 and 4.9 mls for adult vials. Standard data collection for the ICU population was used with a specific
data sheet being filled in daily for the first 3 days of intensive care. We recorded as end-points the patients’ hemoglobin concentrations 72 hours after admission, the total volume of blood taken for phlebotomy and the number of units of blood transfused over the time period. Blood volumes removed were measured at the time of phlebotomy and the volumes recorded contemporaneously.

Results

The volumes of blood removed for analysis and the level of decline in hemoglobin levels are shown in Table 1. The control group had a 65% greater a fall in hemoglobin levels than the study group, though this difference was not statistically significant. There is a statistically significant difference, however, between the study and control groups in terms of the volume of blood drained for analysis; about three times more blood was lost in the control group (15.16 ml vs 45.11 ml). There was no discarded blood in the study group A as compared to almost 25 mls lost by the average patient in the control group B. No patients from either group required blood transfusion during the study.

Discussion

The consequences of anemia in the critically ill are significant both for patients and for healthcare institutions. In managing such patients, the immediate risks of reduced delivery of oxygen to the tissues must be weighed against the adverse long and short-term health effects of transfusion and the financial burden of blood collection and storage.

On the basis of recent research there is a current trend in ICU management to accept lower hemoglobin levels than in previous generations, and thus to transfuse less blood. Nonetheless, about 40% of the critically ill population receive transfused blood during their illness such that, in the United States for example, around 11 million units of red cells are transfused annually.

The administration of blood is subject to increased public scrutiny as, despite best efforts, infectious risks remain. Such risks, due to the ongoing recognition of new pathogens such as West Nile virus, for example, cannot accurately be quantified at present. Non-infectious risks, such as circulatory overload, acute delayed transfusion reactions, microcirculatory dysfunction, immune modulation, hypocalcemia and hypothermia, are also associated with transfusion. Attempts to make the process safer incur increased costs: thus, the introduction of measures to improve the safety and adequacy of the blood supply contributed to a 51% rise in expenditure by the Canadian Blood Services.

Alternatives to transfusion are clearly desirable then, and are the subject of many diverse strands of research. These include the administration of erythropoietin, with or without iron, and therapy with blood cell substitutes or synthetic hemoglobin. Avoiding the need for transfusion is a more rational and cost-effective strategy. Many of the tenets of modern ICU contribute to this strategy-optimising patient nutrition, avoiding drugs associated with bone marrow depression, and minimising diagnostic phlebotomy, for example.

Diagnostic phlebotomy may contribute substantially to the anemia encountered in ICU. In

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Test (Group A)</th>
<th>Control (Group B)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
</tr>
<tr>
<td>Fall in hemoglobin after 3 days</td>
<td>20</td>
<td>0.79</td>
<td>0.61</td>
</tr>
<tr>
<td>Blood lost on gas sampling</td>
<td>20</td>
<td>5.42</td>
<td>1.14</td>
</tr>
<tr>
<td>Blood discarded</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blood phlebotomised</td>
<td>20</td>
<td>9.72</td>
<td>4.92</td>
</tr>
<tr>
<td>Total blood drained</td>
<td>20</td>
<td>15.15</td>
<td>5.32</td>
</tr>
</tbody>
</table>
critically ill surgical patients drawn volumes over 200 mls per day, are described in the literature\textsuperscript{14,15}. However, the volumes drawn vary widely in different study populations; values of 40 to 80 mls per day are more representative of medical patients with higher values being typical on the day of admission. Interestingly, a German study found that the total amount of diagnostic blood loss was a strong predictor of later transfusion\textsuperscript{10}. Another American study found that phlebotomy accounted for approximately 50% of the variation in the amount of red blood cell later transfused\textsuperscript{5}. Of course, more severely ill patients are subject to more frequent phlebotomy and thus are at higher risk of transfusion and its consequences\textsuperscript{1,17}. The mean frequency of phlebotomy in critical patients varies widely among published series, ranging from 5 to more than 10 samples per day\textsuperscript{1,4,17}.

Arterial blood gases are the most frequently ordered laboratory test in ICU and may account for almost 40% of blood drawn\textsuperscript{11}. The mean volume per draw depends on the particular blood test, the ICU, and clinical laboratory practice\textsuperscript{15,18,19}. Published estimate vary from 1.5 ml to 10 ml for arterial blood gas and from 4 ml to 10 ml for hematology, coagulation and chemistry samples. The mean volume per draw in a recent study covering 145 European ICUs was 10.3 ml\textsuperscript{1,4,15}. Patients with indwelling arterial catheters are subject to more frequent blood draws and have three fold increases in phlebotomy volumes compared with patients without such catheters\textsuperscript{3,16,17}.

Each blood sample taken via an arterial or central venous catheter tends to result in blood being discarded, as blood is removed to clear infusate which might otherwise dilute the specimen. The volume lost depends on the local medical and nursing practice and it varies from 2 ml to 10 ml of discarded blood\textsuperscript{3,20,21}. The discarded volume is recommended to be twice the volume of the dead space to provide accurate and reproducible blood gas analysis\textsuperscript{20}. This recommendation is probably not well known though; the volume lost is certainly rarely measured.

Our present findings are that through a simple strategy of closed sampling and the use of pediatric blood vials, phlebotomy-induced blood loss can be reduced by about 30 mls per day per patient. This is likely to be sustained through longer admissions, perhaps producing a significant clinical benefit and reducing costs.

The small patient population studied and the relatively short study period (of 3 days) are amongst the limitations of the present study. While a longer study period would probably validate the hypothesis more clearly, longer lengths of stay are difficult to predict, so that complete follow up is difficult, and phlebotomy may become more invasive once arterial cannulae are removed. Most importantly, other causes of blood loss will become more frequent with longer stays, confounding results.

The venous arterial blood management protection system (VAMP) was introduced in 1989 as a simple method for clinicians to draw blood samples without using needles in a closed system\textsuperscript{6}. An added advantage of this is the elimination of the risk of needle stick injuries, with obvious benefits. In our evaluation of the system, no significant problems were encountered and it succeeded in eliminating the loss of blood as discarded dead-space volume. Furthermore, no extra workload was imposed on medical or nursing staff by the introduction of this method of phlebotomy.

Previous authors have found that pediatric collection tubes can reduce blood loss by 42\textsuperscript{22,23}, but their use is nonetheless not commonplace in adult medical practice. Our findings, in conjunction with these, show that it is feasible to use smaller vials in the adult ICU population. In conclusion, we suggest that the combined approach evaluated can make a modest but potentially clinically significant impact on the volumes of blood drawn from critically ill patients without adverse effect and recommend it for further evaluation or use.

**Acknowledgement**

We thank the nursing staff of Intensive Care Unit of Cork University Hospital for their help in study and the intensive care registrars working in the ICU for their help with the collection of data.

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References

INTRA VENOUS DEXMEDETOMIDINE PROLONGS BUPIVACAINE SPINAL ANALGESIA

MahMouD M Al-MUStafa*, IzDIaD Z BaDrAN**, HamDI M AbU-Ali***, BassAM A Al-BaraZanGI*, IsaLM M Massad* anD SubHI M. Al-GhaneM****

Abstract

Background: The prolongation of spinal anesthesia by using clonidine through the oral, intravenous and spinal route has been known. The new α₂ agonist, dexmedetomidine has been proved to prolong the spinal anesthesia through the intrathecal route. We hypothesized that dexmedetomidine when administered intravenously following spinal block, also prolongs spinal analgesia.

Methods: 48 patients were randomly allocated into two equal groups following receiving spinal isobaric bupivacaine 12.5 mg. Patients in group D received intravenously a loading dose of 1 μg/kg dexmedetomidine over 10 min and a maintenance dose of 0.5 μg/kg/hr. Patients in group C (the control group) received normal saline. The regression times to reach S1 sensory level and Bromage 0 motor scale, hemodynamic changes and the level of sedation were recorded.

Results: The duration of sensory block was longer in intravenous dexmedetomidine group compared with control group (261.5 ± 34.8 min versus 165.2 ± 31.5 min, P <0.05). The duration of motor block was longer in dexmedetomidine group than control group (199 ± 42.8 min versus 138.4 ± 31.3 min, P <0.05).

Conclusion: Intravenous dexmedetomidine administration prolonged the sensory and motor blocks of bupivacaine spinal analgesia with good sedation effect and hemodynamic stability.

Keywords: Anesthesia, spinal; dexmedetomidine; bupivacaine; intravenous.
Introduction

Spinal analgesia is a well-known technique used in urological procedures; transurethral resection of prostate (TURP), transurethral resection of bladder tumors (TURT) or Tension-free Vaginal Tape (TVT). The operative blood loss in TURP and TURT in spinal anesthesia is less in comparison to inhalational general anesthesia\(^1\). An intra-operative cough test helps to correctly position the tape in the TVT surgery during spinal anesthesia.

Different agents, like epinephrine, phenylephrine, adenosine, magnesium sulfate and clonidine, have been used as adjuncts to local anesthesia for prolonging the duration of spinal analgesia via the intrathecal route. Small doses of dexmedetomidine (3 µg) used in combination with bupivacaine in humans in spinal anesthesia produces a shorter onset of motor block and a prolongation in the duration of motor and sensory block with preserved hemodynamic stability and lack of sedation\(^2\). Clonidine an α\(_2\)-agonists, has been used widely in the intrathecal route\(^3,4,5,6\). It has been used intravenously within one hour after the spinal block and found that it prolonged bupivacaine spinal anesthesia for approximately one hour without adverse effect\(^7\).

Dexmedetomidine, also an α\(_2\)-agonist, has been used for pre-medication and as an adjunct to general anesthesia\(^8,9,10\). Intravenous Dexmedetomidine decreases the inhalational anesthesia and opioid requirements during general anesthesia\(^11\). We hypothesize that intravenous dexmedetomidine, might prolong the duration of spinal analgesia similar to clonidine.

The aim of this study, therefore was to evaluate the prolongation of spinal analgesia by the intravenous dexmedetomidine administration after the spinal block, and to assess the hemodynamic changes and the level of sedation.

Methods and Materials

Following approval of the Ethical Committee and obtaining written informed consent from patients, forty eight patients, ASA I-III, scheduled for TURP, TURT or TVT were enrolled in the study. Patients using α\(_2\)-adrenergic receptors antagonists, calcium channel blockers, angiotensin converting enzyme inhibitors, having dysrhythmia by ECG, body weight more than 120 Kg, or height less than 150 cm, were excluded from the study. All patients were pre-hydrated with 300 ml of Ringer’s Lactate solution via an 18-gauge IV cannula in the dorsum of the hand. Standard monitoring was used, including non-invasive arterial blood pressure (BP), ECG, heart rate (HR) and pulse oximetry. Patient motor power and sensation to cold using alcohol solution up to T10 dermatome were examined in both lower extremities. All patients received 4 L/min of O\(_2\) by simple face mask.

With the patient in the sitting position, spinal analgesia was performed at the level of L3-L4 through a midline approach using a 25-gauge Quincke spinal needle (B/Braun Medical, Messenger, Germany) with the hole pointing upwards. If the spinal block failed at the level of L3-L4, we changed the level to L2-L3. In case of failure at both levels; the procedure was abandoned, general anesthesia administered and those patients were excluded from the study. The spinal injection rate of bupivacaine 0.5% was 1ml/3-4 seconds in all patients. Using a computer-generated random list, patients were divided into two groups of 24 each. Control group (group C), received normal saline intravenously and the dexmedetomidine group (group D), received intravenous dexmedetomidine.

Isobaric 0.5 % bupivacaine, 12.5 mg (2.5 ml), was injected intrathecally in all patients. 50 cc syringe was prepared with either normal saline or dexmedetomidine. (Precedex 100 µg/ml; Hospira, Inc.) diluted with normal saline in a concentration of 4µg/ml. Immediately after spinal analgesia patients were laid back to supine position. Patients allocated to group D received intravenously through the intravenous infusion pump a loading dose of 1 µg/kg/hr dexmedetomidine over 10 min and a maintenance dose of 0.5 µg/kg/hr till the end of surgery. Patients in group C received also in 10 min, the same calculated volume normal saline of loading and maintenance dose as in group D.

The intravenous formula was prepared by an anesthetist doctor and was passed on to the doctor who performed the spinal analgesia who was blinded as to which group the patient was allocated. The anesthesiologist to perform the block recorded the baseline value of vital signs (blood pressure, heart rate...
and peripheral oxygen saturation). After performing the spinal block, the vital signs were recorded at 2, 5, and every 5 minutes in the operation room and every 15 minutes in the Post Anesthesia Care Unit (PACU) until the patient was discharged to his ward, after having achieved complete reversal of sensory and motor block.

In the PACU, the sensory level and Bromage scale was recorded every 15 minutes until the patient was discharged from the PACU. The times of regression to the S1 dermatome and reach Bromage scale 3 in PACU were recorded. The sensory level was assessed by cold sensation using alcohol swab along the mid-clavicular line bilaterally. The motor level was assessed according to the modified Bromage scale:

Bromage 0, the patient is able to move the hip, knee and ankle;

Bromage 1, the patient is unable to move the hip, but is able to move the knee and ankle;

Bromage 2, the patient is unable to move the hip and knee, but is able to move the ankle;

Bromage 3, the patient is unable to move the hip, knee and ankle. All durations were calculated considering the time of spinal injection as time zero. When sensory levels of anesthesia were not equal bilaterally, the higher level was used for the statistical analysis. Patients were discharged from the PACU after sensory regression to the S1 segment and Bromage scale 0.

For the purpose of this study, hypotension was defined as a systolic blood pressure of less than 90 mmHg and if maintained, was treated with a bolus administration of 300 ml of lactated Ringer’s solution over 10 min and 6 mg of intravenous ephedrine. Bradycardia was defined as HR <50 beats/min, and if maintained was treated with 0.5 mg of intravenous atropine.

The level of sedation was evaluated intra-operatively and post-operatively every 15 min using Ramsey Level of Sedation Scale:

1. Patient anxious, agitated, or restless;
2. Patient cooperative, oriented, and tranquil alert;
3. Patient responds to commands;
4. Asleep, but with brisk response to light glabellar tap or loud auditory stimulus;
5. Asleep, sluggish response to light glabellar tap or loud auditory stimulus.
6. Asleep, no response.

All sedation scores were recorded considering the time of start infusion as time zero.

Two weeks following discharge, all patients were evaluated in the outpatient clinic. The doctor in charge assessed any new onset of neurological impairment related to spinal anesthesia such as back, buttock or leg pain, headache or any new neurological deficit.

**Statistical Methods**

Statistical analysis was done using statgraphics Centurion XV (Statpoint, Herdon, Virginia – USA). Data was expressed as either mean and standard deviation or numbers and percentages. The demographic data of patients were studied for each of the three groups. The means of the continuous variables (Age, BMI, and duration of surgery) were compared between the three groups using analysis of variance ANOVA, while the demographic data for the categorical variables (sex, ASA class) were compared using chi-square test. Adverse effects and treatment factors (blood transfusion, nausea/vomiting, occurrence of hypotension, bradycardia, use of ephedrine, use of additive analgesia, the use of atropine) were also compared using the chi-square test. The P value of <0.05 was considered significant.

**Results**

Forty eight patients (Cn = 24) (Dn = 24) were enrolled, completed the study protocol and were included in the data analysis. The demographic data did not differ between the two study groups (Table 1).

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td>Demographic data. Values are the means ± standard deviations or numbers</td>
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<td>Table 1</td>
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<tr>
<td>Age</td>
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<tr>
<td>Sex (Male/Female)</td>
</tr>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>ASA I/II/III</td>
</tr>
<tr>
<td>Surgery – TURT/TURP/TVT</td>
</tr>
</tbody>
</table>
Time to regression to S1 dermatome and Bromage scale 0, was significantly prolonged in group D in comparison with group C. The regression time to S1 in group C was 165.2 ± 31.5 min and group D 261.5 ± 34.8 min, the P value <0.0001. The regression time to reach the Bromage 0 scale was 138.4 ± 31.3 min in group C and 199.9 ± 42.8 min in group D, the P value <0.0001 (Table 2).

<table>
<thead>
<tr>
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<th>C (n=24)</th>
<th>D (n=24)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Motor block regression to Bromage 0</td>
<td>138.4 ± 31.3</td>
<td>199.9 ± 42.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sensory regression to S1 segment</td>
<td>165.2 ± 31.5</td>
<td>261.5 ± 34.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

The duration of surgery, need to give ephedrine or atropine, bradycardia, hypotension, need to additive analgesia, blood transfusion, nausea or vomiting in the intraoperative or PACU time, were comparable in the two groups (P >0.05). The total amount of fluids administered following spinal anesthesia was higher in group C as compared to D group (910.8 ± 280.1 versus. 864.5 ± 172.8; p = 0.025) (Table 3).

<table>
<thead>
<tr>
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<th>C (n=24)</th>
<th>D (n=24)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total IV infusion</td>
<td>910.8 ± 280.1</td>
<td>864.5 ± 172.8</td>
<td>0.025</td>
</tr>
<tr>
<td>Duration of Surgery</td>
<td>42.8 ± 7.5</td>
<td>45.1 ± 8.3</td>
<td>0.32</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1/23</td>
<td>1/23</td>
<td>0.46</td>
</tr>
<tr>
<td>Additive analgesia</td>
<td>1/23</td>
<td>0/24</td>
<td>0.58</td>
</tr>
<tr>
<td>Nausea&amp;Vomiting</td>
<td>1/23</td>
<td>0/24</td>
<td>0.32</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>2/22</td>
<td>4/20</td>
<td>0.46</td>
</tr>
<tr>
<td>Hypotension</td>
<td>4/20</td>
<td>0/24</td>
<td>0.15</td>
</tr>
<tr>
<td>Atropine</td>
<td>0/24</td>
<td>2/22</td>
<td>0.65</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>1/23</td>
<td>0/24</td>
<td>0.60</td>
</tr>
</tbody>
</table>

The mean values of mean arterial pressure in the first hour after performing the spinal anesthesia and the first hour in the PACU (Recovery room) were comparable between the tow groups (Fig. 1).

The mean value of heart rate was significantly decreased in group D in comparison to group C in the first hour in the operation room and comparable in the PACU (Fig. 2).

Ramsey sedation scale was 2 in all patients in group C, and ranged from 2-5 in group D, the maximum score was 5 in 3 patients, 4 in 19 patients, and 3 in one patients, and the maximum mean score of sedation (3.96 ± 0.55) was achieved 30 min after starting dexmedetomidine infusion (Fig. 3).

The oxygen saturation was higher than 95% in all patient in the two groups either in the intraoperative or in the PACU time.

Two weeks following discharge from the outpatient clinic, the follow up did not show any neurological impairment related to spinal analgesia such as back, buttock or leg pain, headache or any new neurological deficit.

**Discussion**

Different drugs have been used as adjuvant to local anesthesia in order to prolong the duration of spinal analgesia. Clonidine an α2 agonist, has been used widely in the intrathecal, oral and intravenous routes to prolong the duration of spinal analgesia. It is known to have prolonging effect on sensory and motor blocks when used as an oral premedication within 2 h before bupivacaine spinal anesthesia. The intravenous administration of clonidine within 1 h after the spinal block prolonged bupivacaine spinal analgesia for approximately 1 h without adverse effect. Dexmedetomidine, also an α2 agonist, is pharmacologically related to clonidine, has 8 times more affinity for α2 receptors than does clonidine. It produces sedation and anxiolysis by binding to α2 receptors in the locus ceruleus, which diminishes the release of norepinephrine and inhibits sympathetic activity, thus decreasing heart rate and blood pressure. It produce analgesia by binding to adrenoreceptors in the spinal cord. It has been used as adjuvant to local anesthesia in the intrathecal route and has significant effect on onset and duration of spinal anesthesia.
Fig. 1
Comparison of Mean arterial pressure (MAP) levels among group C and D in first hour after spinal analgesia and first hour in Recovery room (R). Values are expressed as mean ± SD

Fig. 2
Comparison of Heart Rate (HR) levels among group C and D in first hour after spinal analgesia and first hour in Recovery room (R). Values are expressed as mean ± SD

Fig. 3
Comparison of Ramsay sedation score among group C and D. Values are expressed as mean ± SD
such as hypotension and bradycardia, are dose dependent. Infusion of loading dose over 10 min and then infusing the maintenance dose decreases the incidence of those side effects.

Jorm et al\textsuperscript{13} found that dexmedetomidine has an inhibitory effect on the locus ceruleus (A6 group) located at the brain stem. This supraspinal action could explain the prolongation of spinal anesthesia after intravenous administration of dexmedetomidine. The noradrenergic innervation of the spinal cord arises from the noradrenergic nuclei in the brain stem including the locus ceruleus, the A5, and the A7 noradrenergic nuclei. Neurons in the locus ceruleus are connected to the noradrenergic nuclei in the brain stem. Axon terminals of the noradrenergic nuclei reach lamina VII and VIII of the ventral horns of the spinal cord. The activity of the noradrenergic neurons is decreased by agonists acting at \(\alpha_2\)-adrenergic receptors on the locus ceruleus cell bodies. Therefore, inhibition of the locus ceruleus results in disinhibition of the noradrenergic nuclei and exerted descending inhibitory effect on nociception in the spinal cord\textsuperscript{15}. In group D, the prolongation of motor block is less in comparison to its sensory block (199.9 ± 42.8 min versus 261.5 ± 34.8 min). The mechanism of motor block is unclear, the analgesic effects of \(\alpha_2\)-adrenergic agonists could be mediated through supraspinal, spinal, and peripheral actions\textsuperscript{16}. There is some evidence that clonidine results in direct inhibition of impulse conduction in the large, myelinated A\(\alpha\) fibers and the 50\% effective concentration (EC\textsubscript{50}%) measured approximately 4-folds of that in small, unmyelinated C fibers\textsuperscript{17}. This could explain the less prolonged motor block compared with sensory block, as conduction of motor nerve fibers was less inhibited than sensory nerve fibers at the same concentration of clonidine. The same process might be applied to dexmedetomidine, and would explain the more sensory than motor block prolongation.

Dexmedetomidine is known to have sedation effect\textsuperscript{18}; providing better conditions for the surgeon and the patient, provided that hemodynamic stability is preserved. In our patients, Ramsay sedation scores ranged from 2-5, the maximum score in group D was 3.96 ± 0.55. The heart rate decreased significantly after the start of intravenous infusion loading dose and extended in the PACU (Fig. 2). This decrease in the heart rate was more clear and significant in group D in comparison with group C. The lower HR observed in group D could be explained by the decreased sympathetic outflow and circulating levels of catecholamines that are caused by dexmedetomidine\textsuperscript{19,20}. Other studies support the finding that the bradycardia effect of dexmedetomidine is long lasting when used as a premedication drug\textsuperscript{21,22}. Six patients developed bradycardia (HR <50 beat/min), only two patients in group D needed to have atropine to reverse the bradycardia, and statistically and clinically this was not significant.

Previous studies have shown that the hypotensive effect of dexmedetomidine persists in the intraoperative as well as in the postoperative period\textsuperscript{22,23}. In our patients the mean arterial pressure was also decreased in the D group as well as the C group (Fig. 1) and clinically was not significant. There was no further decrease in the blood pressure after adding intravenous dexmedetomidine to spinal anesthesia. Only one patient in group C received ephedrine because of decrease the systolic blood pressure lower than 90 mmHg, which statistically was not significant. The total intravenous fluid administered during surgery was less in group D in comparison with group C (864.5 ± 172.8 versus 910.8 ± 280.1, \(p = 0.025\)).

In conclusion, supplementation of spinal anesthesia with intravenous dexmedetomidine produces significantly longer sensory and motor block than spinal analgesia alone. Adverse side effects were avoided by the slow infusion of loading and the maintenance dose of dexmedetomidine. All patients reached good sedation levels that enabled their cooperation and better operating conditions for the surgeon without significant respiratory depression.
References


ATTENUATION OF HEMODYNAMIC RESPONSES FOLLOWING LARYNGOSCOPY AND TRACHEAL INTUBATION

- Comparative assessment of Clonidine and Gabapentin Premedication

SEYED MOJTABA. MARASHI, MOHAMMAD HOSSEIN. GHAFARI* AND ALIREZA SALIMINIA

Abstract

Objective: The present study was conducted to compare the effect of clonidine and gabapentin premedication in modifying the hyperdynamic response following laryngoscopy and tracheal intubation.

Methods and Materials: Seventy-five ASA I-II patients of both sexes (37 males (49.3%), 38 females (50.7%)) 18 to 45 years (mean 32.8 ± 8.65yr.) were randomly allocated into three equal groups (25 each). Group-1 received 0.2 mg clonidine, Group-2 received placebo and Group-3 received 900 mg gabapentin, 120 minute before operation. Heart rate, systolic, diastolic and mean arterial blood pressure were measured before induction of anesthesia, before laryngoscopy, and 1, 3, 5, 10 min after intubation.

Results: Analysis revealed that the heart rate, systolic, diastolic and mean arterial blood pressure significantly differed between groups (p<0.001, p = 0.003, p<0.001, p<0.001, respectively). The highest rates of heart rate, systolic, diastolic and mean arterial blood pressure were in the placebo group and in one minute after laryngoscopy, and the lowest rate were in the gabapentin group at the time of 1, 3, 5 and 10 after laryngoscopy, except that the lowest rate of heart rate in 10 min after laryngoscopy was in clonidine group.

Conclusion: The data propose that both clonidine and gabapentin have effective role in blunting hyperdynamic responses after laryngoscopy, more so with gabapentin.
Introduction

Manipulation of the respiratory tract such as in laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increased circulating catecholamines, heart rate, blood pressure, myocardial oxygen demand, tachycardia and dysrhythmias\textsuperscript{1,2}. In the recent decade, several studies have focused on clonidine and newly on gabapentin premedication to attenuate the hemodynamic responses following laryngoscopy and intubation. However, there was no comparative study.

Clonidine is a $\alpha_2$-adrenoceptor agonist with sedative and analgesic effects, also has the beneficial effect of blunting hyperdynamic responses due to laryngoscopy and tracheal intubation\textsuperscript{2-8}. In addition gabapentin, a structural analogue of the $\gamma$-aminobutyric acid (GABA) is known as an anticonvulsant drug that has various analgesic effects. Recently, its role in attenuating of hemodynamic responses following laryngoscopy and intubation has been noticed\textsuperscript{9,10}.

The present study was performed to compare the effect of clonidine and gabapentin on modifying the hemodynamic responses following laryngoscopy and tracheal intubation.

Methods and Materials

Data source

Written informed consent from all patients was obtained and the study was approved by the Hospital’s Ethics Committee.

This is a double-blind, placebo-controlled randomized study. Seventy-five ASA I-II patients aged 18-45 years (mean 32.8 ± 8.65 years) of both sexes comprised of 37 male (49.3%) and 38 female (50.7%) were enrolled into the study. Patients were scheduled for elective orthopedic and general surgical procedures under general anesthesia. Exclusion criteria consisted of urgent surgical procedures, body mass index (BMI) more than 30, hiatal hernia, gastroesophageal reflux, history of allergy to clonidine or gabapentin, history of cerebrovascular, neurologic, cardiovascular, respiratory, hepatic and renal disease, hypertension and pheochromocytoma, patients with history of drug or alcohol abused, patients who were administered daily $\beta$-blocker, antidepressant, anti-anxiety, anticonvulsant or antipsychotic drugs, any history of immunity response to muscle relaxant drugs or history of neuromuscular disease that would made muscle relaxants contraindicated, difficult intubation (Mallampati class III-IV or laryngoscopic grade III-IV), prolonged laryngoscopic time (more than 30 second).

Randomization and drugs

Patients were randomly divided to three equal groups (25 each) according to a computerized random table. All patients received premedication drugs 120 minute before admission to the operating room.

Group-1, patients received 0.2 mg clonidine ($0.2 \text{mg} \times 1$ capsule + 2 placebo capsules).

Group-2, patients received placebo (3 capsules).

Group-3, patients received 900 mg gabapentin ($300 \text{mg} \times 3$ capsules).

Technique of anesthesia

Following insertion of intravenous catheter, all patients were infused with 5 ml/kg normal saline. Routine monitoring comprised, ECG, pulse oximetry, and non-invasive blood pressure.

2.5 $\mu$g/kg Fentanyl and 0.03 mg/kg midazolam intravenous as premedication was administered before induction of anesthesia. Patients were preoxygenated for 3 minutes with oxygen 100% and anesthesia was induced with 5 mg/kg thiopental sodium and 0.5 mg/kg atracurium. Three minutes later, laryngoscopy using Macintosh blade size 3 and intubation using intratracheal tube (size 7.5-8) were performed by an anesthetist or by a two-year trained resident in anesthesiology. Heart rate, systolic, diastolic and mean arterial blood pressure were recorded before induction of anesthesia, before laryngoscopy, and 1, 3, 5, 10 min after intubation.

Statistical analysis

Data was represented as mean ± standard deviation for interval and count (relative frequency) for categorical variables. Baseline data were compared among study groups by one-way analysis of variance (ANOVA) for interval and Chi-square (and Fisher’s
exact) test for categorical data. Repeated measure ANOVA model was used to compare variations in different time intervals and among study groups. A p-value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS 11.5 for Windows (SPSS Inc., Chicago, Illinois).

Results

Table 1 shows distribution of sex, mean of age and weight in each group with no significant differences between the three groups (respectively; p = 0.5, p = 0.2, p = 0.4).

**HR:** The placebo group recorded highest mean HR 101.16 ± 16.48 (beat/min) in one minute after laryngoscopy. The clonidine group recorded the lowest HR 69.12 (beat/min) in 10 minutes after laryngoscopy. Heart rate differed with regard to groups (p<0.0001) also with regard to time between groups (p<0.0001). HR profile is shown in (Fig. 1).

**SAP:** The highest mean SAP 148.88 ± 14.12 (mmHg) belonged to placebo group in one minute after laryngoscopy and the lowest one was 99.76 ± 14.69 (mmHg) belonged to gabapentin group in 10 minutes after laryngoscopy. SAP differed with regard to group (p = 0.003) also with regard to time between groups (p<0.0001). SAP profile is shown in (Fig. 2).

**DAP:** The highest mean DAP was 98.60 ± 11.49 (mmHg) belonged to placebo group in one minute after laryngoscopy and the lowest one was 65.72 ± 9.70 (mmHg) belonged to gabapentin group in 10 minutes after laryngoscopy. DAP differed with regard to group (p<0.0001) also with regard to time between groups (p<0.0001). DAP profile is shown in (Fig. 3).

**MAP:** The highest mean MAP was 115.36 ± 11.40 (mmHg) belonged to placebo group in one minute after laryngoscopy and the lowest one was 77.07 ± 10.43 (mmHg) belonged to gabapentin group in 10 minutes after laryngoscopy. MAP differed with regard to group (p<0.0001) also with regard to time between groups (p<0.0001). MAP profile is shown in (Fig. 4).

Discussion

Gabapentin is a known anticonvulsant drug with wide spread effects on pain. Its efficacy on attenuating hemodynamic responses following laryngoscopy was revealed by Fassoulaki and colleagues in 2006. They showed SAP and DAP significantly were lower in the gabapentin group than in the control group (p<0.05) immediately also in 1, 3, 5 and 10 minute after laryngoscopy but HR did not differ between two groups at any of the times. Kayan and colleagues in 2008 demonstrated attenuation of gabapentin on MAP in the first 10 minutes following endotracheal intubation.

The attenuating effect of clonidine has previously been documented by many studies. Our data also confirmed HR, SAP, DAP and MAP significantly differ with regard to groups and to times (all the p-values were less than 0.05). Between the groups, the highest rate of HR, SAP, DAP and MAP were in the placebo group especially in one minute after laryngoscopy. It follows that both clonidine and gabapentin have effective roles in blunting hemodynamic responses following laryngoscopy.

The type of surgery and the quantity of surgical stimulation in the first 10 min of anesthesia induction was not exactly adjusted in all patients. These can be

<table>
<thead>
<tr>
<th>characteristics</th>
<th>Clonidine group (Group-1)</th>
<th>Placebo group (Group-2)</th>
<th>Gabapentin group (Group-3)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Male</td>
<td>13(52%)</td>
<td>14(56%)</td>
<td>10(40%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12(48%)</td>
<td>11(44%)</td>
<td>15(60%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>32.88 ± 8.57</td>
<td>30.72 ± 7.59</td>
<td>34.96 ± 9.51</td>
<td>0.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.88 ± 11.25</td>
<td>67.12 ± 14.65</td>
<td>71.32 ± 10.68</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Values are presented as n (%) or mean ± SD.
considered as our study limitation; however, an effort was made to start surgery 10 min after anesthesia induction.

Conclusions

Results of our study suggest that both clonidine and gabapentine have effective roles in blunting the hyperdynamic responses following laryngoscopy, more so with gabapentine. It also suggests that there are significant differences between gabapentin, clonidine and placebo in modifying the hemodynamic responses in the first 10 min after laryngoscopy. It is recommended that further studies be done to compare the effects of gabapentine and its dosage, with the newer $\alpha_2$ adrenoreceptor, like dexmedetomidine, on modifying the hemodynamic variables following laryngoscopy.
ATTENUATION OF HEMODYNAMIC RESPONSES FOLLOWING LARYNGOSCOPY AND TRACHEAL INTUBATION

References


Pediatric Cancer Pain Management at a Regional Cancer Center: Implementation of WHO Analgesic Ladder

Seema Mishra*, Sushma Bhatnagar**, Manisha Singh***, Deepak Gupta****, Roopesh Jain***, Himanshu Chauhan***, and Gaurav Nirwani Goyal***

Abstract

Purpose: To collect data on the prevalence of various types of cancer pain in a sample of children with cancer, and to implement the WHO Analgesic Ladder in the management of pain in pediatric cancer.

Methods: Eighty four pediatric patients suffering of cancer pain were studied during the period 2001-2006. Patients were requested to rate their global intensity of pain on 0-100 mm visual analogue scale (VAS 0 = no pain 100 = maximum pain). Pain management was performed in accordance with the WHO Analgesic Ladder for cancer pain. Patients were followed up weekly for three weeks.

Results: Of the 84 pediatric children with cancer, pain was nociceptive in 26 (31%), neuropathic in 12 (14.3%) and mixed in 46 (54.8%). Almost 7 (8.3%) of patients were on WHO step 3 at baseline. Thereafter the WHO step 3 increased; first week visit 36 (43%) patients; second week visit 58(69%), and third week 69 (82.1%). At baseline, 40 (47.6%) patients took NSAID only, 2 (2.4%) patients took adjuvant, while 38 (45.2 %) patients took combination of NSAID and adjuvant treatment. There was statistically significant (p = 0.000) reduction in VAS as time progressed.

Conclusion: Cancer pain in pediatric age group can be well managed in accordance with the WHO Analgesic Ladder. Aggressive symptoms and control of treatment of related side effect are also needed to ensure successful implementation and the WHO Analgesic Ladder.
Introduction

The provision of pain management to the pediatric oncology population presents special challenges. The pediatric oncology population is chronically ill, often young with a doubtful prognosis, labile disease course, receiving aggressive therapy with a debilitating side effects. Patients and their families experience severe disruption to their daily lives with frequent clinic visits, scheduled and unscheduled admission. Although there have been major advances in the treatment of childhood cancer with on overall survival rate of more than 70%, cancer continues to be the leading cause of death in children resulting from disease.

Pain control is an integral component of pediatric palliative care. Children may experience many different types of pain from invasive procedures, cumulative effects of toxic therapies, progressive disease or psychological factors.

The pain is often complex with multiple sources, comprised of nociceptive and neuropathic components. Children’s perception of pain is defined by their age and cognitive level; their previous pain experiences, against which they evaluate each new pain; the relevance of the pain or disease causing pain; their expectation for obtaining eventual recovery and pain relief and their ability to control the pain themselves.

In this study the pediatric cancer pain was managed in accordance to the WHO analgesic ladder. The aim was to collect data on the prevalence of different types of cancer pain in a sample of children with cancer pain and report on pain management in pediatric cancer with respect to the WHO ladder approach at a regional cancer set up.

Keywords: Cancer pain, Pediatric cancer pain, Palliative care, WHO analgesic ladder.

Materials & Methods

The present study was conducted on outpatients in the Pain and Palliative Care Clinic at Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India. 84 pediatric patients 5-15 years (mean 11 yrs), (73% males, 27% females) suffering of cancer pain were included in this prospective study during the period 2001-2006.

Initial work up of patients in the Pain Clinic included general medical and neurological examination and a specific examination of the site of pain and surrounding anatomic regions. Patients who were lost to follow up after single visit, were excluded from this study. Patients were followed up weekly for three weeks. Patients were asked to rate their global intensity of pain on 0-100 mm visual analogue scale (VAS 0 no pain and 100 mm is maximum pain).

Pain treatment was performed in accordance to the WHO analgesic ladder for cancer pain:

- NSAIDs for mild pain (WHO Step 1),
- Weak opioids and NSAIDs for mild to moderate pain (WHO Step 2),
- Morphine for moderate to severe pain (WHO Step 3).

Every step was accompanied by various adjuvant drugs for various indications (Table 1). All patients were followed up weekly for three weeks.

### Table 1

<table>
<thead>
<tr>
<th>Types of Drugs</th>
<th>Drugs</th>
<th>Doses (mg/kg/day)</th>
<th>Various Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressant</td>
<td>Amitriptyline</td>
<td>0.2-0.5</td>
<td>Neuropathic pain</td>
</tr>
<tr>
<td>Anticonvulsant</td>
<td>Gabapentin</td>
<td>5-30</td>
<td>Neuropathic pain</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Dexamethasone</td>
<td>4-16 mg/day</td>
<td>Neuropathic pain, Bone pain, metastasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Poor quality of life</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>Metoclopramide</td>
<td>10-30 mg/day</td>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td></td>
<td>Ondansetron</td>
<td>8.5-0.15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Granisetron</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Antihistamine</td>
<td>Promethazine</td>
<td>0.5-2</td>
<td>Pruritus, Nausea/vomiting</td>
</tr>
<tr>
<td></td>
<td>Diphenhydramine</td>
<td>1-4</td>
<td></td>
</tr>
<tr>
<td>Laxatives</td>
<td>Bisacodyl</td>
<td>5-15 mg/day</td>
<td>Constipation</td>
</tr>
<tr>
<td></td>
<td>Sodium picosulphate</td>
<td>5-15 mg/day</td>
<td></td>
</tr>
</tbody>
</table>

Laxatives were given prophylactically to all patients who were on opioids. In follow up visits, patients were asked about pain intensity, nausea/vomiting, sedation, constipation, generalized weakness, lack of appetite. Patients were asked to rate their symptoms on verbal rating score (VRS-1 not at all; 2 mild grades; 3 moderate grades; 4 severe grades).
Statistical Analysis

The appropriate descriptive statistics were used for presentation of each of the covariates. Exploratory exercise was also done for applying the appropriate statistical tools. One way analysis of variance was used to compare the VAS among the different types of pain. Kruskal Wallis test was used to compare the age among the different types of pain. Chi square test was performed to evaluate the association of various outcomes at baseline with different types of pain. Repeated measure of analysis of variance was used for seeing the changes in the VAS as time increases as well as effect of different types of pain (Neuropathic, mixed and nociceptive pain). Cochran Q test was used to look at the differences in proportion of nausea/vomiting, constipation, sedation and pruritus as the time increases. For seeing the changes in the generalized weakness and loss of appetite as the time changes, Friedman test was applied for each of the different types of pain. The p-values less than 5% were considered as a significant result. SPSS 11.5 was used for statistical analysis.

Results

Of the total 94 patients enrolled, 10 patients did not turn up after 1st visit so were excluded. 84 patients were followed up weekly for 3 weeks during the period 2001-2006.

52% of patients were referred from the medical oncology, 30% patients from radiotherapy and 2% patients from surgical oncology, whereas 16% patients were direct referred to pain clinic.

Of the pediatric cancer patients studied 38% had not taken any prior treatment 21% patients had taken chemotherapy only, 19% patients had taken chemotherapy and radiotherapy and 12% patients had taken surgery, chemotherapy and radiotherapy prior to referral.

26 (31%) patients had nociceptive pain (somatic, bony, and visceral). 12 (14.3%) patients had neuropathic pain, 46 (54.8%) patients had mixed pain (Table 2).

Almost 8.3% of pediatric patients were in the WHO step 3 at baseline. Thereafter the WHO step 3 steadily increased at first weekly visit 36 (43%) patients, second visit 58 (69%) patients, and third visit 69 (82.1%) (Fig. 1).

In addition, at baseline, 40 (47.6%) patients took NSAID only, 2 (2.4%) patients took adjuvant while 38 (45.2%) patients took combination of NSAID and adjuvant treatment. The proportion of patients taking combination of NSAID and adjuvant were increasing continuously as time increased. The median morphine dose at baseline, first and second weekly visits was same i.e. 30 mg. However, median morphine dose at third visit rose to 40 mg.

There was statistically significant (p = 0.000) reduction in VAS as time increased while no effect of different types of pain and no interaction effect of time and different types of pain could be found (Fig. 2).
At baseline the nausea/vomiting was moderate grade in 2 patients and severe grade in 1 patient. At second weekly visit no patient had severe grade nausea/vomiting while 6 patients had moderate grade nausea/vomiting. Similarly, none of the patients had severe grade constipation at any visit. 1 patient had pruritus at baseline, 2 patients had moderate grade pruritus and 1 patient had severe pruritus at first visit. One patient had moderate grade pruritus at second visit and no patients developed any type of pruritus at third visit (Fig. 3).

Since the number of patients presented with nausea/vomiting or pruritus or constipation at any visit was not much, therefore the category with occurrence of symptom or no symptom was made for further analysis. However, in case of generalized weakness and loss of appetite, the level of severe grade (VRS 4) patients was less so that patients were pooled with patients having VRS 3. The comparisons of baseline characteristics are shown in Table 2.

The significant deterioration (p = 0.000) in nausea/vomiting was found as time increased. However no significant changes in the proportion of patients could be seen in constipation. In addition, the significantly increased changes in generalize weakness was found whereas no significant changes were for loss of appetite. There was no effect of different types of pain on any of the outcomes separately.

**Discussion**

Pain control is an intrinsic component of pediatric palliative care. Since children may experience complex pains due to myriad physical and psychological factors, pain control must be child centered rather than disease centered. The management of pain in the palliative care of children is somewhat different from that in adults. It also differs in approach from the management of other types of acute and chronic pain in childhood. But in this present study it was found that pain management

![Fig. 3](image)

**Fig. 3**

Distribution of various outcomes according to time

<table>
<thead>
<tr>
<th>Variables</th>
<th>Neuropathic (n = 12)</th>
<th>Mixed (n = 46)</th>
<th>Nociceptive (n = 26)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>9.25 ± 4.49</td>
<td>10 ± 3.52</td>
<td>11.14 ± 3.03</td>
<td>0.256</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>5:7</td>
<td>37:9</td>
<td>19:7</td>
<td>0.027</td>
</tr>
<tr>
<td>Visual analogue scale (VAS)</td>
<td>77.5 ± 18.64</td>
<td>83.26 ± 16.33</td>
<td>80.38 ± 22.53</td>
<td>0.163</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>5 (41.7%)</td>
<td>13 (28.3%)</td>
<td>12 (46.2%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Constipation</td>
<td>3 (25%)</td>
<td>17 (37%)</td>
<td>12 (46.2%)</td>
<td>0.446</td>
</tr>
<tr>
<td>Sedation</td>
<td>2 (16.7%)</td>
<td>2 (4.3%)</td>
<td>1 (3.8%)</td>
<td>0.237</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (3.8%)</td>
<td>0.323</td>
</tr>
<tr>
<td>Generalized Weakness</td>
<td>7 (58.3%)</td>
<td>19 (41.3%)</td>
<td>8 (30.8%)</td>
<td>0.302</td>
</tr>
<tr>
<td>Mild Weakness</td>
<td>1 (8.3%)</td>
<td>2 (4.3%)</td>
<td>4 (15.4%)</td>
<td></td>
</tr>
<tr>
<td>Moderate Weakness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>7 (58.3%)</td>
<td>20 (43.5%)</td>
<td>9 (34.6%)</td>
<td>0.182</td>
</tr>
<tr>
<td>Mild</td>
<td>1 (8.3%)</td>
<td>10 (21.7%)</td>
<td>11 (42.3%)</td>
<td></td>
</tr>
</tbody>
</table>

n = Total number of patients.
in pediatric cancer pain according to WHO analgesic ladder, is as good as in adult patients.

In the present study 14.3% patients were having neuropathic, and 54.6% patients from mixed (nociceptive and neuropathic) and 31.1% from nociceptive pain. In adult patient’s the incidence of neuropathic pain ranged from 16-31%, as quoted by various authors6,7,8 but it is not clearly mentioned the component of nociceptive in their population.

Mean pain intensity at base level in all types was insignificant. There was statistically significant reduction in VAS as time increased, while no effect of different types of pain and no interaction effect of time and different types of pain could be found. This study therefore demonstrated that neuropathic pediatric cancer pain can be relieved in most patients and the efficacies of pediatric cancer pain treatment following the WHO guideline was as good as in neuropathic and mixed, as in nociceptive pain. It has previously been thought that opioids were highly dangerous drugs unsuitable for use in children. However, opioids have now taken their place as the mainstay for provision of good analgesia to manage moderate to severe pain in malignant conditions9,10. Similar findings were observed in the present study where at the end 82.1% patients were on opioids as compared to 8.3% at base line, and the mean dose of morphine used at the end of study was 40 mg with statistically significant decrease in VAS as compared to base line.

No extreme sedation or respiratory depression was observed in any of our patient, similar to others9. Itching was found in 2 children and out of these two one was having itching before coming to our clinic and another had itching after starting morphine which subsided following antihistaminic therapy. Total of 6 (7.1%) patients had nausea/vomiting but out of these six patients 2 patients had nausea/vomiting before coming to our clinic, findings similar to findings observed by Still et al9 but different from Kasai et al11, as incidence of nausea and drowsiness were 52.9% and 41.2% respectively. They proposed the two step Analgesic Ladder.

Effective management of some difficult but common pain syndromes such as shooting or burning neuropathic pain, requires techniques “beyond the ladder”. These patients require different classes of drugs, such as tricyclic antidepressants and anticonvulsants. Unfortunately many of these nonopioid adjuvant drugs have not been studied in children and when prescribed, are “off label”12.

The adjuvant analgesics comprise a diverse group of medications with different primary indications like antidepressants, anticonvulsants steroids13,14. Various adjuvant drugs used in our study; amitryptiline, gabapentine and corticosteroids, as was used by various authors and found to be effective, though it is not evidence based15,16. Future studies are therefore needed to determine the effectiveness of these adjuvant analgesics.

Conclusion

Cancer pain in pediatric age group can be very well managed in accordance with the WHO analgesic ladder. Aggressive control of related side effects, is needed to ensure successful implementation of the analgesic ladder.
References

THE PROPHYLACTIC EFFECT OF RECTAL ACETAMINOPHEN ON POSTOPERATIVE PAIN AND OPIOID REQUIREMENTS AFTER ADENOTONSILLECTOMY IN CHILDREN

Gholam Ali Dashti*, Shahram Amini**, and Elham Zanguee***

Abstract

Background: Postoperative pain in children is common after adenotonsillectomy. Rectal acetaminophen has been used effectively for postoperative pain management in small children. The aim of this randomized double blind study was to evaluate the prophylactic effect of rectal acetaminophen on postoperative pain management and opioid requirements in children undergoing adenotonsillectomy.

Materials and Methods: 104 children, 7 to 15 yr, ASA I or II scheduled for elective adenotonsillectomy were recruited for the study. Patients were randomized to receive either rectal acetaminophen 40 mg/kg or nothing after induction of standard anesthesia. The postoperative pain was assessed using visual analog scale (VAS) every 2 hours for the first 6 hours. The need for rescue analgesic, intravenous pethedine of 0.5 mg/kg, was recorded at 24 hours after surgery.

Results: Pain scores were significantly lower in acetaminophen group at different times (p<0.001) and needed less rescue analgesic (p<0.001).

Conclusion: We conclude that prophylactic rectal acetaminophen is effective in reducing pain after adenotonsillectomy and postoperative analgesic requirement.

Key words: acetaminophen, analgesia, adenotonsillectomy, suppository.

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Introduction

Adenotonsillectomy is one of the most frequent ENT operations performed in children with over 2 million cases in the United States and 2.3/1000 for the population aged under 12 yr in the UK each year.

Postoperative pain may influence the child’s ability to tolerate oral pain medication and fluid intake, resulting in nausea and dehydration in a considerable number of children postoperatively. Operation is associated with pain in more than 80% of children on the first day after operation. It is assumed that pain is not adequately treated in one half of all surgical procedures.

Although opioids are used widely in the management of postoperative pain, their side effects especially respiratory depression, bradycardia, nausea and vomiting, have resulted in decreased use of these analgesics especially in children.

Both acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) have been used extensively with very good results in reducing pain and postoperative opioid requirements after adenotonsillectomy in children and adults. NSAIDs act on prostaglandin synthesis for pain reduction with adverse effects such as bleeding problems in both gastrointestinal tract and from the surgical site and potential renal dysfunction that have caused some concerns in their widespread application. Although some investigators have shown their preference alone or in combination with acetaminophen, other studies failed to reveal such an effect. Acetaminophen is the most commonly used analgesic in children. It is also frequently used as an adjuvant for postoperative pain management in pediatric patients. However, there are reports that failed to show any benefits in reducing postoperative opioid requirements of rectal acetaminophen in infants and small children undergoing elective cleft palate repair or have showed that only high doses of rectal acetaminophen of 40-60 mg/kg was effective in day care surgery in children.

The purpose of this randomized, double blind study was to investigate the efficacy of rectal acetaminophen on postoperative pain management after adenotonsillectomy.

Materials and Methods

After approval from Research Committee of Medical School and procuring parents informed consent, 104 children, 7 to 15 yr, ASA I or II, to undergo elective adenotonsillectomy at a teaching hospital, were recruited for the study. Exclusion criteria included a known allergy to acetaminophen, renal or hepatic dysfunction, ingestion of analgesics in the past 24 hours, drug abuse (because of high prevalence in the region), a known case of G6PD deficiency, diarrhea, dehydration, and bleeding disorders.

No premedication was used. After IV cannulation, patients received 5 ml/kg crystalloid, 0.05 mg/kg midazolam, and 1 µg/kg remifentanil. General anesthesia was induced using 5 mg/kg thiopental sodium. Atracurium (0.6 mg/kg) was used to facilitate endotracheal intubation.

Following induction, the children were randomized based on blocks of 10 to receive either nothing (control group) (n = 51) or rectal acetaminophen 40 mg/kg (n = 53), by a surgical nurse who was blinded to the study and did not participate in the postoperative care of the child. Patients received a total of 10 ml/kg of crystalloids intraoperatively. 0.2 mg/kg of IV dexamethasone was given to reduce postoperative nausea and vomiting. Anesthesia was maintained with halothane 0.5-1% and remifentanil was used in doses of 0.1-0.2 µg/kg/min to maintain heart rate and blood pressure within 20% range from the baseline. Patients were ventilated with 40% oxygen in nitrous oxide.

Standard monitoring included respiratory rate, pulse rate, noninvasive blood pressure, and pulse oximetry. At the end of the surgery, the residual neuromuscular block was reversed with neostigmine 0.05 mg/kg IV, and atropine 0.2 mg/kg IV. All the operations were performed by a single surgeon. Patients were extubated when fully awake and were transferred to postanesthetic care unit (PACU). No patients received local anesthetics at the tonsillar base and coagulation was achieved by electrocautery. Patients were transferred to the ward if they were alert and cooperative, with no or slight pain, no bleeding, hemodynamically stable, and without nausea and vomiting. They stayed in the hospital for 24 hours postoperatively.
Postoperative pain was assessed by using VAS by trained independent blinded nurses on the ward (based on a 0-100 scale) with 0 indicating no pain and 100 indicating the worst intolerable pain ever experienced. Parents were also blind to the study. A pain score of more than 40 was considered as unsatisfactory and resulted in administration of 0.5 mg/kg of pethedine IV (with the minimum interval of 4 hours).

Any adverse effects (nausea, vomiting, respiratory depression, and bleeding) were recorded during their stay in the hospital.

Differences between the groups were analyzed using Student’s t-test. The chi-square test was applied to non-parametric data. SPSS version 13 was used for statistical analysis. P value less than 0.05 was considered significant.

Results

There was no statistical difference in ASA status, mean age, weight, and sex between the groups (Table 1).

The pain scores were significantly lower after arrival at the ward in the acetaminophen group (63.83, SD = 25.30 vs. 77.98, SD = 17.94, P value <0.002). Patients in acetaminophen group experienced less pain at 2, 4, and 6 hours postoperatively compared with the control group (Table 2).

The number of patients who required rescue analgesic was significantly higher in the control compared with acetaminophen group (31 out of 51 vs 22 out of 53 P value <0.001). Opioid requirements were less in the acetaminophen group (6.48 mg SD = 8.52) compared with the control group (17.09 mg SD = 12.12), P value <0.001] (Table 3).

None of the patients in either group developed significant bleeding requiring reoperation. No one had respiratory depression, oxygen desaturation, and bradycardia after receiving pethedine. Two patients in the no acetaminophen group, developed nausea and vomiting in the postoperative period requiring intervention.

Discussion

Our study revealed that rectal acetaminophen reduces pain intensity and postoperative analgesic requirements compared to group without acetaminophen after adenotonsillectomy. Our study was in concordance with those using rectal acetaminophen for postoperative pain management after adenotonsillectomy.

Pain is a common complication after adenotonsillectomy in children and results in 80%
analgesic requirements. Nikanne et al showed that more than 20% of children experienced severe pain at home after adenotonsillectomy. Pain removal would result in less discomfort, nausea and vomiting, faster postoperative oral intake and discharge from the hospital.

It has been shown that postoperative oral pain medication is difficult because children refuse to take oral medication and may result in nausea, vomiting and altered gastrointestinal motility. On the other hand, preventing the initial neural cascade could lead to long term benefits by eliminating the hypersensitivity produced by noxious stimuli.

Although opioids are used widely in the management of postoperative pain, their adverse effects such as respiratory depression and nausea and vomiting have reduced their application. Non steroidal anti-inflammatory drugs (NSAIDS) have replaced opioids for postoperative pain management because of lack of respiratory depression and nausea and vomiting. However, their side effects such as increasing bleeding tendency from the surgical site and gastrointestinal tract, GI upset, and renal and hepatic dysfunction, may affect their liberal application.

Tawalbeh et al suggested that diclofenac was more effective than paracetamol in decreasing the pain associated with swallowing after adenotonsillectomy without considerable adverse effects. In contradistinction, Rusy et al showed that ketorolac was no more effective than high dose acetaminophen for analgesia in the patient after tonsillectomy.

Acetaminophen is the most commonly used analgesic in children. It is almost safe and effective in comparison to opioids and NSAIDS. Rectal acetaminophen has been shown to be a good alternative to oral administration in postoperative pediatric adenotonsillectomy patients. However, doses as high as 40-60 mg/kg could be satisfactorily effective. Bremerich et al reported that acetaminophen up to 40 mg/kg had no opioid sparing effect and did not result in analgesia.

In contrast to our findings, previous studies have found that rectal acetaminophen may provide erratic and inconsistent analgesia after tonsillectomy. This variation may be explained by differing analgesic requirements with different surgical techniques, different doses of acetaminophen, or the concurrent use of other analgesic agents. In addition is the type of surgery performed as adenotonsillectomy might be more painful than adenoidectomy alone.

Acetaminophen has been shown to be more effective when combined with NSAIDs in the postoperative pain management. Combination of NSAIDs and other analgesics have been proposed for pain management but there is not a general agreement on their efficacy. Issioui et al concluded that oral premedication with a combination of acetaminophen (2000 mg) and celecoxib (200 mg) was highly effective in decreasing pain and improving patient satisfaction after ambulatory ENT surgery. However, Hiler et al have shown that a combination of paracetamol and diclofenac was not more effective than paracetamol alone for analgesia after tonsillectomy.

In summary, we were able to show that rectal acetaminophen in dose of 40 mg/kg is effective in reducing pain intensity and postoperative analgesic requirements after adenotonsillectomy in children. It is recommended to administer prophylactic rectal acetaminophen in order to decrease the child’s postoperative discomfort and pain after adenotonsillectomy.
References


PREGNANCY AT TERM DOES NOT ALTER THE RESPONSES TO A MECHANICAL AND AN ELECTRICAL STIMULUS AFTER SKIN EMLA APPLICATION

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and Argyro Fassoulaki****

Abstract

Background: Pregnancy is associated with reduced local anesthetic requirements and increased pain thresholds, possibly due to hormonal changes and activation of endogenous opioids.

Methods: We compared the responses to a mechanical and an electrical stimulus in 30 pregnant women (pregnant group) scheduled for cesarean section and 30 healthy female volunteers (control group) matched for age. Pain was assessed by Visual Analogue Scale (VAS) on two different days after skin application of EMLA or placebo cream on the forearms. EMLA and placebo cream were randomly applied on the medial surface of both forearms for 30 min in a blind cross over manner and the subjects received a mechanical stimulus generated through a pressor palpator followed by an electrical stimulus generated through a nerve stimulator.

Results: Average VAS values from both trials did not differ between pregnant and control group exposed to the mechanical or electrical stimulus after EMLA application or after mechanical or electrical stimulus after placebo cream application.

Conclusions: Late pregnancy is not associated with increased sensitivity to local anesthetics (EMLA) applied to the skin, under our study conditions.

Key words: pregnancy, pain perception, mechanical stimulus, electrical stimulus, local anesthesia; EMLA.
Introduction

Decreased local anesthetic requirements during regional analgesia, increased sensitivity to local anesthetics and increased pain thresholds have all been reported during pregnancy. Mechanical factors such as increased lumbar lordosis and/or distension of the epidural veins, or hormonal alterations, such as increased progesterone and estrogen levels, have been implicated to explain the above changes.

The present study was designed to investigate in pregnant women of 38 weeks of gestation the response to a mechanical and an electrical stimulus after skin application of Eutectic Mixture of Local Anesthetics (EMLA). These responses were compared to the responses obtained from nonpregnant young women treated similarly.

Materials and Methods

Study population

After Institutional Review Board approval and patient written informed consent, 30 parturients ASA I-II with singleton pregnancy (24 primiparas and 6 multiparas) of completed 38 weeks of gestation scheduled for elective cesarean section, and 30 healthy female volunteers matched for age range, were enrolled in this prospective study. Exclusion criteria consisted of body weight more than 20% of the ideal body weight for volunteers and more than 20 Kg weight gain during pregnancy for parturients, complicated pregnancy, thyroid gland disease, central or peripheral nerve disease, diabetes mellitus, hypertension, analgesic consumption or illegal drug abuse, alcoholism and non-Greek speaking language.

Study protocol

The mechanical and electrical stimuli were demonstrated to all participants and the Visual Analogue Scale (VAS) was explained the day before. Tests were performed by the same investigator (A.K) on two consecutive days in both the parturients and the controls. All subjects were tested in the sitting position in a quiet room during the morning hours.

Day 1: An independent anesthesiologist filled syringes of 2 ml with EMLA, or placebo creams, and applied these on the medial surface of the forearm in the middle of the distance between the wrist and the elbow. Both creams were covered with Tegaderm™ tape. The forearm right versus left to receive EMLA cream was determined by tossing a coin, heads indicating EMLA application on the right and tails on the left forearm. Thirty minutes later the creams were removed and the responses to a mechanical and electrical stimulus were assessed by Visual Analogue Scale (VAS).

Day 2: Both parturients and control subjects were exposed to the same tests on the following day but in a reverse order regarding EMLA and placebo application on the right versus the left forearm.

Unless contraindicated, epidural analgesia was the technique of choice. Mechanical and Electrical Stimuli.

Mechanical stimulus was applied for 3 sec by a pressure palpator (Pressure Feeler 650 gr Sedatelec®; Chemin des Muriers, Irigny, France) exerting a standard force on its end of 650 gr. This was followed by an electrical stimulus consisted of a 2Hz, 0.25 msec square wave electrical impulse, generated by a peripheral nerve stimulator (Organon®).

The primary endpoint of our study was the VAS scores obtained in pregnant and nonpregnant women after applying a mechanical and an electrical stimulus on the skin exposed to EMLA and to placebo cream.

Statistical Analysis

Statistical analysis was conducted using the SPSS version 13.0 (SPSS Inc., Chigago IL). Patient characteristics between the two groups were compared with Student’s t-test and smoking habit was analyzed with X² test.

VAS scores obtained after EMLA application on the right and left forearm of the same subject were averaged. Similarly were treated VAS scores after placebo cream.

VAS scores obtained after mechanical and electrical stimuli following EMLA application as well as VAS scores obtained after mechanical stimulus following placebo cream application did not follow a normal distribution (Kolmogorov-Smirnov test) and were compared between the groups with Mann-Whitney test. VAS scores after electrical stimulus following placebo cream followed normal distribution.
PREGNANCY AT TERM DOES NOT ALTER THE RESPONSES TO A MECHANICAL AND AN ELECTRICAL STIMULUS AFTER SKIN EMLA APPLICATION

Animal studies have shown that pregnancy results in a progressive increase of pain thresholds\(^5\,^6\) possibly due to activation of endogenous opioid system\(^1^4\) and to steroid hormone elevation\(^1^0\). Nevertheless these results have not been reproduced in human studies in the same consistent manner. Staikou et al., in a similar setting as in our study, found no difference between pregnant and control subjects regarding pain responses to mechanical and electrical stimuli\(^1^1\). Also Dunbar at al., reported no differences in VAS scores after nociceptive thermal stimuli before or after pregnancy, although no control group was investigated\(^1^5\). Coolkasian et al., found that pregnant women are more willing to report pain than non pregnant subjects\(^1^6\). Saisto et al., reported reduced pain tolerance and increased VAS scores after cold pressor test in pregnant women fearing labor pain than pregnant women not fearing labor pain. All subjects reported increased VAS scores before than after delivery but no change in pain endurance\(^1^7\).

In contrast Cogan et al., reported increased pain thresholds, after a pressure stimulus, before delivery than after delivery and increased discomfort thresholds between pregnant and controlled subjects\(^1^8\).

Also electrical stimuli of 5, 250 and 2000 Hz have resulted in increased pain thresholds during pregnancy with greatest reduction observed at 5Hz stimulation. Nevertheless no control group was included in this study and the study population was small\(^1^9\). Carvalho et al., in a recent controlled study found increased heat pain tolerance in pregnant women a finding not reproduced by cold pressor stimulus\(^2^0\).

The controversial results in humans might be attributed to lack of control group in most studies, to different stimuli used to access the pain perception, to different time points of testing, but also to interindividual variability\(^2^1\).

Enhancement of local anesthetic effects has been also documented during pregnancy, and although the reason is not clear, hormonal and mechanical factors have been investigated. Datta et al, found decreased latency of conduction block of nerve fibers from pregnant rabbits to bupivacaine, suggesting either increased sensitivity or enhanced diffusion to receptor site due to increased progesterone levels during pregnancy\(^4\). Flanagan et al in two studies showed that chronic exposure of rabbit nerve fibers to progesterone

(Kolmogorov-Smirnov test) and were compared between the two groups with Students t-test.

**Results**

Patients’ characteristics in each group are shown in Table 1. Weight was significantly higher in the parturient women compared to the control group (\(p = 0.0005\)). Twenty one of the parturients received epidural anesthesia and 9 received general anesthesia.

<table>
<thead>
<tr>
<th></th>
<th>Pregnant (N = 30)</th>
<th>Controls (N = 30)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.6(3.7)</td>
<td>31.6(4.8)</td>
<td>0.338</td>
</tr>
<tr>
<td>Body weight(kg)*</td>
<td>77.6(10.4)</td>
<td>61.4(1.3)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.66(0.06)</td>
<td>1.66(0.07)</td>
<td>0.338</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12(40.0)</td>
<td>7(23.3)</td>
<td>0.165</td>
</tr>
<tr>
<td>No</td>
<td>18(60.0)</td>
<td>23(76.7)</td>
<td></td>
</tr>
</tbody>
</table>

The VAS values did not differ between the two groups after the mechanical or electrical stimulus regardless of treatment with EMLA or placebo cream (Table 2).

**Table 2**

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Pregnant</th>
<th>Controls</th>
<th>p</th>
<th>Z</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical</td>
<td>EMLA</td>
<td>20(18)</td>
<td>19(10.8)</td>
<td>0.58</td>
<td>-0.54</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>20(14.5)</td>
<td>19(11.8)</td>
<td>0.883</td>
<td>-0.14</td>
</tr>
<tr>
<td>Electrical</td>
<td>EMLA</td>
<td>26(22)</td>
<td>24(16.6)</td>
<td>0.853</td>
<td>-0.18</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>21.4(15)</td>
<td>17(10.1)</td>
<td>0.21</td>
<td>1.24</td>
</tr>
</tbody>
</table>

**Discussion**

The results of the present study failed to show increased sensitivity of, pregnant women to topical EMLA application compared to non pregnant women, as assessed by pain perception after mechanical or electrical stimuli.
alters local anesthetic sensitivity\textsuperscript{22,23}.

Long term exposure to progesterone might play the key role as Bader et al, could not find an effect of acute progesterone treatment in conduction blockade of isolated rabbit vagus nerve\textsuperscript{24}. Hirabayashi et al., found that pregnancy at second, third trimester and at term, enhances the spread of hyperbaric amethocaine compared to nonpregnant or to first trimester pregnant women, which again supports the role of progesterone rather than mechanical factors producing these changes\textsuperscript{3}. Progesterone alterations have also been proposed to explain the decrease halothane\textsuperscript{25}, enflurane\textsuperscript{26} thiopental requirements during pregnancy\textsuperscript{27} although the mechanism remains unknown.

Nevertheless, mechanical factors cannot be excluded to explain subarachnoid block alterations during pregnancy. James et al., in a non blinded study, have shown increased anesthetic requirements in preterm women (28-35 weeks of gestation) than at term women (38-42 weeks of gestation) presenting for cesarean section\textsuperscript{28}. They also found a strong correlation between fundal height taken from the symphysis pubis to the fundus and the block height achieved. Fassoulaki et al, found higher level of subarachnoid sensory block with hyperbaric lidocaine in pregnant compared to non pregnant women\textsuperscript{2}.

Our results are in contrast to the results of Butterworth et al., who found increased susceptibility of the median nerve to 5 ml of 1\% lidocaine HCL in pregnant women\textsuperscript{29}. We chose EMLA cream which penetrates the intact skin and successfully obliterates pain during pinprick\textsuperscript{30}, so the local anesthetics used in Butterworth and in our study are not comparable. Eogan et al., found prolonged median nerve latencies in pregnant compared to non pregnant subjects which might be the underlying reason of the results of Butterworth\textsuperscript{31}.

A limitation of our study is the short time of EMLA application (30 min), as it has been shown that increased time of application or increased time between removal of the EMLA and stimulus application results in more effective blockage of nociceptive receptors as assessed with laser stimulus\textsuperscript{32,33}.

In conclusion, the response to a mechanical and an electrical stimulus after EMLA or placebo cream application to the skin, did not differ between pregnant and non-pregnant women.
References


ROBOTIC LAPAROSCOPIC RADICAL CYSTECTOMY
INHALATIONAL VERSUS TOTAL INTRAVENOUS
ANESTHESIA: A PILOT STUDY

MOHAMED M. ATALLAH* AND MAHMoud M. othMAN**

Summary

Background: Robotic assistance may refine laparoscopic radical cystectomy. Steep Trendelenburg tilt (TT) and pneumoperitoneum (PP) are challenging anesthesia maneuvers. In view of those maneuvers, would inhalational anesthesia or total intravenous anesthesia (TIVA) be the more appropriate anesthetic management for this kind of surgery?. This issue is under consideration in this clinical trial.

Methods: 15 patients scheduled for robotic laparoscopic radical cystectomy (RLRC) were randomly allocated into two groups to be anesthetized by either isoflurane anesthesia (ISO n = 8) or ketamine-midazolam-fentanyl total intravenous anesthesia (TIVA n = 7). The hemo-respiratory dynamics, oxygenation and biochemical variables were monitored taking into consideration the system organ function as primary outcomes, and operative conditions and recovery profile as secondary outcomes.

Results: The PP and TT increased the mean arterial and airway pressures and decreased lung compliance, and were associated with respiratory acidemia, while changes in heart rate remained within normal range. The duration of PP was shorter in TIVA patients but mean arterial pressure was higher than ISO group. ISO was associated with increased plasma concentrations of prothrombin, fibrinogen and aspartate aminotransferase.

Conclusions: Though the number of patients is small in this study (n = 15), it nevertheless brings to light the advantages of TIVA during the robotic laparoscopic radical cystectomy (RLRC), by shortening the duration of PP without an increase in prothrombin and fibrinogen concentrations. A larger number of clinical trial are needed to further clarify this issue.

Keywords: anesthesia, inhalation, isoflurance; anesthesia, intravenous, ketamine, midazolam, fentanyl; surgery, radical cystectomy.
On the morning of surgery, patients were premedicated with 7.5 mg midazolam and 300 μg clonidine given orally two and one hour respectively, before transfer to the operative suite. These doses were reduced by 50% to patients ≥60 years old. Patients were allocated by computer generated random numbers to receive either isoflurane anesthesia (ISO n = 8) or ketamine-midazolam-fentanyl total intravenous anesthesia (TIVA n = 7).

Age-adjusted single dose upper lumbar extradural analgesia was performed in the sitting position in both groups before induction using bupivacaine 0.5% mixed with morphine. Arterial and central venous cannulation were secured.

The ISO group was induced with 1 μg/kg⁻¹ fentanyl, 0.1 mg/kg⁻¹ midazolam and sleeping dose of thiopentone and maintained by isoflurane at end-tidal concentrations adjusted to help minimizing changes in HR and arterial BP. The TIVA group was induced with fentanyl 1 μg/kg⁻¹, midazolam 100 μg/kg⁻¹ and ketamine 2 mg/kg⁻¹ and maintained by separate infusion of the three drugs (Table 1). Before creation of PP, ketamine dose was reduced by 25%, and midazolam and fentanyl doses were reduced by 50%. These were normalized following the creation of PP. Pipecuronium was used to facilitate tracheal intubation in both groups to maintain adequate surgical muscle relaxation and was replaced by vecuronium when repeated serum creatinine level was >1.5 mg/dL⁻¹. The lungs were ventilated with oxygen enriched air (FIO₂ = 0.35) and ventilation was manipulated to minimize excessive increases in end-tidal CO₂ concentrations.

After induction, the patients were placed in an extended lithotomy position with a 45° TT. Sufficient padding was applied around the shoulder and pressure points and the arms were tucked in.

Following RLRC, the resected bladder specimen was removed through a mini-subumbilical laparotomy incision. A neobladder was then fashioned from the terminal ileum. The ureters were re-implanted to the neobladder. The latter was relocated into the pelvis. The wound was then closed. Finally, the neobladder was then anastomised to the urethral stump via laparoscopic approach.
Results

This prospective randomized clinical trial was performed with 15 patients who underwent RLRC and open surgery neobladder creation. Patient demographic data and durations of operative interventions are displayed in Table 2.

The median durations of PP and RLRC were shorter during TIVA by 32% and 36% respectively.

HR changes did not display any significant difference between both groups (Fig. 1). PP and TT increased MBP in both groups, with more higher values in TIVA patients. Following PP deflation, MBP returned to within normal range in both groups (Fig. 1). Stepping up anesthetic doses prevented excessive increases in BP in five and two patients in ISO and TIVA respectively. Nitroglycerine infusion (0.5-10 μg/kg·min⁻¹) was needed in the rest of the patients. Two patients in TIVA needed additional sodium nitroprusside (0.5-2 μg/kg·min⁻¹).

Table 2
Patients data and durations of operative intervention
Values are median ± SD (range).

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane (n = 8)</th>
<th>TIVA (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic data:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>58 ± 7 (47-66)</td>
<td>56 ± 5 (50-63)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>71 ± 10 (54-80)</td>
<td>80 ± 14 (58-95)</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>167 ± 24 (105-181)</td>
<td>170 ± 4 (165-175)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>6/2</td>
<td>7/0</td>
</tr>
<tr>
<td>Duration of intervention (h)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trendelenburg tilt</td>
<td>4.4 ± 0.7 (2.8-5.2)</td>
<td>3.8 ± 0.5 (3.0-4.5)</td>
</tr>
<tr>
<td>Pneumoperitoneum</td>
<td>4.0 ± 0.8 (2.4-4.8)</td>
<td>2.7 ± 0.8 (1.9-4.0)*</td>
</tr>
<tr>
<td>Robotic cystectomy</td>
<td>3.6 ± 0.8 (2.1-4.5)</td>
<td>2.3 ± 0.8 (1.5-3.8)*</td>
</tr>
<tr>
<td>Open surgery</td>
<td>3.5 ± 1.0 (1.8-4.5)</td>
<td>4.0 ± 0.6 (3.0-4.5)</td>
</tr>
<tr>
<td>Total anesthetic duration</td>
<td>8.8 ± 0.8 (8.0-10.0)</td>
<td>8.0 ± 0.5 (7.3-8.8)*</td>
</tr>
</tbody>
</table>

* Significant intergroup difference (P < 0.05)

Preoperative condition: 3 hypertensives in TIVA group, 1 diabetes mellitus in TIVA group, 6 C-virus hepatitis, 4 in isoflurane group and 2 in TIVA group.

Monitoring consisted of continuous 5-lead ECG, pulse oximetry, capnography, invasive arterial pressure, central venous pressure, core body temperature and respiratory dynamics. Arterial blood samples were periodically withdrawn for gasometry, Hb conc, Het%, and biochemical variables (albumin, bilirubin, transaminases, creatinine, fibrinogen and prothrombin conc.). Plasma cortisol and growth hormone concentrations were respectively quantified by fluorescence polarization immunoassay (Axsym, USA) and enzyme-linked immuno-sorbant assay (DSL, USA).

The increases in HR and arterial pressure induced by the creation of pneumoperitoneum (PP) and steep Trendelenburg tilt (TT) were ameliorated by the stepping up anesthesia concentration and infusion of nitroglycerine and sodium nitroprusside. Warming was carried out throughout the procedure. Cautious initially restricted fluid replacement was achieved by warm crystalloids. Residual neuromuscular block was antagonized with neostigmine at the end of the operation. In the recovery room, patients were observed and their physiological signs assessed.

Statistical Analysis

Data were processed by SPSS program and presented as median and SD. For intergroup significance evaluation Mann-Whitney U-Wilcoxon rank sum test was used. For significance of differences from the basal values, Wilcoxon-matched pairs signed ranks test was used. P-value <0.05 was considered statistically significant.
Mean airway pressure was increased, and lung compliance was decreased following PP creation and TT. However, following deflation, TIVA patients showed higher lung compliance values (Fig. 1).

PP produced respiratory acidemia which gradually resolved postoperatively (Fig. 2). Plasma albumin decreased in all patients during the 7 days study period, while prothrombin and fibrinogen increased only following ISO (Fig. 3). Serum aspartate aminotransferase (AST) increased on the third postoperative day following ISO, but serum bilirubin and alanine aminotransferase were within normal values (Fig. 4). Serum sodium, potassium, and creatinine were within normal ranges during the study period.

Growth hormone and cortisol increased in all patients during operative intervention (Table 3). By the end of surgery, growth hormone returned to normal values in TIVA patients, but remained high following ISO. Cortisol levels remained high in both groups. Intraoperative blood loss was minimal in 13 patients. One patient in each group needed two units of blood.

Recovery was delayed for 60 min in one patient following ISO and for 45-150 min in 5 patients following TIVA. The latter needed pressure support ventilation. Surgical emphysema affecting the medial aspects of the thighs and lower abdomen was observed in 4 and 3 patients following ISO and TIVA respectively. This extended to the face in one patient in each group. Periorbital edema was observed. Patients did not complain of pain from the surgical incisions and postoperative analgesics were needed for patients with extended surgical emphysema. There was no incidence of pneumothorax, pneumomediastinum, pulmonary edema or any other system organ affection during the postoperative period.

**Discussion**

RLRC was performed with limited number of patients anesthetized by either ISO or TIVA. The creation of PP and TT increased mean arterial and airway pressures and decreased lung compliance, and was associated with respiratory acidemia, while changes in HR remained within normal range. The duration of PP was shorter in TIVA patients but MBP was higher than ISO group. ISO was associated with increased plasma concentrations of prothrombin, fibrinogen and AST. Recovery was more delayed following TIVA.

Peritoneal insufflation with carbon dioxide and modification in patient position with 45° TT were applied to provide adequate visual and operative conditions. PP induces widespread changes in cardiovascular system. Experimental data demonstrated a decrease in cardiac output and MBP. Elevated preload and afterload and decreased cardiac output and ejection fraction were reported in clinical studies. Head

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**Table 3**

<table>
<thead>
<tr>
<th></th>
<th>Growth hormone (mg/ml&lt;sup&gt;1&lt;/sup&gt;)</th>
<th>Cortisol (μg/ml&lt;sup&gt;-1&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ISO</td>
<td>TIVA</td>
</tr>
<tr>
<td>Basal</td>
<td>0.1 ± 0.3 (0.1-1.0)</td>
<td>0.4 ± 0.9 (0.1-2.6)</td>
</tr>
<tr>
<td>End of:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robotic cystectomy</td>
<td>8.0 ± 7.1* (0.8-21.0)</td>
<td>3.2 ± 4.5* (0.9-12.0)</td>
</tr>
<tr>
<td>Open surgery</td>
<td>1.2 ± 1.3* (0.4-3.6)</td>
<td>1.1 ± 1.0 (0.3-3.1)</td>
</tr>
<tr>
<td>Postoperative (2h)</td>
<td>0.5 ± 0.9 (0.1-2.2)</td>
<td>1.1 ± 1.7 (0.3-5.1)</td>
</tr>
</tbody>
</table>

* Significant difference (P<0.05) from basal value.
Fig. 1
Perioperative median values of mean blood pressure (MBP, mmHg), heart rate (HR, bpm), compliance (Comp., ml/cm H₂O), and mean airway pressure (Paw, cmH₂O) during isoflurane anesthesia (ISO) and TIVA.

Fig. 2
Perioperative median values of pH, arterial carbon dioxide tension (PaCO₂, mmHg), and serum bicarbonate (HCO₃, mmol/L) during isoflurane anesthesia (ISO) and TIVA.

Fig. 3
Postoperative median serum concentrations of prothrombin, Fibrinogen, and albumin after isoflurane anesthesia (ISO) and TIVA.

Fig. 4
Postoperative median serum concentrations of bilirubin, Aspartate aminotransferase (AST), and Alanine aminotransferase (ALT) after isoflurane anesthesia (ISO) and TIVA.
down position either increased these changes\textsuperscript{3,11} or had no more effect\textsuperscript{12}, but none of these clinical studies had adopted this steep TT.

Respiratory acidosis and decreased lung mechanics together with transient reduction of the pulmonary shunt were demonstrated after PP in clinical settings\textsuperscript{5,13}.

The cerebral blood flow velocity increased and the cerebral vascular resistance decreased, while maintaining the vasoreactivity unaffected\textsuperscript{14-16}.

During pneumoperitoneum, the blood flow to the abdominal organs is variably affected. Hollow viscous organs are less disturbed than solid organs\textsuperscript{10}. Experimental data demonstrated a decrease in total hepatic blood flow, mostly through a decrease in portal vein blood flow, with contradictory reports on hepatic artery buffer response\textsuperscript{9,10,17,18}. Cirrhotic liver showed a similar decrease in total hepatic blood flow\textsuperscript{19}. Clinical studies reported a decrease in hepatic blood flow and increase in hepatic enzymes, being more following cholecystectomy than after colectomy, suggesting impairment of hepatic function specially in elderly patients\textsuperscript{4,20}. PP and hypovolemia markedly alter renal blood flow\textsuperscript{21}. In our study, abdominal organ function was not affected apart from mild increase in AST following ISO.

Most experimental studies investigating the effects of PP on “organ function” have been conducted mostly on small animals without organ disease, while the majority of the clinical reports were young adults and mostly with healthy system organs. With RLRC, the denominator is different. Patients are likely to be elderly adult or older, sicker and with significant underlying disease demonstrating lower threshold for physiologic decompensation. Perioperative risk factors include preexisting system organ dysfunction, hypovolemia and possibly any other iatrogenic intervention. Risk-adjusted strategy should be adopted. Preexisting disease have to be optimally managed. Perioperative optimization of vital functions and minimization of postoperative pain avoid further deterioration of preexisting diseases. PP pressure and the degree of head down have to be the least compatible with good surgical conditions. Adequate anesthesia and prompt replacement of fluid and blood loss minimize the surgical stress response.

Inhalational anesthetics have a cardioprotective effect. This has been reported in vitro studies\textsuperscript{22,23}, and clinically in coronary surgery patients\textsuperscript{24}. In this pilot study, ISO anesthesia was followed by increased plasma concentrations of prothrombin, fibrinogen and AST suggesting incomplete stress and hepatic protection. The clinical advantages of TIVA during radical cystectomy has been recommended\textsuperscript{6, 7}. It provided better operating conditions and a more acceptable recovery profile. The absence of significant changes in plasma concentrations of prothrombin, fibrinogen and AST following TIVA suggests a satisfactory stress and hepatic protection.

Which of the two techniques is more favourable for RLRC is still speculative. The results of this limited-number clinical trial do not equate to that coming from reasonably powered study. Although the duration of PP was shorter in TIVA patients and the measured plasma concentrations of the coagulation factors were within normal range, yet a definite advantage for TIVA would be claimed following a clinical trial with adequate number of patients.

In conclusion, the study is limited in number and the patients were carefully chosen from cancer bladder population to be of appropriate age and body weight with minimal organ system dysfunction. While this study refers to an advantage of TIVA during RLRC, yet a large number clinical trial are needed to confirm these advantages.

Acknowledgment: We acknowledge the statistical analysis by Mrs Sahar A. Rahman, Statistician at the Urology & Nephrology Center.
References


THE EFFECT OF NITROGLYCERIN AS AN ADJUVANT TO LIDOCAINE IN INTRA VENOUS REGIONAL ANESTHESIA

RAHMAN ABBASIVASH*, EBRAHIM HASSANI*,
MIR MOUSSA AGHDASHI**,
AND MOHAMMAD SHIRVANI***

Implication Statement

The present study is the second to assess nitroglycerin as a new adjuvant for intravenous regional analgesia. Its addition to lidocaine, nitroglycerin appears to shorten the sensory and motor block onset time in closed reduction of forearm fractures and provides acceptable analgesia for 24 hours after operation.

Abstract

Purpose: The disadvantages of intravenous regional anesthesia (IVRA) include slow onset, poor muscle relaxation, tourniquet pain, and rapid onset of pain after tourniquet deflation. In this randomized, double-blind study, we evaluated the effect of nitroglycerin (NTG) in quality improvement when added to lidocaine in IVRA.

Methods: Forty-six patients (20-50 yrs), were randomly allocated in two equal groups. Under identical condition, the control group received a total dose of 3mg/kg of lidocaine 1% diluted with saline, and the study group received an additional 200 µg NTG. Vital signs and tourniquet pain, based on visual analog scale (VAS) score were measured and recorded before and 5, 10, 15, 20, and 30 min after anesthetic solution administration. The onset times of sensory and motor block were measured and recorded in all patients. After the tourniquet deflation, at 30 min and 2, 4, 6, 12 and 24h, VAS score, time to first analgesic requirement, total analgesic consumption in the first 24 h after operation, and side effects were noted.

Results: The sensory and motor block onset time were shortened in study group (2.61 vs. 5.09 and 4.22 vs. 7.04 min, respectively) (p <0.05). The recovery time of sensory and motor block and onset of tourniquet pain were also prolonged (7.26 vs. 3.43, 9.70 vs. 3.74 and 25 vs. 16.65min., respectively) (p <0.05). Analgesia time after tourniquet deflation was prolonged and tourniquet pain intensity was lowered in study group (p <0.05). Intraoperative fentanyl and meperedine requirement during first postoperative day and pain intensity at 4, 6, 12 and 24 h postoperatively were lower in the study group (p <0.05). There were no significant side effects.

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Conclusion: The NTG adding to lidocaine in intravenous regional anesthesia shortens onset times of sensory and motor block and decreases the tourniquet and postoperative pain, without any side effect.

Keywords: Intravenous regional anesthesia, Nitroglycerin, Lidocaine.

Introduction

The technique of intravenous regional anesthesia (IVRA) was first introduced by German surgeon August Bier in 1908. It consists of injecting local anesthetic solutions into the venous system of an upper or lower extremity that has been exsanguinated by compression or gravity and that has been isolated by means of a tourniquet from central circulation. The resultant anesthesia is produced by direct diffusion of local anesthetic from the vessels into the nearby nerves. This technique is easy, cost-effective and its efficacy in emergency and out patients setting has been proved.

Complications of IVRA are a few and mostly limited to systemic toxicity from local anesthetic that is related to problems with the technique. The risk mainly comes from an inadequate tourniquet application or equipment failure at the beginning of the procedure.

Its slow onset, tourniquet pain during the procedure, limited operating time (<1 h), possible nerve damage and insufficient postoperative analgesia are among a few disadvantages of this technique.

Algesic effects of transdermal Nitro-glycerin (NTG) have been reported in several studies and recently Nitro-glycerin has been used as an adjuvant in IVRA and its effects on tourniquet pain and intraoperative and postoperative analgesia were promising. We decided to conduct a similar study in patients scheduled for close reduction of forearm fracture and evaluate the duration of analgesic effect for 24 hours postoperatively.

The essence of science implies that study findings must be replicated in a different study before firm conclusion can be drawn. Thus, the present study is the second to assess the efficacy and safety of using Nitroglycerin in IVRA as an adjuvant.

Methods and Materials

Informed patient consent and ethical and research committees approval were obtained. In a prospective, randomized double-blinded study, forty six ASA I – II patients age 20-50 years scheduled for closed reduction of forearm fractures were included in two equal groups. The sample size was calculated based on a type I error of \( \alpha = 0.05 \), \( p_1/p_2 \) equal to 2.75 and \( p_2 = 0.15 \). Enrollment of 23 patients in each group was required. Patients with sickle cell anemia, Reynaud disease, and history of drug allergy, antihypertensive drug and NTG consumption were excluded.

In operating room, patient’s vital signs (arterial blood pressure, heart rate, SpO2, ECG) were monitored by Datascope passport 2. Premedication for both groups consisted of IV midazolam 0.15 mg/kg and 1 µg/kg fentanyl. An intravenous cannula (gauge 20) was placed in a distal vein of the hand in preparation for IVRA. The arm was elevated for six minutes then a rubber Esmarch bandage was wound around the arm spirally to exsanguinate the arm. A double pneumatic tourniquet was placed around the upper arm and the proximal cuff was inflated based on LOP (Limb Occlusion Pressure) with safety margin of about 50 mmHg.

Absence of radial pulse and loss of pulse oximetry tracing was considered as an adequate isolated circulation of the arm. In study group IVRA was administered with 200 µ NTG, (Trinitrosan 5 mg/1ml, Merck KGaA, Darmstadt, Germany) plus 3 mg/kg lidocaine (LIGNODIC®, Lidocaine 1%, Caspian Tamin Pharmaceutical Co., Rasht-Iran)) diluted with saline to a total volume of 40 ml. In control group 3 mg/kg lidocaine diluted with saline to the same volume was injected over 60 seconds by an anesthesiologist blinded as to group assignments.

To assess the sensory block, pinprick with a 22 gauge short-beveled needle was performed in the dermatomal sensory distribution of median, ulnar and radial nerves. Complete motor block was noted when no voluntary movement in patients wrist and fingers was possible. Sensory and motor block onset times were recorded.

After the onset of sensory and motor block, distal cuff of tourniquet was inflated to 250 mmHg and the
proximal cuff was deflated. BP, HR, SpO₂ and Visual Analog Scale (VAS) scores (0 = no pain and 10 worst pain) was monitored before and at 5, 10, 15, 20, 25, 30 min after tourniquet deflation. When pain was >3 on the VAS scale, patients were given intravenous fentanyl 1 μg/kg. Times and total dose of intraoperative fentanyl were recorded. Tourniquet was not deflated sooner than 30 min. At the end of surgery through cyclic deflation technique, it was deflated. Sensory and motor block recovery time was noted. Vital signs and pain intensity (VAS) were monitored 30 min and 2, 4, 6, 12 and 24 h postoperatively. Patients with VAS >3 received 30 mg IM meperidine and the total dose of meperidine in first 24 h after surgery was recorded. Quantitative and qualitative data were analyzed by Independent sample student’s t-test and Fischer’s exact χ² test respectively.

Results

The demographic data in both groups were similar and no significant difference was noted (p >0.05, Table 1).

![Table 1: Patient Characteristic](image)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study G</th>
<th>Control G</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) ± SD</td>
<td>33.83 (±10.66)</td>
<td>34.57 (±12.83)</td>
<td>0.833*</td>
</tr>
<tr>
<td>Sex (F/M) ± SD</td>
<td>4F/19M</td>
<td>5F/18M</td>
<td>0.713 **</td>
</tr>
<tr>
<td>Weight (Kg) ± SD</td>
<td>72.30 (±9.57)</td>
<td>79.35 (±18.04)</td>
<td>0.105*</td>
</tr>
<tr>
<td>ASA II/II</td>
<td>18 I / 5 II</td>
<td>16 I / 7 II</td>
<td>0.507 **</td>
</tr>
</tbody>
</table>

* Independent samples Student’s t-test, ** Fischer’s exact χ² test.

The same surgeon performed surgical procedure (closed reduction of forearm fracture). There was no statistically significant difference in vital signs (MAP, HR) in both groups intraoperatively and after tourniquet deflation (p >0.05).

The onset time of sensory and motor block in the study group were shorter (2.65 vs. 5.09 and 4.22 vs. 7.04 min, respectively, p <0.05) and the recovery time for sensory and motor block were slower (7.26 vs. 3.43 and 9.07 vs. 3.74 min, respectively) (p <0.05). The study group took longer time to complain of tourniquet pain and analgesia lasted longer in study group (25.00 vs. 16.65 and 130.32 vs. 38.21 min, respectively) (p <0.05, Table 2).

Although there was no significant difference in pain intensity 15 minutes from the start of operation, yet during the next 15 minutes pain intensity and tourniquet pain, determined by VAS was lower in study group compared to control group (p <0.05).

The average dose of intraoperative IV fentanyl in study group was less than control one (18.26 vs. 78.04 μg, respectively, p <0.05) (Table 3). The average pain intensity in 4, 6, 12 and 24 hour postoperation in study group was less compared to control group (p <0.05) but maximum pain intensity in first day postoperatively as determined by VAS, was similar in both groups (p <0.05). In study group intramuscular meperidine injection (35.42 mg) was also less compared to control group (55.65 mg) (p <0.05) (Table 3).

No adverse effect was noted in both groups.

Discussion

The results of this study suggest that the addition of NTG to lidocaine for IVRA in closed reduction of forearm fractures, without any notable side effects, improved the onset and duration of sensory and motor block and anesthesia quality, decreased tourniquet pain in terms of both onset and duration and intraoperative and postoperative analgesic consumption.

Several studies have reviewed the use of adjuncts (i.e., opioids, non steroid anti-inflammatory drugs10, α₂ agonists11,12 neostigmine13, muscle relaxants, magnesium14 and sodium bicarbonate) to intravenous regional anesthesia. Selda Sen et al performed the first study on adding NTG to IVRA for hand and forearm surgery such as tendon release, trigger point and carpal

![Table 2](image)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study G</th>
<th>Control G</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory block onset time (min)</td>
<td>2.65 (± 0.99)</td>
<td>5.09 (± 1.86)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sensory block recovery time (min)</td>
<td>4.22 (± 0.99)</td>
<td>7.04 (± 1.87)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Motor block onset time (min)</td>
<td>7.26 (± 1.42)</td>
<td>3.43 (± 0.99)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Motor block recovery time (min)</td>
<td>9.07 (± 1.14)</td>
<td>3.74 (± 0.91)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Analgesia duration after tourniquet deflation (min)</td>
<td>130.52 (± 37.61)</td>
<td>38.22 (± 21.65)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean ± SD, p-values were <0.0001
effects and analgesia by blocking hyperalgesia and the neurogenic component of inflammatory edema through NO production.

Direct stimulation of peripheral fibers, similar to locally applied acetylcholine is another possible mechanism for analgesic effect of NTG. The above mentioned mechanisms or combination of them, might contribute to the analgesic effects of NTG added to lidocaine in IVRA.

NTG as an adjuvant in IVRA, nearly halves the onset of sensory and motor block, which has beneficial effects in patients managed by IVRA.

NTG increases the onset time of tourniquet pain and reduces its intensity. It seems that although high doses of NTG can cause hypotension and headache but no adverse effect was noted with small doses added to lidocaine.

Conclusion

The results of this study suggest that with addition of NTG to lidocaine in IVRA improves the quality of the block, decreases tourniquet pain and opioid consumption in first postoperative day. Further study might be undertaken to evaluate the local anesthetic sparing effect of NTG in IVRA.
EFFECT OF NITROGLYCERIN AS AN ADJUVANT TO LIDOCAINE IN INTRAVENOUS REGIONAL ANESTHESIA

References

EVALUATION OF THE TOURNIQUET LEAK DURING FOREARM INTRAVENOUS REGIONAL ANESTHESIA

- Manual vs Automatic Pump Injection -

ROSHDI ROSHDI AL-METWALLI*

Summary

Background: The present study was conducted to compare the effect of pump injection versus manual injection on the venous pressure, during forearm intravenous regional anesthesia (IVRA) and the incidence and the magnitude of lidocaine leak.

Methods: A crossover randomized study of IVRA with a forearm tourniquet was conducted on 14 male healthy volunteers. This study was performed, once using manual injection of local anesthetic and once using automatic pump injection, on two separate sessions. In both techniques, 0.3 ml/kg lidocaine 0.5% was injected over 90 seconds. The occlusion pressure, continuous venous pressure and the serum lidocaine two minutes at end of injection, were recorded.

Results: The mean occlusion pressure 161.6 (17.2) mmHg was always higher than the mean initial arm systolic blood pressure 131.7 mmHg. The maximum venous pressure was significantly higher in the manual technique 176.7 (15.4) mmHg than in the pump technique 161.3 (12.3) mmHg (p = 0.04). The incidence of lidocaine leak was significantly lower (35.71%) in the pump technique compared to (78.5%) in the manual technique (p = 0.02). Moreover; the mean lidocaine plasma concentrations was significantly higher [0.86 (0.5) µg.ml⁻¹] in the manual technique compared to [0.32 (0.4) µg.ml⁻¹] the pump technique (p = 0.04).

Conclusion: The use of pump injection for forearm IVRA could significantly decrease the maximum venous pressure, and decrease the incidence and the magnitude of lidocaine leak past the tourniquet.

Keywords: Anesthetic technique: regional intravenous. Drug: lidocaine. Measurements: Venous pressure, Lidocaine plasma conc.

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Introduction

Intravenous regional anesthesia (IVRA) is a safe and effective technique for providing anesthesia as well as a bloodless field during hand surgery, with published success rates ranging from 94% to 98%\(^1\text{,}^2\). IVRA is easy to perform and the only necessary technical skill is inserting an intravenous (IV) cannula.

Traditionally, an upper arm tourniquet has been used for these procedures. However, the recommended doses of local anesthetics for upper arm IVRA do have the potential risk of systemic toxicity\(^3\text{,}^4\).

Forearm IVRA, however, allows the dose of local anesthetic to be decreased by up to 50% without affecting the quality of analgesia\(^5\text{,}^6\). In addition, the forearm tourniquet can be tolerated longer and was consistently rated as less painful when compared with the upper arm tourniquet\(^7\). However, this technique was unpopular in the past because it was thought that “compression forces of an inflated forearm tourniquet cannot obliterate the anterior and posterior interosseous arteries seated in the deep ‘valley’ between the prominent radius and ulna”\(^8\). It was therefore assumed that tourniquet leakage was inevitable, thus increasing the possibility of local anesthetic toxicity and block failure. A quantitative study showed that forearm IVRA results in tourniquet leakage comparable with upper arm IVRA\(^9\).

During intravenous regional anesthesia, leakage of local anesthetic agent past the tourniquet into the systemic circulation could occur if the tourniquet pressure was inadequate to maintain occlusion of the underlying vessels in the face of the venous pressures generated by the injection\(^10\). Previous studies had measured venous pressure during actual or simulated upper arm IVRA, at different injection rates and volumes. To my knowledge, limited data of using automatic pump injection for forearm IVRA are available.

The main objective of the present trial is to study venous pressure during lidocaine forearm IVRA, using manual versus automatic pump injection, and evaluate its effect on the possible leak past the tourniquet.

Methods and Materials

Following the Institutional Ethics Committee approval and volunteer informed written consent, a prospective randomized study of IVRA with a forearm tourniquet was conducted on 14 male healthy volunteers, each volunteer acting as his own control. This study was performed, once using manual injection of local anesthetic and once using automatic pump injection, on two separate sessions. The sequence of the technique of IVRA (manual or pump technique) for each session, was allocated randomly and separated by at least one week.

For each session, immediately before the start of the procedure, arterial blood pressure was measured in the contra lateral arm with a standard adult cuff using a mercury sphygmomanometer. An 8 cm wide pneumatic tourniquet was placed over padding on the forearm 1 cm below the medial epicondyle of the humerus. An automatic pneumatic tourniquet machine (Zimmer A.T.S. 2000) was used for inflating the pneumatic tourniquet. The gauge on the machine was calibrated against a mercury column before each operating session.

“Occlusion pressure”, the tourniquet pressure required to occlude the radial blood flow was measured. This was determined by slowly lowering the tourniquet pressure from well above the systolic value and recording the tourniquet pressure at which the radial pulse first became palpable. Having found the occlusion pressures, the pneumatic tourniquet was removed and placed in a similar manner over the forearm to be operated on. A 20-gauge Teflon catheter was inserted in a dorsal vein of the hand and used for injection of local anesthetic. A similar cannula was inserted in a vein just distal to the tourniquet for venous pressure recording during the injection. The limb distal to the pneumatic tourniquet was exsanguinated by an Esmarch’s bandage, starting from the finger tips. The tourniquet was then inflated to a pressure equal to the occlusion pressure plus 50 mmHg (inflation pressure), and the Esmarch’s bandage was removed.

The calculated amount of 0.5 per cent preservative-free lidocaine solution (0.3 mL.kg\(^{-1}\) body weight) was injected over 90 second in all volunteers, by either the same anesthesiologist (manual technique) or by using automated infusion pump [Baxter Flogard. FAAM.3047K] (pump technique), through the intravenous cannula on the dorsum of the hand. Venous
pressure distal to the tourniquet was recorded every 10 seconds during injection by another anesthesiologist using pressure transducer connected to the proximal venous catheter.

In all patients two venous blood samples were taken for estimation of lidocaine concentration from an indwelling intravenous catheter placed in the contra lateral upper limb, before and two minute after lidocaine injection. The tourniquet was deflated 15 minutes after injection.

**Statistics**

The sample size was determined assuming a paired design in which forearm IVRA using different mode of injection would be applied to each volunteer on two separate occasions. To have an 80% probability of detecting 17% difference (from a pilot study) of maximum intravenous pressure, between the two techniques (\( \beta = 0.2 \)), and testing at the 0.05 level (\( \alpha = 0.05 \)), the sample size was found to be 14 patients. Data was analyzed using a paired \( t \)-test to compare venous pressure and lidocaine serum level. Fisher’s exact test was used to compare the incidence of leak. Statistical significance was assumed to be achieved at \( P < 0.05 \).

**Results**

The mean age of the volunteers was 33.7 (7.7) yr, mean height was 172.3 (7.2) cm, mean weight was 74.7 (5.1) kg and the mean forearm circumference was 25.9 (3.2) cm.

The occlusion pressure 161.6 (17.2) mmHg was always higher than the initial arm systolic blood pressure 131.7 (11) mmHg and the difference between them which ranged from 5 to 50 mmHg (29 ± 12.6) did not show any correlation with either the initial systolic blood pressure measured over the upper arm, (\( R^2 = 0.008 \)), or the circumference of the forearm at a point 1 cm distal to the medial epicondyle of the humerus (\( R^2 = 0.03 \)).

There was significant difference in the incidence of lidocaine leak past the pneumatic cuff into the systemic circulation prior to tourniquet release, between the manual technique 11/14 (78.5%) and the pump technique 5/14 (35.71%) \( p = 0.02 \). The lidocaine plasma concentrations was 0.86 (0.5) \( \mu g.ml^{-1} \) in the manual technique and 0.32 (0.4) \( \mu g.ml^{-1} \) in the pump technique with significant difference between both techniques (\( P < 0.04 \)).

Venous pressure before exsanguinations, before and during injection is presented in Fig. 1. There was a significant difference between the maximum venous pressure in the manual technique 176.7 (15.4) mmHg and in the pump technique 161.3 (12.3) mmHg (\( p = 0.02 \)).

There was significant correlation between the maximum venous pressure and the lidocaine plasma levels in both manual (Fig. 2) and pump techniques (Fig. 3) (\( R^2 = 0.82 \) and 0.68 respectively).

**Discussion**

The present crossover randomized study, showed a significant higher value of venous pressure during forearm IVRA when using manual injection than when using pump injection, with significant lower incidence and magnitude of the leak (lidocaine plasma level) in the pump group compared to the manual group.

One important factor affecting the success of IVRA is the tourniquet pressure. The present study used 8 cm wide pneumatic cuff, which is much narrower than the standard adult sphygnomanometer cuff used for measuring blood pressure. As the narrow cuff is less able to transmit tourniquet pressure to blood vessels lying deep inside the limb\(^{11,12}\), this could explain why the occlusive pressure was always higher than systolic blood pressure. Similarly this could explain why the difference between them was smaller in the present study 29.6 (12.6) mmHg using 8 cm wide cuff than Chan, et al study 67 (25) mmHg using 5 cm wide cuff\(^5\).

In the present study, the highest venous pressure was observed at the end of injection in both techniques, with significant higher value in the manual injection technique. This could be expected, as the use of infusion pump for injection could induce a steady rise of venous pressure given a chance for the veins to distend over the time with a final lower pressure at the end of injection.

To my knowledge none of the previous studies had evaluated the effect of using pump injection versus
Fig. 1
Evaluation of venous pressure for the manual (•) and pump (○) techniques during the 90 sec. of injection.

Fig. 2
Correlation between the maximum venous pressure achieved at the end of injection and the lidocaine plasma level in the Manual technique.

Fig. 3
Correlation between the maximum venous pressure achieved at the end of injection and the lidocaine plasma level in the pump technique.
manual injection on the venous pressure during forearm IVRA. However, El-Hassan et al.\textsuperscript{12} had compared the effect of different rates of infusion on the rate of rise of venous pressure on one volunteer during simulated Bier’s block. They reported that the slower the rate of injection the lower was the venous pressure.

It has been suggested that, the occurrence of convulsions during the performance of intravenous regional analgesia with the tourniquet \textit{in situ} may be partly explained by the generation of exceptionally high pressures in the venous system of the arm. The pressures generated were greater than or equal to the occluding pressure of the tourniquet. This in turn may lead to flow of injectate under the tourniquet and into the systemic circulation\textsuperscript{14-16}.

In the present study, although non of the volunteer in both techniques had a maximum venous pressure that exceeded the inflation pressure, leak of lidocaine had occurred in 11 out of 14 cases (78.5\%) in the manual technique, and 5 out of 14 cases (35.7\%) in the pump technique with a magnitude of 0.86 (0.5) µg.ml\textsuperscript{-1} and 0.32 (0.4) µg.ml\textsuperscript{-1} respectively. This in agreement with Kalso et al.\textsuperscript{13}, and Chan et al.\textsuperscript{5}, who reported a lidocaine leakage rate of 55\% and 67\% respectively.

More interestingly, the present study reported a linear correlation between the magnitude of the leak and the maximum venous pressure in both techniques. The possible explanation is that, decrease in the pressure gradient between the inflation pressure and the venous pressure could exacerbate the unavoidable leak through the interosseous vessels which are assumed to be protected from the tourniquet pressure.

Limitations of this study consist of, First; this trial would be strengthened if it used different rates of injection as well as different levels of inflation pressure, but this necessitated multiple sessions which was refused by the volunteers. However; this could be an idea for further study. Second; the present study did not test the clinical efficacy of the performed block, this is because the clinical efficacy of forearm IVRA had been proven by many of previous studies\textsuperscript{5,17,19}, as well as for ethical reason as this study was done on volunteers.

The present study concluded that the use of pump injection for forearm IVRA could significantly decrease the maximum venous pressure, and reduce the incidence and the magnitude of lidocaine leak past the tourniquet. This possibly will increase the duration of the block and further decrease the incidence of potential systemic toxicity.

**Acknowledgements**

I wish to thank all members of the Department of Anaesthesia in King Fahad Hospital, Al-Kobar, Saudi Arabia with special thanks to Dr. S. Abdulfatah, Dr. M. Al-Tahhan, Dr. H. Mowafi and Mr. S. Abdulrahman, for their help and support.
References


TIME TO EXTUBATION IN INFANTS UNDERGOING PYLOROMYOTOMY

- Isoflurane Inhalation vs Remifentanil Infusion -
SONIA BEN KHALIFA, SAMI BLIDI, MEHDI TRIFA,
ALIA SKHIRI, MEHDI DRIRA, TAREK REGAYA
AND AMJED FEKIH HASSEN

Abstract

Background: Infantile hypertrophic pyloric stenosis (IHPS) associated with metabolic alkalosis, could induce late anesthesia recovery, especially when opioids are used. The aim of this study was to compare the time of extubation and the quality of perioperative analgesia in infants scheduled for pyloromyotomy, receiving either isoflurane inhalation or remifentanil infusion.

Methods: Thirty full-term infants scheduled for pyloromyotomy were prospectively studied. A standardized anesthetic induction was performed. For maintenance of anesthesia, infants were randomly allocated to receive either isoflurane 0.75% of inspired concentration (GI n = 15), or remifentanil as a continuous infusion of 0.4 μg.kg⁻¹.min⁻¹ (GR n = 15). At the beginning of skin closure, the anesthetic was discontinued and 15 mg.kg⁻¹ of paracetamol administered. Non parametric tests were used in statistical analysis.

Results: The time to extubation was similar in both groups. The intraoperative heart rate was significantly lower in the GR group.

Conclusion: Remifentanil provided better intraoperative analgesia than isoflurane in infants undergoing pyloromyotomy without increasing time to extubation.
**Introduction**

Infantile hypertrophic pyloric stenosis (IHPS) is one of the most common infant gastrointestinal disorders requiring surgery. Pyloric outlet obstruction causes projectile vomiting thus inducing electrolyte and metabolic disturbances. The classic abnormality is a hypochloremic metabolic alkalosis that could induce late anesthesia recovery, especially when opioids are used\(^a\). Therefore, inhalational agents are usually used as maintenance anesthetics.

The aim of the present study was to compare time to extubation and quality of perioperative analgesia with the use of remifentanil infusion and compare it to that of isoflurane inhalation, in infants scheduled for pyloromyotomy.

**Methods and Materials**

Following the Ethics Committee’s approval and written parent’s informed consent, thirty ASA I or II full term infants (gestational age ≥37 weeks) admitted for IHPS, were prospectively included in a randomised single-blind study. They underwent pyloromyotomy after normalization of their metabolic and electrolyte imbalance (serum bicarbonate ≤30 mmol.L\(^{-1}\), serum sodium ≥130 mmol.L\(^{-1}\)). Infants who presented difficult intubation were excluded from the study.

Infants were not premedicated. Induction was performed with propofol 5 mg.kg\(^{-1}\) and succinylcholine 2 mg.kg\(^{-1}\). For maintenance, infants were allocated, using a random-number table, to receive nitrous oxide and oxygen (50%50%), with either isoflurane at 0.75% inspired concentration (GI n = 15), or remifentanil as a continuous infusion at 0.4 µg.kg\(^{-1}.mn^{-1}\) (GR n = 15).

If signs of light anesthesia appeared (movement, increases in systolic arterial blood pressure (SABP) and/or in heart rate (HR) 20% above basal values), the inspired concentration of isoflurane and the infusion rate of remifentanil were increased by respective increments of 0.25% (GI) and 0.05 µg.kg\(^{-1}.mn^{-1}\) (GR) until a maximum infusion rate of 2 µg.kg\(^{-1}.mn^{-1}\) (GR) was reached. In infants who developed hypotension (decreases in SABP 20% of basal value), the inspired concentration of isoflurane and the infusion rate of remifentanil were respectively decreased by 0.25% (GI) and 0.05 µg.kg\(^{-1}.mn^{-1}\) (GR). Bradycardia, defined as a decrease of the HR 30% compared to the previous value, was treated with atropine 20 µg.kg\(^{-1}\).

At the beginning of skin closure, the anesthetic maintenance was discontinued and intravenous paracetamol 15 mg.kg\(^{-1}\) was administered. Extubation was performed when infant was awake, had regained his airway reflexes and was adequately warmed.

In the PACU, the BP, HR and PSO\(_{2}\) were monitored. The postoperative pain was assessed by Amiel-Tison score, which is a behavioral approach using facial expressions, body movements, intensity and quality of crying as indices of response to nociceptive stimuli\(^b\). If the score was higher than 7, nalbuphine 0.2 mg.kg \(\mu g^{-1}\) was administered by i.v. route.

The following data were collected: demographics, time to extubation, duration of surgery, intraoperative HR and SABP at induction, after intubation, at the skin incision, and then at five-minute intervals until the end of surgery. Postoperatively, the Amiel-Tison score was recorded every 20 min. after extubation for 2 hours. Occurrence of intraoperative incidents (movement at incision, bradycardia) were noted.

Data were analysed using package SPSS 13.0. Statistical analysis involved Chi-square and Mann-Whitney tests. P values \(\leq 0.05\) were considered statistically significant.

**Results**

No statistical difference was noted between the two groups with regard to demographics, time to extubation, duration of surgery, intraoperative HR and SABP at induction, after intubation, at the skin incision, and then at five-minute intervals until the end of surgery. Postoperatively, the Amiel-Tison score was recorded every 20 min. after extubation for 2 hours. Occurrence of intraoperative incidents (movement at incision, bradycardia) were noted.

The following data were collected: demographics, time to extubation, duration of surgery, intraoperative HR and SABP at induction, after intubation, at the skin incision, and then at five-minute intervals until the end of surgery. Postoperatively, the Amiel-Tison score was recorded every 20 min. after extubation for 2 hours. Occurrence of intraoperative incidents (movement at incision, bradycardia) were noted.

Data were analysed using package SPSS 13.0. Statistical analysis involved Chi-square and Mann-Whitney tests. P values \(\leq 0.05\) were considered statistically significant.

**Table 1**

| Patient characteristics and intraoperative data among infants anesthetized for pyloromyotomy |
|---------------------------------------------|-----------------|-----------------|-----------------|
| Age (days)                                  | GI 43 ± 12      | GR 37 ± 14      | 0.12 |
| Weight (Kg)                                 | 3.85 ± 1        | 3.51 ± 0.5      | 0.13 |
| Sex-ratio                                   | 5               | 5               | 1               |
| Duration of surgery (min.)                  | 33 ± 9          | 31 ± 9          | 0.70 |
| Basic HR (beats per minute)                 | 148 ± 18        | 137 ± 19        | 0.06 |
| Basic SABP (mmHg)                           | 88 ± 12         | 84 ± 15         | 0.39 |

Data are mean ± SD except for sex-ratio of patients. No significant difference (p >0.05) was found between the two groups.
On admission, biochemical findings showed metabolic alkalosis (serum bicarbonate ≥30 mmol.L⁻¹ in 7 cases), hypokalemia (serum potassium ≤3.7, in 3 patients) and hyperkalemia (serum potassium ≥4.8 mmol.L⁻¹ in 3 other infants). After preoperative correction, serum bicarbonate and natremia were similar in the two groups (Table 2).

| Table 2: Preoperative biochemical findings among infants scheduled for pyloromyotomy |
|-------------------------------------------|-----------|-----------|
| Serum bicarbonate (mmol.L⁻¹) | GI 24 ± 2 | GR 24 ± 5 | 0.62 |
| Natremia (mmol.L⁻¹) | GI 135 ± 3 | GR 134 ± 3 | 0.34 |
| Data are mean ± SD. No significant difference (p >0.05) was found between the two groups |

Time to extubation was similar between the two groups: 17 ± 10 min (GI) and 20 ± 11 (GR), p = 0.42. The intraoperative HR was lower in GR compared to GI group:

<table>
<thead>
<tr>
<th>GR</th>
<th>GI</th>
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<tbody>
<tr>
<td>At skin incision 118</td>
<td>135 p = 0.01</td>
</tr>
<tr>
<td>5 min. 119</td>
<td>132 p = 0.022</td>
</tr>
<tr>
<td>10 min. 122</td>
<td>133 p = 0.049</td>
</tr>
</tbody>
</table>

Intraoperative tachycardia requiring increases of the inspired concentration of isoflurane occurred in one patient of GI. No statistical difference could be found between the groups regarding intraoperative SABP.

There was no significant difference between the groups with regard to postoperative Amiel-Tison score, HR and SABP.

At skin incision, movement was recorded in 3 infants in each group. Three patients in GT group had developed episodes of bradycardia, but with favourable progress.

**Discussion**

In view of its metabolic disorders, there is no ideal anesthetic technique for the care of IHPS: the use only of inhalational agents for the maintenance of anesthesia neglects intraoperative analgesia, while the administration of opioids could induce late anesthesia recovery due to persistent cerebrospinal fluid alkalosis³.

The use of remifentanil, a short-acting opioid, provides analgesia during pylorotomy without increasing time to extubation, meanwhile, narcosis is ensured by propofol and N₂/O₂ mixture. The open-label study comparing halothane to remifentanil in infants who underwent pylorotomy, inspired our trial⁴.

In our study, we chose isoflurane instead of halothane. The time to tracheal extubation as comparable in both groups: 16.8 ± 10.2 in GI group versus 19.6 ± 10.6 in GR group (p = 0.47). A similar result was found in Davis⁵ study (7.7 ± 3.2 versus 7.4 ± 6.3). A retrospective cohort study showed a shorter time to discharge from the OR when remifentanil was used as maintenance anesthetic with propofol (12.5 ± 10.6 min), compared to isoflurane (14.2 ± 7.8), sevoflurane (18.5 ± 11.7) and halothane (24.8 ± 11.1) (p<0.01)⁶.

Intraoperative analgesia was assessed by SABP and HR variation during surgery and movement at surgical incision. Intraoperative HR was significantly lower in GR group when compared to GI group at skin incision, and after 5 and 10 minutes, showing a better analgesia for the remifentanil-anesthetized infants (Fig. 1). Davis et al did not find differences between the two groups regarding intraoperative hemodynamic parameters⁴. In our study, movement at skin incision was observed in 3 infants of each group and required deepening of anesthesia.

**Fig. 1**

*Intraoperative heart rate (HR) among infants scheduled for pyloromyotomy: comparison between remifentanil (GR) and isoflurane (GI). HR was lower in GR compared to GI at skin incision (p = 0.01), 5 (p = 0.022) and 10 minutes after (p = 0.049).*
Postoperative pain, as assessed by the Amiel-Tison score, was higher in GR, but without any significant difference. No infant of the two groups required supplementary analgesic during the two postoperative hours. Davis et al, had found a similar result in the postoperative period comparing halothane to remifentanil, in infants undergoing pylorotony^4^, while children who received remifentanil had worse postoperative pain scores in other kinds of surgery. The comparison of remifentanil to fentanyl in tonsillectomy and adenoidecotomy in pediatric ambulatory surgery, found higher postoperative pain scores in the remifentanil than in the fentanyl groups^6^.

After elective strabismus surgery, pain scores were also higher in the remifentanil group, compared to children who received alfentanil, propofol or isoflurane^7^.

Bradycardia occurred in 3 infants in GR group, whereas hypotension occurred in one patient in each group. The occurrence of bradycardia in the GR patients could be related to the flow of remifentanil and the lack of administration of atropine at induction in our infants^8^,^9^.

No postoperative respiratory complication was found among our infants. In Davis’ study^4^, only children belonging to halothane group had developed episodes of postoperative apnea. The incidence of postoperative apnea and hypoxia was similar with remifentanil compared to propofol and isoflurane, but lower than with alfentanil^7^.

**Conclusion**

Remifentanil in association with an \( \text{N}_2\text{O}/\text{O}_2 \) mixture provided better intraoperative analgesia than did isoflurane, thus providing proper narcosis and a comparable time to extubation. Quality of postoperative analgesia was similar in both groups. Therefore, a remifentanil-based anesthesia is an interesting alternative to the inhaled anesthetic technique of isoflurane, for IHPS.

**References**

CASE REPORTS

ANESTHETIC IMPLICATIONS OF ACUTE METHYLENEDIOXYMETHAMPHETAMINE INTOXICATION IN A PATIENT WITH TRAUMATIC INTRACEREBRAL HEMORRHAGE

- Case Report-

SAMUEL DEMARIA JR*, ETHAN O BRYSON**, AND ELIZABETH A.M. FROST***

Abstract

The use of the street drug methylenedioxymethamphetamine (MDMA), commonly referred to as ecstasy, has become increasingly prevalent amongst teenagers and young adults in the United States and many other parts of the world. While most anesthesiologists are facile with the intricacies of managing patients intoxicated by alcohol, cocaine and narcotics the new “club” drugs present a challenge, especially under emergency conditions. MDMA, in particular, is the most commonly abused club drug and potentially one of the most dangerous in the perioperative period. We present a case report of traumatic subarachnoid hemorrhage in a patient with acute MDMA intoxication and a review of the anesthetic implications.

Case

A 19-year-old man with an unknown medical and surgical history presented to the Emergency Department after a motor vehicle collision in which he was the unrestrained driver. The patient presented initially with a Glasgow Coma Score (GCS) of 9 and was emergently intubated in the field. A passenger in the vehicle stated the patient was at a “rave” before the accident. He did not know whether the patient took any illicit substances but stated that there was “X” at the party.

The patient was of average height and weight. Initial vital signs upon arrival to the Emergency Department included heart rate 115 beats per minute, blood pressure 157/88 mmHg, respiratory rate 12 breaths per minute, and O₂ saturation 99% on FiO₂ 0.4 via mechanical ventilator. Rectal temperature was 38.2°C. He had numerous facial abrasions but no open lacerations or obvious fractures. Neurologic examination did not reveal any focal deficits and the patient was moving all four limbs spontaneously. His lungs were clear and his cardiovascular exam was remarkable only for tachycardia. Laboratory evaluation indicated sodium of 124 meq/L. Cerebral computed tomography revealed a left-sided intracerebral hematoma and blood in the fourth ventricle with slight midline shift.

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Ecstasy is a hallucinogenic amphetamine analog known amongst recreational drug users as XTC, X, E and Adam. The drug is classified as a club drug along with GHB (gamma hydroxybutyrate), ketamine and flunitrazepam because of its use predominantly at dance parties (“raves”) and dance clubs. MDMA was patented in 1914 by Merck Pharmaceuticals as an appetite suppressant. Given its purported entactogenic effects (i.e., feelings of enhanced communication with and closeness to others), it was promoted as a psychotherapy adjunct in the 1970’s. Despite this potential clinical use, abuse of MDMA prompted the Drug Enforcement Administration (DEA) to issue a schedule 1 drug classification in 1985. Since that time, MDMA abuse in the US has steadily climbed.

MDMA is most often abused orally as a small pill or capsule. As it is produced illegally, the purity of street MDMA is highly variable, with numerous compounds commonly mixed into the final product. Indeed, the concentration of MDMA itself may vary and accidental overdoses are likely. Any acute MDMA intoxication should be approached as polysubstance intoxication.

MDMA closely resembles the hallucinogen mescaline and the stimulant amphetamine. These structural relationships are predictive of its effects. MDMA increases the release and decreases the reuptake of serotonin and dopamine and may also have direct agonist properties at serotonergic and dopaminergic receptors as well as monoamine oxidase (MAO) inhibitor effects. In vitro studies suggest an indirect agonist effect on norepinephrine release5. Effects may be felt within 20 minutes of ingestion and can last up to 8 hours.

Effects include heightened alertness, “closeness” to others, increased emotional lability, decreased aggression and increased sexual arousal. Hypertension, tachycardia and hyperpyrexia are common. Mydriasis, bruxism, sweating and agitation with later lethargy, fatigue, anorexia and depressed mood follow.

The drug is metabolized principally through the cytochrome P450 (CYP450) 2D6 enzyme. Phase II metabolism of MDMA is poorly understood. One metabolite has been shown to be a 2D6 inhibitor in vitro. 2D6 inhibitors (e.g., cocaine, methadone, haloperidol, fluoxetine, paroxetine) block the main
metabolic pathway of MDMA and may substantially increase the effects. Benzodiazepines are metabolized principally by the 3A4 enzyme and likely have limited metabolic interaction with MDMA. Pro-serotonergic drugs (e.g., fluoxetine, amphetamines, St. John’s wort, tramadol, lithium,) may increase the severity of MDMA’s pro-serotonin effects.

Hyperthermia is the most common adverse effect and a leading cause of MDMA-related mortality. The mechanism relates most likely to serotonergic effects in the hypothalamic thermoregulatory center compounded by sustained muscle hyperactivity from long periods of dancing in a warm environment (e.g., club), increased metabolic rate and rigidity. In genetically susceptible pigs, MDMA has been identified as a trigger of malignant hyperthermia (MH). Hyperpyrexia leading to rhabdomyolysis, disseminated intravascular coagulation (DIC) and multi-organ failure is the most dreaded consequence. Increased temperature increases cerebral blood flow and intracranial pressure and could worsen head trauma. Also, hyperthermia is not uncommon after head injury which will thus compound the differential diagnosis.

Sympathetic stimulation from MDMA intoxication increases myocardial oxygen demand and causes tachycardia, vasoconstriction, hypertension and occasionally acute myocardial infarction and dilated cardiomyopathy if prolonged. Cerebral autoregulation may fail, allowing dangerous increases in cerebral blood flow. Significant hypotension and low cardiac output may be encountered after the initial hyperdynamic state due to catecholamine depletion or autonomic dysregulation.

Electrolyte disturbances in MDMA abusers are particularly dangerous. Hyponatremia which often results from excessive water intake from increased physical activity (i.e., dancing at parties where MDMA is present) has been associated with MDMA-related seizures, stupor and incontinence. Increases in plasma ADH levels can be induced by MDMA use which may compound the increased intake of water by users. The occurrence of severe hyponatremia is an unusual complication in young patients with mild head injuries. One retrospective review of patients in a Thai hospital demonstrated that of over one thousand mild head injuries reviewed, only three patients demonstrated severe hyponatremia. All three of these patients were found to have recently ingested MDMA.

Other effects attributed to acute MDMA intoxication include hepatotoxicity with hepatonecrosis and fulminant liver failure, pneumothorax and pneumomediastinum, acute renal failure from rhabdomyolysis and creatine phosphokinase elevations lasting up to 4 days after hospitalization. Cerebrovascular events like subarachnoid hemorrhage, cerebral infarct and venous sinus thrombosis are relatively uncommon.

Most toxicology screens will not detect MDMA and its metabolites and a history is vital although often not available. A directed physical exam is also critical, with particular attention directed to vital signs (with suspicion heightened if patient is hyperthermic) and cardiopulmonary findings. Initial studies that may help the anesthesiologist’s approach are mostly nonspecific tests such as the electrocardiogram and electrolytes.

Succinylcholine should be used cautiously given the risk of compounded the malignant hyperthermia-like effects of the drug, raising intracranial pressure or potentially worsening hyperkalemia, if present. Also, the bruxism often associated with ecstasy may make intubation more challenging in spite of patient habitus. If the patient is conscious and capable of protecting his or her airway, anxiolysis with midazolam or diazepam may be useful and also raises seizure threshold.

Management of hyperthermia, cardiovascular instability, electrolyte derangements and renal and hepatic dysfunction are imperative. Wide swings in hemodynamic parameters are to be avoided given these patients’ higher risk of cardiomyopathy and coronary or cerebral vasospastic events. An intra-arterial blood pressure monitor, placed prior to induction, is advised.

Propofol and thiopental are appropriate induction agents as ketamine may induce catecholamine release from potentially exhausted stores. Etomidate tends to have stable hemodynamic effects but may increase seizure activity, which may be attenuated by pre-induction benzodiazepines. Paralysis with a non-depolarizing agent immediately slows heat production and help lower body temperature. Also, unlike succinylcholine, non-depolarizers are not associated with malignant hyperthermia. For this reason,
rocuronium may be ideally situated to both initiate a rapid sequence induction and maintain paralysis. Severe hypertension and raised intracranial pressure may occur during direct laryngoscopy and commonly used methods to blunt this response (e.g., intravenous lidocaine, opioids) are correct.

Maintenance of anesthesia for head trauma is generally with volatile anesthetics. However, volatile gases are known triggers of malignant hyperthermia and are best used conservatively if a patient has ingested MDMA. A narcotic infusion with remifentanil, which is metabolized by blood and tissue esterases, serves the dual role of blunting sympathetic output and lowering the amount of gaseous anesthetic necessary for surgery. Other narcotics, such as fentanyl, are also suitable. Serial sodium measurements and appropriate correction are important.

Potential intraoperative pitfalls are many. Intraoperative hypertension and tachycardia should be treated with labetalol, with its alpha and beta blocking effects. Pure beta blockade worsens hypertension by tipping the balance of catecholamine action to alpha-1 receptors. Intraoperative hypotension requires rapid infusion of crystalloid or the use of direct alpha-1 agonists. Avoiding indirect agonists such as ephedrine prevents the theoretical catastrophe generated when an already exhausted sympathetic nervous system is prompted to release catecholamines.

Hyperthermia must be treated promptly to avoid rhabdomyolysis and DIC. Basic measures include cold fluids, active cooling with ice packs and avoidance of warming blankets. Given the presumed central mechanism of MDMA-induced hyperthermia, dantrolene use is controversial as the drug inhibits the release of calcium from sarcoplasmic reticulum. Dantrolene may help exertional heat stroke which may be similar to MDMA-induced hyperthermia. Hall and Henry noted that during hyperthermia, the calcium levels required for excitation-contraction coupling are reduced such that hyperthermia alone can cause contraction and subsequent heat production and increased metabolic demand\textsuperscript{10}. They suggested that dantrolene, which raises the calcium requirements for excitation-contraction coupling, may be of some benefit even if it does not directly counteract central causes of hyperthermia.

In summary, patients acutely intoxicated by ecstasy may be hyperthermic, hyperdynamic and have many other dangerous complications. Neurological sequelae, in particular, present a challenge in terms of evaluation and treatment of the patient. We present a case of traumatic intracranial hemorrhage possibly worsened by concurrent ecstasy abuse. A conservative approach to such patients using thorough preoperative assessment, a gentle anesthetic induction and appropriate monitoring is crucial to a good outcome.

References
HUMAN POISONING AFTER INGESTION OF PUFFER FISH CAUGHT FROM MEDITERRANEAN SEA

- A Case Report -

SUHEIL CHUCRALLAH CHAMANDI*, KAMAL KALLAB**, HANNA MATTAR*** and ELIE NADER****

Abstract

Puffer fish poisoning is due to a powerful neurotoxin produced by bacteria living in this kind of fish. Though the sea of Lebanon (Mediterranean) is not endemic of puffer fish and incidence of its serious poisoning is rare, yet occasional incidences do occur. The purpose of this presentation is to raise the awareness of fishermen, fish-restaurant frequenters, public health organizations and the Ministry of Health, of its serious symptomology and to seek medical help as soon as possible.

Case Report

A 68 year-old woman, with hypertension and diabetes, was brought to the Emergency Department of the Hopital Universitaire de Notre Dame De Secours, in January 2008 complaining of proximal limb weakness and dyspnea.

Four hours prior to her arrival, the patient had eaten a half-cooked fish liver. Three hours and thirty minutes later, she started feeling a tingling sensation in the perioral region and in the tip of her fingers associated with blurred vision, head heaviness, nausea and one episode of vomiting.

Ten minutes later, she lost her ability to hold her head up and had developed weakness of her upper and lower extremities. This was accompanied by mild abdominal distention and urinary urgency. The patient then developed quadriplegia, hypophonia and dysarthria. She complained of dyspnea, ophtalmoplegia and had an absent gag reflex. Subsequently, the patient underwent endotracheal intubation.

After intubation, the neurological examination revealed normal consciousness and orientation, bilateral third, fourth and sixth nerve palsies, normal pupillary reflexes, absent gag and cough reflexes and the deep tendon reflexes. Computed Tomography (CT) scan of the brain did not show any abnormalities.

Upon further questioning on the following day, the family reported that the fish was a blowfish and identified it by picture comparisons, as Lagocephalus scleratus (Fig.1 & 2).

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Four days later she was extubated and recovered fully without any neurological sequelae.

**Fig. 1**
*Dr. S. Chamandi holding a Puffer fish caught from our sea*

**Fig. 2**
*Puffer fish caught in the Mediterranean sea*

**Discussion**

Puffer fish is the general name for fish of the family Tetraodontidae, class Osteichthyes order Tetraodontiformes. The *Lagocephalus scleratus* is known to be one of the most dangerous puffer fish species. These fish can swell their bellies to a shape resembling a ball. They are geographically distributed in waters surrounding Japan, the Indian and South Pacific Oceans and North American waters (lesser degree). The Mediterranean coasts is not known as an endemic region.

Between 1974-1983, the incidence of puffer fish intoxication was estimated to be as high as 200 cases per year, with mortality approaching 50%. Puffer fish poisoning is most commonly seen in Japan. Sporadic cases have been reported in the United States.

The different bacteria living in puffer fish liver, gonads, intestines and skin, are known to synthesize a very potent heat stable neurotoxin called “tetrodotoxin”.

Historically, the first recorded cases of tetrodotoxin poisoning were from the logs of Captain James Cook, the British explorer, navigator and cartographer during his voyages to the Pacific Ocean, late part of the 18th century. He recorded that his crew were eating some local tropic fish (puffer fish), and feeding the remains to the pigs kept on board. The crew experienced numbness and shortness of breath, while the pigs were all found dead the next morning. It is clear that the crew received a mild dose of tetrodotoxin, while the pigs ate the puffer fish body parts that contained most of the toxin, thus killing them.

The toxin was first isolated and named in 1909 by Japanese scientist Yoshizumi Tahara: Tetrodotoxin (anhydrotetrodotoxin 4-epitetrodotoxin, tetrodonic acid, TTX) (Fig. 3 & 4).

**Fig. 3**

**Fig. 4**

Poisoning from tetrodotoxin is of particular public health concern in Japan. “Fugu” is a traditional delicacy, prepared and sold in special restaurants where trained and licensed chefs carefully remove the *viscera* to reduce the danger of poisoning.

**Pathophysiology**

The toxin blocks the action potentials in nerves by binding to the pores of the voltage-gated, fast sodium channels in nerve cell membranes. Tetrodotoxin binds
Tetrodotoxin intoxication is divided into four stages based on neurologic signs:

1. Rapidly after ingestion (10 min to 2 hours) numbness and/or paresthesias of the lips and tongue and often of fingers occur.

2. Sensory symptoms progress markedly.

3. Muscular paralysis of extremities occur. Motor incoordination progresses and paralysis develops, but consciousness is maintained. Voice production is difficult because of bulbar muscle paralysis.

4. Consciousness may progressively deteriorate and respiratory paralysis can cause death.

Our patient had eaten the liver of Lagocephalus scleratus, known to be one of the most dangerous fish species. The different bacteria living in puffer fish liver, gonads, intestines and skin, are known to synthesize a very potent heat stable neurotoxin “tetrodotoxin”. The diagnosis was made on the clinical manifestations and the recent dietary history. The onset of symptoms in our patient was more delayed than usual. Although she reached the third stage, she remained hemodynamically stable. Her consciousness was intact during all the paralytic period, and she returned to her baseline status over a short period. Even though the tetrodotoxin level was not determined in serum or urine, the clinical history, the progressive recovery and the kind of fish eaten (confirmed later by presenting the rest of the fish ingested by the patient), were all consistent with the diagnosis of puffer fish poisoning.

Clinical Picture

The clinical manifestations typically develop within 30 min. of ingestion, but may be delayed by up to 4 hours. Death has occurred within 17 min. of ingestion. Usually, paresthesias of the lips and tongue is followed by several signs as simple as sweating to life threatening, such as severe hypotension, respiratory failure, cardiac arrhythmias and even coma (Table 1).

<table>
<thead>
<tr>
<th>Signs &amp; symptoms of puffer fish poisoning</th>
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<tbody>
<tr>
<td>sialorrhea</td>
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<td>headache</td>
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<td>lethargy</td>
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<td>tremor</td>
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<td>dysphagia</td>
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<td>dyspnea</td>
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<tr>
<td>bronchospasm</td>
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<td>coma, hypotension</td>
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<td>gastrointestinal symptoms are often severe and include nausea, vomiting...</td>
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<tr>
<td>diarrhea, and abdominal pain.</td>
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Tetrodotoxin intoxication is divided into four stages based on neurologic signs:

1. Rapidly after ingestion (10 min to 2 hours) numbness and/or paresthesias of the lips and tongue and often of fingers occur.

2. Sensory symptoms progress markedly.

3. Muscular paralysis of extremities occur. Motor incoordination progresses and paralysis develops, but consciousness is maintained. Voice production is difficult because of bulbar muscle paralysis.

4. Consciousness may progressively deteriorate and respiratory paralysis can cause death.

Our patient had eaten the liver of Lagocephalus scleratus, known to be one of the most dangerous fish species. The different bacteria living in puffer fish liver, gonads, intestines and skin, are known to synthesize a very potent heat stable neurotoxin “tetrodotoxin”. The diagnosis was made on the clinical manifestations and the recent dietary history. The onset of symptoms in our patient was more delayed than usual. Although she reached the third stage, she remained hemodynamically stable. Her consciousness was intact during all the paralytic period, and she returned to her baseline status over a short period. Even though the tetrodotoxin level was not determined in serum or urine, the clinical history, the progressive recovery and the kind of fish eaten (confirmed later by presenting the rest of the fish ingested by the patient), were all consistent with the diagnosis of puffer fish poisoning.

Conclusion

Since Puffer fish is not endemic in the shores of Lebanon, its poisoning is considered rare and potentially dangerous. Nevertheless with the increasing tourism and foreign fish importation, puffer fish poisoning may occur in Lebanon. The purpose of this presentation is to raise the awareness of this poisoning among fish eaters and to coerce the Ministry of Health to take the necessary actions towards the fishermen, the restaurants and educate the public, in order to avoid the ingestion of this kind of fish, to recognize it signs of poisoning, and in case of accidental ingestion to seek medical help as soon as possible.
Recommended readings

FAILURE OF ENDTIDAL CARBON DIOXIDE TO CONFIRM TRACHEAL INTUBATION IN A NEONATE WITH A SINGLE VENTRICLE AND SEVERE PULMONARY STENOSIS

- Case Report -

Sahar M. Siddik-Sayyid*, Anis S. Baraka**, Farah H. Mokadem*** AND Marie T. Aouad****

A 12 day old baby girl (body weight 3.5 kg) with dextrocardia and single ventricle, both great arteries arising from single ventricle, severe valvular and subvalvular pulmonary stenosis and hypoplastic pulmonary artery, and non restrictive atrial septal defect, was scheduled for Blalock-Taussing shunt under general anesthesia.

On the day of surgery, heart rate (HR) was 139 bpm, noninvasive blood pressure (BP) 93/31 mmHg, SpO₂ 81% on room air, and temperature 36.5° C. Patient was preoxygenated with 100% O₂, which increased SpO₂ to 99%.

Anesthesia was induced by face mask with sevoflurane in oxygen with gradual increase in concentration to 6%. Immediately after venous access was obtained, propofol 2 mg/kg⁻¹ was administered. Patient was easy to ventilate and saturation was 99% when intubation was attempted for the first time. Upon laryngoscopy, vocal cords could be visualized and uncuffed endotracheal tube (3.0 mm) was inserted easily.

Although the patient was ventilated, and bilateral air entry by auscultation was detected, no endtidal carbon dioxide (ETCO₂) tracing on the monitor could be seen, and the patient started developing hypoxia (SpO₂ 60%), and BP decreased to around 40/25 mmHg. Intubation was considered esophageal and a repeated attempt of intubation with direct visualization of the tube passing through the vocal cords, showed no improvement in the above findings. Also, patient developed bradycardia (HR 85 bpm), and was given atropine 10 µg/kg⁻¹. Following a transient increase of HR to 120 bpm and saturation to 75%, both values dropped again, and still no ETCO₂ could be detected. Capnograph was checked and no deficiency could be found. However, the chest rise observed and bilateral air entry by auscultation confirmed correct placement of the tube. Since hypotension and bradycardia persisted, a bolus injection of epinephrine 10 µg/kg⁻¹ was given. BP increased to 70/35 mmHg, HR to 115, and SpO₂ to 79%, and low ETCO₂ tracing (20 mmHg) could be detected. When circulation improved, surgery was carried out.

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Discussion

When CO₂ is absent as measured by capnograph, it means either the endotracheal tube is in a wrong position (esophageal) or there is absent/decreased presentation of CO₂ to the lungs. False negative results can occur in many situations, where ETCO₂ is not detected, even though the tube is properly placed in the trachea. Gas sampling problem, such as disconnection of the tracheal tube from breathing apparatus, apnea, equipment failure, a kinked or obstructed tracheal tube, unintentional PEEP to a loosely fitted or uncuffed tube, and dilution of proximal sampling by fresh gas flow in Mapelson D systems and Dryden absorber may be misinterpreted as absent waveform caused by esophageal intubation. A marked decrease in pulmonary blood flow will increase alveolar component of the dead space; this occurs with low cardiac output, hypotension, pulmonary stenosis, pulmonary embolism, tetralogy of Fallot, and kinking or clamping of the pulmonary artery during pulmonary surgery¹.

Propofol use in children with congenital heart disease (CHD) may decrease systemic vascular resistance and lead to a change in the ratio between systemic and pulmonary flow². Also, propofol produces bradycardia by its action on the sinoatrial node and attenuation of the β adrenergic receptors at the level of the ventricular myocytes. Even a relative decrease in HR may be deleterious in infants and young children who depend on HR to maintain cardiac output as they cannot increase stroke volume. Previous study found that induction with sevoflurane decreases BP which returned to baseline values in few min after reducing concentration of inhaled anesthetic⁴.

In our neonate, severe pulmonary stenosis and single ventricle are expected to produce low ETCO₂ values on capnography. Sevoflurane induction combined with propofol may have caused a further reduction in the pulmonary blood flow secondary to reduced systemic vascular resistance, and bradycardia. As a consequence, the cardiac output dropped resulting in an increase of the arterial/ETCO₂ gradient and subsequently alveolar dead space. This caused a completely absent CO₂ waveform on capnography (false negative result). Restoration of the circulation resulted in the reappearance of the waveform.

Repeated attempts of intubation can be complicated in cyanotic neonates by deleterious hypoxia and cardiovascular decompensation. The apneic episodes during repeated attempts of laryngoscopy can result in rapid desaturation because of the low functional residual capacity and high rate of oxygen consumption of the neonate. Also, the basal low saturation places the neonate with cyanotic congenital heart disease in the steep part of the oxyhemoglobin dissociation curve.

In summary, ETCO₂ in neonates with cyanotic CHD associated with pulmonary stenosis and single ventricle consistently underestimates the true arterial CO₂ level. Any additional decrease in pulmonary flow such as that induced by sevoflurane-propofol combination may render ETCO₂ waveform an inadequate tool to confirm tracheal intubation.

Keywords: Congenital heart disease: pulmonary stenosis, single ventricle; Capnography: entidal carbon dioxide; Anesthesia: pediatric.

References

UNEVENTFUL EPIDURAL ANALGESIA IN A PATIENT WITH SEVERE THROMBOCYTOPENIA

- Case Report -

SAMİ M İBRABİM* AND MUSTABA SAŁEĦ EL GAZALI**

Abstract

Epidural analgesia is the most effective method for analgesia in labor. It has, however, contraindications and carries many serious side effects.

Though coagulopathy is an absolute contraindication for epidural and axial blocks, yet there are no absolute limits for platelet counts that stand in the way of providing epidural analgesia. In a patient who is writhing in pain due to severe uterine contractions, and in whom there exists a recent normal platelet screening and no history of bleeding disorders, it is internationally acceptable between anesthetists to provide epidural analgesia without waiting for a new platelet screening.

Introduction

Although epidural analgesia is the most effective method for analgesia in labor, nevertheless it carries risky and serious side effects.

Coagulopathy is an absolute contraindication for epidural analgesia and axial blocks. However, there are no absolute limits for platelet counts beyond which one could refuse to provide epidural analgesia to relieve labor pain. In a patient tormented with pain due to severe uterine contractions, and carrying a recent normal platelet screening and no history of chronic hepatic disease, pre-eclampsia, bruises, ecchymoses, or bleeding disorders, an epidural can be placed with minimal fear of causing a hematoma.

We report, herein, a patient with normal lab findings who received epidural analgesia. After vaginal delivery, the epidural catheter was removed, and severe thrombocytopenia was discovered, with a platelet count of $27 \times 10^9/L$, the patient had no subsequent neurologic or hematologic complications.
Case Report

A 25 year-old gravida 2 para 1, 76 kg with a history of previous cesarean section under general anesthesia, was admitted to the labor room of Hamad Medical Corporation Hospital of Doha-Qatar, for trial of labor. Her history revealed that she had an uncomplicated obstetric history, good natal care and there were no signs or symptoms of any chronic hepatic, renal, or autoimmune diseases. The only pertinent information was that she was taking paracetamol (acetaminophen) regularly (500 mg tablets three times daily for ≥1 month), for abdominal and back pain. There was no history or signs of coagulopathy in the previous pregnancies and there was no bleeding from mucus membranes and no petechiae or bruises noted. The routine hematologic studies were performed two months prior to admission to labor ward in anticipation of a normal vaginal delivery, revealed a platelet count was 200 × 10^9/L. Other complete blood count data were within normal limits.

On admission, patient was normotensive with no albuminuria or manifestations of preeclampsia and her uric acid level was normal. The options for labor analgesia were discussed with the patient, and she chose epidural analgesia. A combined spinal epidural analgesia at L3-L4 was entertained.

Following skin infiltration with a local anesthetic, a 16-gauge Tuohy and a 27-gauge spinal needle were used (combined spinal epidural Minipack: Portex, CSEecure: Hythe,UK). With the loss of resistance saline technique, the epidural space was identified. Twenty-five microgram of fentanyl plus 2.5 mg of bupivacaine were deposited intrathecally through the spinal needle. The epidural catheter was then threaded for 4 cm into the epidural space. The epidural catheter was secured as usual with a transparent dressing. There were no signs of intravascular or intrathecal injection, local anesthetic toxicity, hypotension, arrhythmias or abnormal changes in the fetal heart, were observed. An epidural infusion was started of 50 ml mixture of one mg plain bupivacaine/ml and two mcg of fentanyl/ml, with the infusion rate ranging between six to sixteen ml/hour varying with the intensity of labor pain.

Labor progressed as expected (first stage 180 min, second stage 30 min). Patient delivered a healthy baby, weighing 3300 gm with an Apgar score of 9 and 10 at 1 and 5 min respectively. The pediatrician assessed the baby and whose hematologic studies were sent to rule out any thrombocytopenic disorders, all of which revealed no abnormalities. Two hours following delivery of the placenta and suturing of the episiotomy, the epidural catheter was removed. Bleeding at injection site during removal of the catheter was noted, which was stopped by pressure for 7 min.

Results of the hematologic studies on the sample obtained before the epidural insertion, revealed a platelet count of 50 × 10^9/L (Coulter Counter). This was confirmed by the manual platelet count and a peripheral blood smear examination of the platelets, giving a count of 41 × 10^9/L and a smear showing platelets of large size (Fig. 1).

Serial platelet count estimations were then conducted which manifested a sloping curve of platelet counts in the ensuing 2 days, returning to around normal in a month’s time (Fig. 2). It was expected that

![Peripheral blood smear showing a low platelet count with large size platelets (ITP)](image)
the platelet count would increase following delivery of the placenta, but it did not. Within 2 hours, the platelet count dropped from $50 \times 10^9/L$ to $27 \times 10^9/L$. The thrombin time was normal at 9.5 sec, and the partial thromboplastin time was 34 sec. The liver function tests, although still within the normal ranges, had doubled; AST increased during 22 hours from 17 to 26 U/L, in the same period ALT increased from 11 to 21 U/L.

![Platelet count changes curve](image)

Fig. 2
Platelet count changes curve

No signs of epidural hematoma or neurologic injury were elicited. Patient moved both legs with full power (Bromberg’s score was 2 out of 4 and 1 hour after the epidural, the motor strength was one out of 4 with normal free movements.

Neurologic assessment every hour during the first 6 hours and then every 2 hours during the remaining 24 hours, revealed no neurologic deficits and no abnormal vaginal bleeding. Total blood loss was 300 ml, which is the expected loss after a spontaneous vaginal delivery.

Patient was referred to a hematologist for follow-up of platelet count and coagulation state. For more than 2 months, the follow-up did not reveal any abnormalities in blood cell components and coagulation studies.

**Discussion**

The normal range for human platelet levels is between 150-450 $\times 10^9/L$. Normally, human platelet counts remain relatively stable. In cyclical thrombocytopenia, however, platelet counts may oscillate from very low ($1 \times 10^9/L$) to normal ($150-450 \times 10^9/L$), or even higher. Cyclic thrombocytopenia, a rare manifestation, first described in 1936 and was related to hormonal changes during menstruation and changes that occur over days and months. It may also be of autoimmune origin. It is common in females and usually leading to increased destruction and short life span of platelets. It may also be due to amegakaryocytic origin due to impaired platelet production, usually more common in males.

In obstetric patients, thrombocytopenia ranges from benign disorders to life-threatening syndromes. The idiopathic type of thrombocytopenia (ITP) was been diagnosed by peripheral blood smear examination. It is striking that in our case the changes in platelet count were rapid over few hours and an ITP diagnosis was confirmed by the large-sized platelets in the peripheral blood smear (Fig. 1). The patient had normal platelet count during her last pregnancy and had no predisposing signs of coagulopathy and no signs and symptoms of bleeding dyscrasias in the current pregnancy. Her blood count done 3 months previously, revealed a normal platelet count ($200 \times 10^9/L$). Epidural analgesia had to be started immediately as the patient was in severe labor pain. The analgesia guidelines as adopted in our Institution were implemented (normal platelet counts, not less than $100 \times 10^9/L$ within the previous 2-3 months, and without any predisposing factors of coagulation deficits).

We know of only one case report in which the patient received epidural analgesia uneventfully with a platelet count as low as $26 \times 10^9/L$. This patient had a history of idiopathic thrombocytopenia (ITP) which the then attending anesthetist did not ascertain due to a language barrier. The patient had received corticosteroids to improve the platelet count.

In our case, the patient had normal blood components in the previous and current pregnancy. She had no history of ITP and had normal blood count ($200 \times 10^9/L$) in the previous 3 months and had received good antenatal care. It is probable that the patient platelet count was $\leq 50 \times 10^9/L$ at the time of epidural insertion and which decreased rapidly until delivery, and then started to improve spontaneously without any medications.
In ITP, platelet counts decreases, but the size and activity of platelet, function is enhanced to compensate for the decrease in number\(^1\) (Fig. 1). This may explain the absence of hematoma or neurologic complications.

With regards acetaminophen (paracetamol) there are studies demonstrating that oral acetaminophen does not inhibit platelet function in vivo\(^2,3\). Other studies, however, declare that acetaminophen is a non-steroidal anti-inflammatory drug (NSAID) and may affect platelet count if used chronically.

**Conclusion**

It is highly recommended that antenatal care be provided for all pregnant women and that platelet counts and coagulation profile should be performed on admission to the pregnant women with labor pains to the ER, regardless of whatever previous studies have shown. Patients should be monitored closely for any neurologic dysfunction after a neuroaxial block, especially in conditions with low platelet counts. It is also recommended that prospective studies of platelet screening are needed prior to the performance of epidural analgesia.

**Acknowledgement**

I would like to thank Dr. André Louon and Dr. Anjum Suzan John for their unlimited efforts in editing this case report.

**References**

THE RATE DEPENDENT BUNDLE BRANCH BLOCK

- Transition from Left Bundle Branch Block to Intraoperative Normal Sinus Rhythm -

- Case Report -

SEEMA MISHRA*, PRASHANT NASA#, GAURAV NIRWANI GOYAL##,
HIMANSHU KHURANA#, DEEPAK GUPTA#
AND SUSHMA BHATNAGAR**

Abstract

A chronic hypertensive patient with electrocardiogram (ECG) showing left bundle branch block (LBBB) was given general anesthesia for right modified radical mastectomy. Her ECG reverted to normal sinus rhythm intermittently during peri-operative period. This intermittent rate-dependent LBBB is a rare entity. Though hypertension is one significant co-morbid condition, the risk evaluation of LBBB during anesthesia only on an ECG finding, is not justifiable. Rather patient should be investigated further for any cardiac risk.

Keywords: Left bundle branch block, heart-intra ventricular conduction.

Introduction

Left bundle branch block is a major electrocardiographic abnormality in hypertensive patient. It may signify associated coronary heart disease. Few cases have been reported on such rate-dependent LBBB developing intraoperatively in a patient with normal ECG but without LBBB preoperatively.

We report a case of preoperative LBBB which reverted to normal sinus rhythm below critical hear rate, during perioperative period.

Case Report

A 45 year-old 70 kg female diagnosed as a case of carcinoma right breast T2N1Mx (Stage 2) was posted for modified radical mastectomy. Pre-anesthetic evaluation revealed that she was a known case of hypertension of 6 yrs and was on oral losartan hydrochlorthiazide once a day, with good control of blood pressure. She gave no history of chest pain, syncope or dyspnea on exertion. On systemic examination, there was no significant abnormality in the cardiovascular and respiratory systems.
Her investigations including complete hemogram, renal function tests, blood urea, serum creatinine, blood sugar, liver function test, serum bilirubin, and total proteins, were within normal limits. Her ECG showed LBBB. Fine needle aspiration cytology of right breast was positive for ductal carcinoma. Ultrasonography abdomen showed incidental finding of chronic cholecystitis changes and cholelithiasis. Her bone scan and chest x-ray were normal.

A Dobutamine-stress thallium/$^{99m}$Tc myocardial perfusion imaging was done by a cardiologist whose report revealed mildly hypoperfused anteroseptal region (may be due to breast attenuation or LBBB) and there was no evidence of stress induced ischemia. Left ventricular ejection fraction was 66% (normal >65%) with mildly hypokinetic anteroseptal region. She was taken up for surgery and a mild risk explained to patient.

Premedication consisted of intramuscular glycopyrrolate 0.2 mg, fentanyl 100 µg, and promethazine 25 mg. The induction of general anesthesia was done with intravenous propofol 2 mg/kg$^{-1}$ and fentanyl 2 µg/kg$^{-1}$. Tracheal intubation 7.5 mm internal diameter cuffed endotracheal tube was accomplished with intravenous vecuronium 0.1 mg/kg$^{-1}$. Anesthesia was maintained with oxygen, nitrous oxide in 40:60 ratios and 0.5-1% isoflurane. The patient was mechanically ventilated (tidal volume 8 ml/kg$^{-1}$ and rate 12 breaths minute$^{-1}$).

Intraoperatively after 25 minutes of anesthesia, her ECG reverted to normal sinus rhythm with a heart rate of 55 ± 3 beats per min, and blood pressure maintained within normal limits. This reversal to normal sinus rhythm was observed until the time of reversal. However, at the time of reversal of neuromuscular blockade with inj. neostigmine 0.5 mg/kg$^{-1}$ and inj. glycopyrrolate 8 µg/kg$^{-1}$, ECG started showing a repeat pre-operative LBBB again with heart rate around 100 ± 10 min$^{-1}$. Total anesthesia time was 90 minutes.

In the ICU, the patient was monitored for one hour postoperatively, her ECG again returned to normal sinus rhythm for 10 min at a heart rate of 55 ± 5 min$^{-1}$. However, soon ECG started showing LBBB with no symptoms despite adequate pain relief and normal to stable vital parameters at a heart rate 72 min$^{-1}$ (Fig. 1).
The postoperative period remained uneventful except for asymptomatic LBBB. Holter examination showed that the ECG changes were rate-dependent left bundle branch block.

Discussion

Left bundle branch block is major clinical finding in cases of known hypertension. It may also signify associated coronary artery disease, aortic valve disease or cardiomyopathies. Isolated left bundle branch block in a healthy young adult may be benign, but in hypertensive or older patients it may signify a progressive degenerating myocardium involving cardiac conduction system.

The stress-perfusion imaging of the patient showed a relatively normal cardiac performance. Her ECG which was showing LBBB preoperatively, became normal peri-operatively at a heart rate of <60 beats per minute.

Our hypothesis is that the LBBB in the present case was not of organic origin as proved by stress-perfusion imaging and the fact that LBBB reverted back to normal sinus rhythm. When heart rate was at 60 ± 10 beats per minute intraoperatively, and especially postoperatively for some time, LBBB reverted to sinus rhythm. So pre-operative abnormal ECG rhythm was rate-dependent LBBB, reverting into normal sinus rhythm at lower heart rates (critical heart rates).

The rate-dependent bundle branch block is defined as an intraventricular conduction defect that may return, if only temporarily, to sinus rhythm at lower heart rates. The exact mechanism of such a block is unclear but may result from anatomic or physiological interruptions in cardiac conduction system either due to ventricular enlargement or from neurogenic or functional depression with or without underlying pathological lesions of the conducting tissue. Rate-dependent bundle branch block can revert to sinus rhythm at critical heart rate. The transition from normal to abnormal may occur by alterations in heart rate by only 1 or 2 beats/min. This critical heart rate is dependent on change in heart rate. With rapid decrease in heart rate, sinus rhythm may appear at higher rates and with rapid acceleration in heart rate, it may appear at lower heart rate, as the heart rate increase RR interval shortens and the descending impulses finds one of the bundle branches still in its refractory period.

A clear differentiation of LBBB into a benign rate-dependent LBBB, and LBBB associated with myocardial ischemia or infarction, may avoid the unnecessary postponement of a case because of high cardiac risk. Various convenient methods exist for the diagnoses of rate-dependent LBBB during anesthesia. Manouvers like carotid massage, deep inspiration and pharmacological agents like esmolol, metoprolol, propanolol, neostigmine and edrophonium which all decrease the heart rate and thus change this aberrant conduction block to normal. Holter examination, however, is the gold standard.

In a chronic hypertensive patient with LBBB, it is always better to do further cardiac evaluation, like stress-imaging, in order to rule out an associated CAD.

In conclusion, rate-dependent left bundle branch block is a rare entity. LBBB with other co morbid condition, like hypertension, though a significant finding, yet the evaluation of risk during anesthesia only on an ECG finding, is not justifiable. Rather patient should be further investigated for any associated cardiac co morbid conditions.
References

INTUBATION-INDUCED TRACHEAL STENOSIS

- The urgent need for permanent solution -

- Case Report -

ALI S AL-QAHTANI*, AND FAROUK M MESSAHEL**

Abstract

The most common site for the occurrence of intubation-induced tracheal damage is at the area in contact with the inflatable cuff. After the change from high-pressure to low-pressure cuffs, major tracheal lesions still continue to occur. This is a case of tracheal stenosis that occurred after 7 days of intubation with standard cuffed tube whose cuff pressure was assessed by subjective means. Three weeks later, patient was in need of reintubation, the trachea was found to be stenotic at the site of the previous tube cuff. Emergency tracheostomy had to be performed and computed axial tomography (CT) confirmed the tracheal stenosis. A month later, the patient had another cardiac arrest from which he did not recover. Our message in this report is to throw light and alert clinicians involved in tracheal intubation, of the presence of the Lanz endotracheal tube whose pilot balloon is designed to automatically regulate the intra-cuff pressure and thus prevent the occurrence of tracheal stenosis due to high pressure. We strongly recommend the presence of Lanz tracheal tubes as standard emergency equipment in intensive care settings and in any situation in which cuff pressure is likely to increase.

Keywords: Tracheal Stenosis, Postintubation Tracheal Stenosis, Tracheostomy.

Introduction

When the high-volume low-pressure cuffed tracheal tubes were introduced into clinical practice more than 3 decades ago, hopes were high that major tracheal damage associated with the previously used high-pressure cuffed tubes would be eliminated. However, tracheal stenosis is still occurring, and in one prospective study of critically ill patients, 11% of patients who had been intubated with high volume low pressure cuffed tubes, developed tracheal stenoses that were 10-50% of their tracheal diameter at the cuff site1. Other reports showed more severe tracheal damage at the cuff site2. This is a case report of tracheal stenosis following a week long intubation.

We believe that tracheal intubation is here to stay, albeit for the foreseeable future. Monitoring tracheal cuff pressure by simple devices has decreased the incidence of cuff-related tracheal damage. However, such practice is tedious and time-consuming, in addition it did not eliminate the occurrence of the damage4. To avoid the occurrence of tracheal stenosis, we strongly recommend anesthesiologists and intensivists to be aware of the presence of the Lanz tracheal tube, whose pilot balloon is designed to automatically regulate the intra-cuff pressure.

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Case Report

A 51 year-old, a known hypertensive hospital male employee, developed a cardiac arrest while playing basketball. He received advanced life support resuscitation, at the end of which he was deeply comatose with Glasgow Coma Scale of 4. Patient was mechanically ventilated for seven days until his condition improved then his trachea was extubated. His oxygen saturation was 98% on breathing room air. However, it was noted that he already developed right hemiparesis and dysphasia.

On the 21st post-extubation day, the patient was in obvious respiratory distress with falling oxygen saturation. Attempts at passing decreasing sizes of tracheal tubes were unsuccessful, at which stage tracheal stenosis was diagnosed and an emergency tracheostomy was performed. Computed axial tomography (CT) was done and confirmed the diagnosis (Fig. 1). Unfortunately a month later, the patient had another cardiac arrest from which, he could not recover.

Discussion

The introduction of the tracheal tubes with low pressure cuffs have led to the erroneous belief that cuff-related tracheal damage has been prevented. In fact, once the wall of the tracheal tube cuff comes in contact with the mucous lining of the inside of the trachea, small amounts of air injected into the cuff may result in steep increases in cuff pressure. Changes in the tracheal mucosa may occur as early as 15 min after inflation of the cuff, and ischemic damage may result within a similar period if the cuff pressure increases to greater than 40 mmHg.

An increase in tracheal cuff pressure occurs when nitrous oxide is administered to an intubated patient under general anesthesia. In the ICU, however nitrous oxide is rarely used, in such situation an increase in cuff pressure is the result of injecting excess air into the cuff or the use of opioids, widely used in intensive care settings. Morphine may result in a 21% increase in cuff pressure, while the increase in cuff pressure after fentanyl may reach 44%.

Tracheal stenosis after intubation usually presents as shortness of breath and either or both inspiratory stridor and expiratory wheeze on exertion. Changes in the flow-volume loop are diagnostic of tracheal stenosis (Fig. 2a & 2b).
Tracheal lesions related to excessive cuff pressure may be totally eliminated if the Lanz tracheal tube is used as a standard in intensive care settings and in any situation an increase in cuff pressure is likely\textsuperscript{11-12}. The Lanz pilot balloon has been developed to automatically control and regulate intra-cuff pressure, without the need for additional monitoring. Injecting approximately 40 ml of air to achieve an intra-cuff pressure of 22-25 mm Hg, the system will automatically maintain cuff pressure at a constant level below 25 mm Hg (34 cm H\textsubscript{2}O). (The mean capillary perfusion pressure in the tracheal wall is about 35 mm Hg [48 cm H\textsubscript{2}O]). Any increase in the volume of the tracheal cuff will be offset automatically by regulating valve and will move to the pilot balloon which is visible through outer transparent balloon (Fig. 3a & 3b). The balloon and control valve continuously regulate cuff pressure avoiding over-or underinflation. It also maintains safe cuff pressure at varying altitudes during air transportation.

In conclusion, the aim of this presentation is to alert the awareness of the many anesthesiologists and intensivists to the existence and use of the Lanz endotracheal tube whose automatic pilot-balloon regulating of the cuffed-pressure, thus providing quality medical care, and avoiding considerable patients’ morbidity with its associated human and medical costs. In emergency situations where resuscitation takes place by the available means and the standard endotracheal tube (Fig. 4) is used, this tube can be replaced by a Lanz endotube when patent is in the ICU. It is therefore highly recommended that the Lanz tube should be an integral part of emergency equipment in the ICU.
References


OBSTRUCTION OF ENDOTRACHEAL TUBE; A MANUFACTURING ERROR

- Case Report -

FATEMEH HAJIMOHAMMADI*, ARMAN TAHERI**
AND PAYAM EGHTESADI-ARAGHI***

Manufacturing defects in endotracheal tubes (ETT) are known to occur, and may cause ETT obstruction in various ways1. We report an ETT manufacturing error resulting in partial airway obstruction with a 7.0 mm cuffed tube due to partial perforation of the distal orifice of the ET tube.

Case Report

A fourteen-year-old girl 49 kg, ASA I with chronic sinusitis was scheduled for an elective functional endoscopic sinus surgery. Monitoring equipment including pulse oxymeter, sphygmomanometer, and ECG were applied and her basic vital signs were within normal range.

Patient was premedicated with midazolam 2 mg and fentanyl 100 µg, via an IV route. Anesthesia was induced with thiopentone 250 mg and muscle relaxation was achieved using 25 mg atracurium. The trachea was intubated with a cuffed oral PVC ETT (Supa high volume-low pressure cuff, single use, ID = 7.0 mm) without any complication. ETCO₂ monitoring was established and bilateral lung expansion confirmed by auscultation although bag ventilation was difficult because of high inspiratory pressure. Then the lungs were artificially ventilated at tidal volume of 500 ml (end-tidal CO₂ of 40 mmHg) and rate of 10 breaths per minute with a mixture of oxygen, nitrous oxide (50%) and halothane (1%) for anesthesia maintenance.

Before preparation and draping, a pharyngeal pack was inserted. After several minutes, the peak airway pressure increased from 30 to 65 cmH₂O gradually. This was accompanied by heart rate increase (120 beat/min) and end-tidal CO₂ rise to 60 mmHg. SaO₂ remained unchanged at 100% with FiO₂ of 50%.

Upon noting the rise in ETCO₂ and drop in expired tidal volume, the patient was immediately disconnected from the ventilator and the lungs ventilated manually, nitrous oxide was discontinued and pharyngeal pack was removed. The circuit was checked systematically for kinks, obstructions or leaks, but none was found. ETT marking at the incisor was checked and remained the same at 18 cm. Lung auscultation revealed expiratory wheezing. Visual inspection of the ETT did not reveal any cause of airway obstruction. A 10F suction catheter was then passed down the lumen of the ETT for suctioning of secretion but the suction catheter could not be passed fully down the tube and resistance was encountered. After that, the surgery was delayed and patient’s ETT was substituted.

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with another same size new cuffed ETT under direct laryngoscopy which resulted in marked improvement in ventilation.

Examination of the former tube revealed that there was as a manufacturing error (Fig. 1) consisting of a plastic film covering the distal opening of the tube with a small perforation (approximately 2.5 mm in diameter) at its mid-upper point. The subsequent anesthetic course was uneventful.

**Fig. 1**
Plastic film at the distal end of the ETT that was removed from the patient. Arrow shows the orifice in the plastic film with diameter of approximate 2.5 mm

**Discussion**

Difficulty in ventilating an intubated patient during anesthesia may be ascribed to a variety of causes, basically including anesthesia gas delivery malfunction, obstruction of the breathing circuit (somewhere between the common gas outlet and the end of the ETT), poor pulmonary compliance (extrinsic or intrinsic), esophageal intubation or acute bronchospasm, tension pneumothorax, and endobronchial mass lesion.

Several manufacturing defects in ETT have been described. These include cuff defects leading to herniation of the ETT cuff and intraluminal tracheal obstruction, elliptical defects in the tube wall at the level of the notch cut for insertion of the pilot tube causing air leak, kinking of the ETT and intraluminal plastic films and meniscus causing near complete airway obstruction.

The checking of ETT for defects before tracheal insertion is an integral part of routine checking of anesthetic equipment. This usually includes examining the tube to ensure patency and inflating the cuff to detect air leakage. In our case, routine check of the ETT failed to find the structural problem at the tube end hole. Only after intubation and ventilation for a period of time did the structural defect become obvious.

Barst et al and Kee have described similar cases. Barst et al described a 6-months-old girl that was intubated with an uncuffed 3.5 mm internal diameter Sheridan ETT and following no air entry confirmation she was reintubated with new tube. On inspection, the tube’s lumen was entirely occluded by a plastic meniscus that must have been introduced during the tube’s manufacturing process.

As this case demonstrates, the intrinsic occlusion of the ETT itself should be considered. Increasing airway peak pressure on a volume control mode of ventilation and persistently high ETCO\(_2\) due to hypoventilation were the only early warning signs. The suction catheter was unable to pass through the tube due to the distal end block as the tube was occluded with a plastic film.

This incident was reported to the Supa Corporation together with the tube’s Lot number.

Although this occurrence is rare, we feel that it is timely to highlight this case to relay that any structural defects in the tube may result in significant airway incidents.

In conclusion, inspection of ETT prior to use is still the most crucial factor in confirming tube function. Vigilant monitoring of ventilator pressure and end tidal CO\(_2\) is the key to the early detection of airway obstruction. When airway obstruction is encountered in an intubated patient, it is important to consider both mechanical and pathologic factors. In cases where no other cause for inadequate ventilation is found, it is imperative to replace the ETT.
References

TRACHEAL CARTILAGE FRACTURE WITH THE PERCUTANEOUS DILATATIONAL TRACHEOSTOMY, CIAGLIA METHOD

- Case Report -

KASRA KARVANDIAN*, ATA MAHMOODPOOR**, MOSTAFA MOHAMMADI*, MOHAMMADTAGHI BEGMOHAMMADI* and AFSHIN JAFARZADEH**

Surgical tracheostomy was first introduced by an ENT surgeon (Chevalier Jackson) in 1900. In 1955, Seldinger, a Swedish radiologist, introduced a way of insertion of a tube with the aid of a guidewire into the hollow spaces of body, such as blood vessels. In 1985 Pasquale Ciaglia performed percutaneous dilatational tracheostomy (PDA) with the Seldinger method.

Tracheostomy nowadays is usually performed as PDT in the ICUs1. Most of the PDT methods are performed with the Seldinger method. The basic difference between the various PDT methods, however, is in both the way of dilation and the way of dilator entrance (antegrade vs retrograde). In the Ciaglia method, several dilator tubes are used for tracheal dilation2.

Case Report

A 29 year old man was admitted to ICU because of convulsions and decline in the level of consciousness, with the diagnosis of encephalitis. He underwent an endotracheal (ET) intubation and was put on mechanical ventilation. Twenty days after ICU admission, because of the anticipated long duration of ET intubation and low level of consciousness, a PDT was performed with the Ciaglia method.

Patient was sedated with fentanyl and midazolam. Oral cavity and pharynx were locally anesthetized with lidocaine. The ET tube was withdrawn as tube cuff was placed between vocal cords using bronchoscope. Angiocath was inserted between the first and second tracheal cartilages and a guidewire was inserted through it. The angiocath was then withdrawn and dilator was guided to trachea. During insertion, the inferior (second) cartilage got broken as confirmed by the bronchoscope. The tracheostomy tube was inserted and its correct position confirmed with bronchoscopy and chest x-ray. The patient was under close observation, and two weeks later, he was weaned from ventilator. For the following two months patient did not have any complication due to the fractured tracheal cartilage.
Discussion

Patients with long duration of ET intubation require tracheostomy. The indications for surgical tracheostomy and PDT are the same. The advantages of PDT over the surgical method, consists of decreased bleeding, less tissue incision and injury, less complications, its rapid and cost saving3-6. In addition, long term complications, such as tracheal stenosis and late wound healing, are less with PDT method7,8.

In view of such advantages of PDT, nowadays patients in ICU undergo PDT unless a contraindication exists9,10. Anterior neck infection and coagulopathy are absolute contraindications for PDT method. Large goiter, previous history of neck surgery, less than 17 years old, hypoxemia with positive end expiratory pressure more than 20 cmH2O, FiO2 more than 70%, morbid obesity, or inability to define the tracheal cartilage, thyro-hyoid distance less than 3 cm and emergent situations, are relative contraindications11-13.

Tracheal cartilage fracture is one of the complications of PDT with the Ciaglia method attributable to tracheal anatomy (trachea is angulated backwards as it inserts in the thorax). In the performance of PDT at upper levels, therefore, more force is needed and inserting dilator into the intercartilage space near cricoid cartilage (between the first and second tracheal rings), increases the risk of a fracture. Because the cricoid cartilage is denser than other cartilages, the inserting force and pressure on it are transported to lower tracheal rings, thus increasing the risk of cartilage fracture, especially in patients with short neck and limitation of neck movement. Performing PDT with Ciaglia method from the lower levels of trachea produces less force angle, so dilator and trachea are positioned in nearly straight line (Fig. 1, 2).

It is recommended, therefore, that PDT with Ciaglia method be done in lower levels of trachea, than in the first tracheal cartilages.

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**Fig. 1**
PDT at upper levels of trachea of produces increased pressure on lower cartilage rings.

**Fig. 2**
PDT at lower levels of trachea produces less force angle, bringing dilator and trachea to a nearly straight line.
VENTRICULO-PERITONEAL SHUNT SURGERY
IN AN INFANT WITH DOUBLE AORTIC ARCH,
PATENT DUCTUS ARTERIOSUS
AND ATRIAL SEPTAL DEFECT

- Case Report -
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VISHWAS MALIK² AND HEMANSHU PRABHAKAR¹

Abstract

Double aortic arch with patent ductus arteriosus and atrial septal defect is an uncommon association. Such complex cardiac lesions may complicate an otherwise normal anesthetic course. We came across a case with aqueductal stenosis and hydrocephalus, scheduled for ventriculoperitoneal shunt surgery, on an emergent basis. The child was managed successfully. The anesthetic implications of resultant left-to-right shunt with increased intracranial pressure have been described.

Key Words: Double aortic arch, Patent ductus arteriosus, Atrial septal defect, Anesthesia.

Introduction

Double aortic arch is a rare but life threatening condition, if misdiagnosed¹. Its association with patent ductus arteriosus (PDA) and atrial septal defect (ASD) has been mentioned in association with few genetic abnormalities²,³. However, the anesthetic implications of this association in patients undergoing neurosurgical procedures have never been described in literature.

We present a case of congenital hydrocephalus due to aqueductal stenosis, with associated double aortic arch, PDA, and ASD, scheduled for an emergency ventriculoperitoneal (VP) shunt surgery.
Case Report

A 3-months-old male baby weighing 4 kg was admitted to our hospital with complaints of increasing size of head and upward gazing of eyeballs, for the previous 15 days. This was associated with vomiting and decreased feeding for 2 days. There was no history of seizures or focal neurological deficit. The antenatal history was remarkable for breach presentation and cesarean section delivery from a polyhydramnios mother, at 38 weeks of gestation. He developed bronchopneumonia during the first month of life which improved following antibiotic treatment. On examination, the child was pale but, there was no cyanosis, jaundice, clubbing, or pedal edema. The heart rate was 116 beats.min⁻¹, and respiratory rate 28 breaths.min⁻¹. He had features of hydrocephalus with increased head circumference (42 cm), open and tense fontanelles, and presence of sunset sign. It was noticed that the baby developed bluish discolouration of mouth and lips while crying. On cardiac auscultation systolic murmur was audible. Chest X-ray showed a globular cardiac silhouette with cardiomegaly, bilateral hilar prominence and thickening of bronchovascular markings. ECG showed normal sinus rhythm with no evidence of ventricular hypertrophy. Echocardiography revealed a complex congenital heart disease with presence of ASD (ostium secundum type), PDA, and double aortic arch. There was no evidence of pulmonary hypertension. Peripheral arterial pulsations were feeble bilaterally in the upper limb, whereas they were well felt in the lower limbs. The oxygen saturation on room air was 99%. The child had a reducible umbilical hernia and hypospadiasis as well. Routine blood tests were within normal limits with a hemoglobin level of 14 g/dl. MRI of brain showed gross hydrocephalus with aqueductal stenosis and corpus callosum agenesis. Non-contrast CT scan head showed hydrocephalus and dilated lateral ventricles with periventricular ooze. This child was posted for an emergency ventriculoperitoneal shunt surgery in view of the raised intracranial tension and deterioration of neurological condition.

In the operation theatre, inhalational induction was performed using sevoflurane in oxygen and air mixture. After securing an intravenous (IV) access, fentanyl 2 mcg.kg⁻¹ and rocuronium 1 mg.kg⁻¹ was given. Tracheal intubation was facilitated using a 3.5 mm ID uncuffed endotracheal tube. Anesthesia was maintained with sevoflurane in oxygen (FiO₂ -0.5)-air mixture, fentanyl, rocuronium, and intermittent positive pressure ventilation. Monitoring parameters included ECG, non-invasive BP, SpO₂, end-tidal CO₂, and inspired concentration of inhalational agents. The end-tidal CO₂ was kept between 33 ± 2 mmHg. Posterior tibial artery was cannulated for continuous BP monitoring. Intraoperatively, the mean BP was targeted to keep within 10% of the baseline values. However, there was no episode of desaturation or hemodynamic instability. Serial arterial blood gas analysis revealed metabolic acidosis (Table 1), which was managed with IV supplementation of sodium bicarbonate (4.2%) solution.

Total duration of procedure was 90 minutes. The blood loss was approximately 20 ml, and a total of 80 ml Ringer’s lactate was used as maintenance fluid. Temperature was maintained around 36°C. At the end of procedure, residual neuromuscular blockade was reversed with neostigmine and glycopyrrolate, and trachea extubated, uneventfully. The child was observed in the intensive care unit for 24 hours. Though metabolic acidosis persisted (Table 1), further bicarbonate supplementation was stopped as the child was clinically stable. He was discharged on third postoperative day with an advice for further cardiac evaluation. At 1-month follow-up, the child had improved neurological status.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>pO₂ (mmHg)</th>
<th>pCO₂ (mmHg)</th>
<th>HCO₃⁻ (mmol/L)</th>
<th>BE</th>
<th>SO₂ (%)</th>
<th>Na⁺ (mmol/L)</th>
<th>K⁺ (mmol/L)</th>
<th>Ca²⁺ (mmol/L)</th>
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<tr>
<td>After induction</td>
<td>7.22</td>
<td>184</td>
<td>35.9</td>
<td>14.2</td>
<td>-12.1</td>
<td>100</td>
<td>139</td>
<td>3.9</td>
<td>1.21</td>
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<tr>
<td>Intraoperative</td>
<td>7.254</td>
<td>234</td>
<td>38.0</td>
<td>16.3</td>
<td>-9.6</td>
<td>100</td>
<td>139</td>
<td>3.8</td>
<td>1.05</td>
</tr>
<tr>
<td>Postoperative (ICU)</td>
<td>7.288</td>
<td>190</td>
<td>34.6</td>
<td>16</td>
<td>-9.3</td>
<td>100</td>
<td>139</td>
<td>4.2</td>
<td>1.12</td>
</tr>
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</table>
Discussion

The anesthetic challenge, in this case, is due to the combined presentation of left-to-right shunt with hydrocephalus. Patients with increased intracranial pressure require hyperventilation to reduce cerebral blood flow, at the same time keeping adequate \( \text{PaO}_2 \). On the other hand, the anesthetic management of a patient with left-to-right shunt includes avoidance of pulmonary vasodilation by lowering \( \text{FiO}_2 \) and/or hypoventilation.

Double aortic arch results from an anomalous persistence of fourth aortic arch\(^4\). It causes formation of a vascular ring around esophagus and trachea, producing pressure effects. Infants with double aortic arch or vascular rings may present with harsh cry, inspiratory stridor, respiratory distress, and dysphagia. Airway obstruction may be significant in infants and children with vascular rings\(^4\). Inhalational induction is preferred, as it serves to maintain spontaneous ventilation. The tracheal compression can worsen during induction. Paralysis should be administered only after ascertaining ability to ventilate using intermittent positive pressure ventilation. These patients would require smaller than expected endotracheal tube size. However, in this case, we did not encounter any such problem.

Non-cardiac congenital anomalies are commonly associated (50 to 80\%) with these patients\(^4\). Congenital cardiac anomalies are also present in 20\% of children with double aortic arch\(^5\). Our patient presented with a combination of PDA and ASD (ostium secondum). This combination causes a substantial left-to-right shunt, resulting in increased volume loading of both the ventricular chambers, decreased cardiac output, and increased intra-cardiac and intra-pulmonary pressures. Deterioration of gas exchange and congestive cardiac failure may occur when compensatory mechanisms fail to keep up with excess cardiac work. Decreased systemic blood flow in the presence of left-to-right shunt as a result of PDA can cause pulmonary over circulation. This results an elevation of left atrial pressure due to augmented pulmonary venous return. Diastolic blood pressure may be compromised if cardiac output is reduced or there is a low resistance vascular bed, as in our case. Infants with greatly increased pulmonary blood flow suffer from congestive heart failure secondary to increased volume overload. Obstruction of the large and small airways results in increased airway resistance and poor compliance. The inspiratory pressure needed for adequate positive-pressure ventilation must be adjusted accordingly.

Hyperoxia and hypocarbia cause pulmonary vasodilatation. Hence, it is advisable to reduce the \( \text{FiO}_2 \) and to avoid hyperventilation. Normocapnia is helpful in managing the increased pulmonary blood flow resulting from such complex heart disease. However, in this case, mild hypocapnia was maintained without any untoward event, in order to reduce the intracranial pressure (ICP). Nitrous oxide (\( \text{N}_2\text{O} \)) is best avoided, as it causes sympathetic hyperactivity, increased pulmonary vascular resistance, and interferes when \( \text{FiO}_2 \) requirement is increased\(^7\). It also causes an increase in cerebral blood flow, which is of concern in patients with raised ICP. Metabolic acidosis in this patient was possibly because of decreased systemic blood flow in the preoperative period, despite adequate efforts to maintain PVR and SVR, intraoperatively. Additional anesthetic issues include avoidance of air bubbles in intravenous lines to prevent paradoxical air embolism.

To conclude, we successfully managed a patient of aqueductal stenosis and hydrocephalus with associated double aortic arch, PDA, and ASD, who underwent VP shunt surgery. A detailed history and complete physical examination along with an adequate investigational work up would help in formulating anesthesia plan in such patients.
REFERENCES


ANESTHESIA FOR NELSON’S SYNDROME

- Case Report -

MAHUR MEHTA*, GIRIJA P RATH**, AND GYANINDER PAL SINGH*

Introduction

Adrenalectomy in the setting of residual corticotrope adenoma tissue predisposes to the development of Nelson’s syndrome1; a disorder characterized by rapid pituitary tumour enlargement and increased pigmentation secondary to high ACTH levels. We present the perioperative course of a child with Nelson’s syndrome who underwent sublabial trans-sphenoidal hypophysectomy.

Case Report

A 12 yr-old, 30 kg female child was admitted with history of bilateral adrenalectomy for Cushing’s syndrome 3 years back, following which she developed severe darkening of skin all over body and gradually progressing headache. Her endocrine profile revealed ACTH levels of 220 pg/mL (Normal = 6-76 pg/mL) with cortisol of 1.2 µg/dL (normal = 5-25 µg/dL) for which prednisolone 5 mg and fludrocortisone 50 µg daily were being supplemented. Growth hormone levels were increased (4 ng/mL; normal <2 ng/mL). Well defined hypointense mass (9 × 3 mm) arising from anterior pituitary was evident in CT scan. A diagnosis of Nelson’s syndrome was made and sublabial transsphenoidal hypophysectomy was planned. Child was rendered euthyroid on eltroxin 50 µg daily. Airway examination revealed coarse facies with Mallampati II airway.

Anesthesia was induced with propofol and fentanyl. Tracheal intubation was facilitated with rocuronium. Maintainanence of anesthesia was done with isoflurane and N\textsubscript{2}O in 40% O\textsubscript{2} and intermittent boluses of rocuronium and fentanyl. At end of procedure, neuromuscular blockade was reversed and trachea extubated. Postoperative course was uneventful. Perioperative steroid coverage comprised hydrocortisone 50 mg 8 hourly, started 1 day preoperatively till postoperative day 1, when oral prednisolone 25 mg daily in divided doses was started, subsequently tapered over next 2 days to scheduled preoperative dose. Normal skin colour was restored in 1-2 days, probably indicating successful removal of microadenoma.

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Discussion

The incidence of Nelson’s syndrome has been variably reported to be between 8-38%\(^2\)\(^-\)\(^4\). Younger age and pregnancy are possible associated risk factors. Hyperpigmentation of skin, minimal sellar changes or raised ACTH though suggestive, need neuroradiological confirmation for definite diagnosis of Nelson’s syndrome. The predominant cause of morbidity is from local tumor extension or invasion. Patients with this disorder become deeply pigmented because of excess alpha melanocyte stimulating hormone (a-MSH), a derivative of propiomelanocortin (POMC), the precursor peptide for ACTH. There may be loss of pituitary function because of compression or replacement of normal pituitary tissue or compression of structures adjacent to the pituitary fossa by the tumor. Lateral extension of the tumor may result in invasion of the cavernous sinuses and entrapment or compression of the cranial nerves (III, IV, V and VI). Superior extension of the tumor can lead to compression or invasion of optic apparatus and or the hypothalamus. Headaches are common, are probably due to stretching of the dura of the diaphragma sellae by the tumor. Pituitary adenomas exhibit widely variable endocrine profile.

References

SUDDEN CARDIAC ARREST DURING CESAREAN SECTION
- A Possible Case of Amniotic Fluid Embolism -

- Case Report -

NIKOOSERESHT MAHSHID*, SADEGIAN AHMAD**, MANOCEHRIAN NAHID* and FARHANCHI AFSHIN*

Abstract

Amniotic Fluid Embolism (AFE) is a rare obstetric catastrophe that occurs in approximately 1/50,000 pregnancies and has a mortality rate in excess of 80%. AFE is a condition that is poorly understood and often difficult to diagnose. We report a case of a healthy 27 yr-old gravid two, 35 wk gestation parturient with a previous Cesarean section two years previously, and presently admitted for emergent Cesarean section due to premature uterine contractions.

Induction of general anesthesias was performed with no problem and a male preterm infant with Apgar 8 at 1min was delivered. Amniotic fluid was bloody and 40% placental abruption existed. Following delivery of the placenta, patient suddenly became plethoric and O₂ saturation began to decrease and no pulse could be palpated! Immediate CPR was successful but she was hemodynamically unstable and signs of right heart strain was obvious. Right jugular venous catheterization was performed, vasopressors were administered. After a two hours period of relatively stable vital signs, patient’s reflexes returned to normal, however, profound coagulopathy on lab data was reported and she was treated with 10 unit Packed Red Blood Cells (PRBCs), 10 unit FFP and 8 unit platelets, Sodium bicarbonate, oxytocin and Methergine. The patient remained hemodynamically unstable while laparotomy-hysterectomy was performed to stop the bleeding. Unfortunately attempts were unsuccessful and patient died four hours later in ICU. Post-mortem findings showed signs of Disseminated Intravascular Coagulation (DIC), no fetal squamous cells in pulmonary vasculature were found and special staining of Cytokeratin marker shows no positive cells in lumen of vessels.

The post-mortem diagnosis of AFE is challenging to forensic investigators and pathologists and can be confirmed by histological confirmation of amniotic fluid contents in the pulmonary vasculature, although they may be difficult to identify. In recent years it has been suggested that AFE is an anaphylactoid reaction to fetal antigens and an elevated serum tryptase level is increasingly being used to support the diagnosis.

Sudden onset of cardiovascular collapse and early signs of right heart strain and fulminant DIC supports the diagnosis of AFE in this case, although no fetal debri could be find in pathologic staining.
Right jugular venous catheterization was performed and infusion of dopamine 5μg/kg/min and epinephrine 5 μg/min was started. She had relatively stable vital signs for two hours and her reflexes (cough, spontaneous ventilation, pain withdrawal…) returned to normal. However, profuse vaginal bleeding was observed and patient’s systolic blood pressure fell to 40 mmHg. Lab data reported metabolic acidosis and profound coagulopathy on lab data were reported (PT >2 min & PTT >3 min). She was treated with 10 units of Packed Red Blood Cells (PRBCs), 10 unit FFPs and 8 unit platelets, sodium bicarbonate, oxytocin and methergine. The patient remained hemodynamically unstable, in the meantime laparotomy-hysterectomy was performed to stop the bleeding. Unfortunately attempts were unsuccessful and patient died four hours later in ICU.

Post-mortem findings showed signs of Disseminated Intravascular Coagulation (DIC), no fetal squamous cells in pulmonary vasculature were found and special staining of Cytokeratin marker showed no positive cells in lumen of vessels.

Discussion

Amniotic Fluid embolism (AFE) has been reported during pregnancy, labour, Cesarean section and the postpartum period. While the syndrome remains poorly understood, it can be described as a two-stage process. In the first stage, amniotic fluid and fetal cells enter the maternal circulation, triggering the release of several endogenous mediators. Pulmonary artery vasospasm and pulmonary hypertension lead to elevated right ventricular pressure, and the resultant hypoxia causing myocardial and pulmonary capillary damage. Approximately half of all patients who survive enter a second stage characterized by hemorrhage and DIC, possibly because amniotic fluid contains Thromboplastin.

The post-mortem diagnosis of AFE is challenging to forensic investigators and pathologists and can be confirmed by histological confirmation of amniotic fluid contents in the pulmonary vasculature of the mother, although difficult to identify as some contests are lodged in small pulmonary capillaries. Multiple lung sections are submitted when diagnosing AFE which increases the probability of finding elements of...
SUDDEN CARDIAC ARREST DURING CESAREAN SECTION: A POSSIBLE CASE OF AMNIOTIC FLUID EMBOLISM

In recent years it has been suggested that AFE is an anaphylactoid reaction to fetal antigens and an elevated serum Tryptase level is increasingly being used to support the diagnosis\textsuperscript{2,4,8,9.}

In the absence of a definitive diagnostic test, Benson proposed a clinically based definition of AFE. According to his criteria, a diagnosis of AFE would be appropriate for any patient experiencing sudden onset of cardiovascular collapse during pregnancy or 48 hours postpartum. Other illnesses ought to ruled out that might explain the signs and symptoms\textsuperscript{10.}

The sudden onset of cardiovascular collapse in this case preceded by plethoric discoloration of the patients face suggests anaphylactoid reactions, and early signs of right heart strain\textsuperscript{5} followed by progressive fulminant DIC\textsuperscript{6}, supports the diagnosis of AFE, though no fetal debri could be found in the pathologic staining of pulmonary vasculature.

References

PERIOPERATIVE CARE OF A CHILD WITH ULLRICH CONGENITAL MUSCULAR DYSTROPHY

- Case Report -

Neesann Puangsuvan, BS¹, Robert A Mester, BS¹, Venkataraman Ramachandran, MD³ and Joseph D Tobias, MD⁴*

Abstract

Ullrich congenital muscular dystrophy (UCMD) is a severe form of congenital muscular dystrophy manifesting axial muscle contractures and distal joint hyperlaxity. Severe hypotonia and associated respiratory failure may occur early in the disease process. Given the various associated orthopedic conditions, anesthetic management may be required during surgical interventions to correct skeletal deformities or these patients may present with surgical conditions unrelated to their primary illness. We present a 4-year-old with UCMD who required operative intervention for a ruptured appendix. Anesthetic care implications included the need for a rapid airway control to limit the risks of aspiration due to the intra-abdominal process, choice of neuromuscular blocking agent for rapid sequence intubation, associated airway issues related to micrognathia and limited mouth opening, and the potential for involvement of the cardiovascular and respiratory systems. The perioperative management of patients with UCMD is discussed including the use of propofol and remifentanil for rapid sequence intubation to avoid the need for neuromuscular blocking agents.

Introduction

Ullrich’s congenital muscular dystrophy (UCMD) is a severe form of congenital muscular dystrophy manifesting axial muscle contractures and distal joint hyperlaxity. It generally presents as hypotonia at birth. The disorder was first described in 1930 by Otto Ullrich, who encountered two children with proximal joint contractures and severe distal joint hyper-extensibility. He subsequently named the disorder congenital atonic-sclerotic muscular dystrophy, but over the years, it has become known as Ullrich’s congenital muscular dystrophy. UCMD is inherited as an autosomal recessive trait although cases of spontaneous mutation have been described.

Other distinctive clinical features include a high-arched palate, protuberant calcanei, and rigid spine syndrome. Despite the extensive muscular involvement, intelligence and development are generally normal¹. Early involvement of the diaphragm leads to early respiratory failure in many patients as well as resulting in the predisposition to recurrent chest infections.

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intubation with cricoid pressure. The first attempt at laryngoscopy with a MacIntosh 2 blade was difficult due to the microstomia and limited mouth opening. This attempt at laryngoscopy was aborted and while cricoid pressure was maintained, a second attempt at laryngoscopy with a Wis-Hipple 1.5 laryngoscope revealed a short epiglottis with a grade II view of the airway. The patient’s trachea was intubated with a 5.0 mm uncuffed ETT. Maintenance of anesthesia consisted of desflurane (expired concentration 4-8%) in 50% air/oxygen supplemented with fentanyl (total of 3 µg/kg). No neuromuscular blocking agents were administered. The laparoscopic procedure was completed without difficulty in approximately 75 minutes.

After completion of the procedure, a caudal epidural block was performed with 1.2 mL/kg of 0.25% bupivacaine with 1 µg/kg of clonidine. She was transported to the post-anesthesia care unit. No supplemental pain medication was required for the initial 10 postoperative hours. Subsequently, pain was easily controlled with ketorolac (0.5 mg/kg) administered every 6 hours around the clock, supplemented with as needed doses of nalbuphine (0.05 mg/kg). The remainder of her postoperative course was uneventful.

Discussion

The congenital muscular dystrophies are comprised of a heterogeneous group of diseases affecting muscular architecture including Ullrich congenital muscular dystrophy (UCMD), merosin-deficient congenital muscular dystrophy, and rigid spine syndrome. The congenital muscular dystrophies present similarly during infancy and the neonatal period with decreased intrauterine movement, hypotonia, and delays in the achievement of motor milestones. However, there are specific signs and symptoms which may suggest the diagnosis of UCMD including spinal rigidity, hyperlaxity of the joints of the hands and feet, and early diaphragmatic involvement with chronic respiratory infections or respiratory failure.

Biochemically, collagen type VI is a large, ubiquitous, extracellular matrix protein which forms a highly branched, microfilbrillar network of the skeletal muscle providing structural support including cell-to-cell adhesions and stability. Interactions have
been described between collagen type VI and the major constituent of the muscle basement membrane, collagen type IV indicating that it functions as an anchor for the basement membrane to underlying connective tissue. Likewise, a variety of other matrix components have been shown to interact with collagen type VI particularly proteoglycans and other types of collagen to form structurally critical cellular networks for skeletal muscle. The interactions between proteoglycans such as chondroitin sulfate, biglycan, and decorin and collagen VI provides important mechanisms for transmembrane signaling in a variety of tissues including: skeletal muscle, blood vessels, and cartilagenous tissues throughout the body. These molecular interactions aid in cellular maintenance of homeostasis as well as processes of wound healing through interactions with fibronectin microfibrillar networks.

Structurally, collagen type VI is composed of 3 separate α-chains which are encoded by 3 separate genes located on chromosomes 2 and 21. Mutations in these genes result in 2 specific types of muscular dystrophies including Bethlem myopathy and UCMD. Although Bethlem myopathy is generally a more benign disease with a more variable onset and a slower progression, UCMD presents in the neonatal period with severe wasting of the axial musculature and distal joint hyperlaxity. Of significant importance to the perioperative care of these patients is the frequent early involvement of the diaphragmatic musculature which may progress to early and severe respiratory failure. However, there remains significant interpatient variability depending on the severity of the mutations in the collagen VI gene resulting in a wide range of clinical presentations and manifestations. These can range from as mild as scoliosis or abnormal scar formation and wound healing to neonatal hypotonia with failure to achieve independent ambulation and an early requirement for ventilatory support.

In our patient, anesthetic considerations included not only her primary disease process, but also the need to secure the airway using rapid sequence intubation due to the presence of an intra-abdominal process with delayed gastric emptying and the associated risk for aspiration. In an effort to avoid the potential for aspiration during anesthetic induction, we pretreated our patient with an H2-antagonist and the motility agent metoclopramide, followed by rapid sequence intubation with cricoid pressure. Of primary concern in such patients is the choice of medications to allow for the rapid accomplishment of endotracheal intubation. Given the risks of rhabdomyolysis, hyperkalemia and cardiac arrest with succinylcholine, this agent is absolutely contraindicated in patients with muscular dystrophies. Conversely, non-depolarizing neuromuscular blocking agents (NMBA's) are considered safe in patients with various muscular dystrophies. However, even with intermediate-acting agents such as atracurium or vecuronium, doses which are normally used for endotracheal intubation can result in a prolonged duration of action as increased sensitivity to these agents has been established in patients with muscular dystrophies.

Prior to their withdrawal, rapacuronium and mivacurium, two short-acting NMBA’s, could have been considered in this scenario although rapacuronium may have been preferred given its rapid onset. Frankowski et al. reported their experience with the use of rapacuronium in 2 patients (9-years of age and 10-years of age) with Duchenne muscular dystrophy. There was a prolonged clinical duration (return of T1 to 25% of its baseline, 16.4 and 18.4 minutes vs. 13.8 ± 7.2 minutes in the general population), a doubling of the recovery index, and doubling of the spontaneous recovery time (return of T4/T1 ≥ 70%). Mivacurium has also been suggested as a possible agent in patients with muscular dystrophy. In a cohort of 7 patients with Duchenne muscular dystrophy, a dose of 0.2 mg/kg resulted in complete suppression of all four Twitches of the train-of-four in 1.5 to 2.6 minutes. Time to recovery of the first twitch varied from 12 to 18 minutes.

Given that these short-acting neuromuscular blocking agents are no longer available, we chose to use an alternative technique of rapid sequence intubation without a neuromuscular blocking agent. Several investigators have reported the successful use of a combination of remifentanil and propofol to allow for endotracheal intubation without the need for neuromuscular blocking agents. Batra et al. reported that propofol (3 mg/kg) and remifentanil (3 µg/kg) could be used to allow for endotracheal intubation.
within 90 seconds without the use of a NMBA in children ranging in age from 5 to 10 years. Similar efficacy has been reported in a cohort of adult patients when using propofol (2 mg/kg) and remifentanil (3 µg/kg). In adult patients, Alexander et al. evaluated the suitability of tracheal intubation 60 seconds following the administration of propofol (2 mg/kg) and remifentanil in doses ranging from 2 to 5 µg/kg. Good or excellent conditions were present in 95% of patients who received 4 µg/kg of remifentanil versus only 60% of those who received 3 µg/kg.

In our patient, the combination of propofol (3 mg/kg) and remifentanil (3 µg/kg) produced excellent conditions within 60-90 seconds although a second attempt at laryngoscopy was necessary due to our patient’s airway abnormality and the need to use a direct laryngoscope blade.

Although anecdotal, previous reports exist regarding the potential for difficulties with airway management in patients with various muscular dystrophies including both Duchenne and Emery-Dreifuss variants. As with our case, these difficulties resulted from the combination of limited mouth opening and restricted flexion/extension of the neck. These issues are likely related to fibrotic changes in the associated muscle groups including the masseter muscles which may limit mouth opening. Furthermore, in these cases reports and our patient, associated micrognathia and a short thyromental distance further complicated airway management. It remains unknown whether these issues are sporadic occurrences or somehow related to the muscle dystrophy.

In addition to the concerns outlined above regarding rapid sequence intubation and airway management, the underlying muscular dystrophy may also predispose these patients to both respiratory and cardiac problems. Of particular importance would be the risk of postoperative respiratory failure. The effects of residual anesthetic agents combined with poor muscular function may predispose these patients to upper airway obstruction. Poor cough reflex, pre-existing muscle weakness, and diaphragm impairment may further increase the risk for postoperative atelectasis and respiratory failure. Although our patient underwent a laparoscopic, we chose to place a caudal epidural block at the completion of the procedure to ensure adequate postoperative analgesia. Supplemental postoperative analgesia was then easily achieved with a combination of ketorolac and nalbuphine thereby avoiding the need for strong opioids and their potential for associated adverse effects. We would suggest that use of a regional anesthetic technique with a combination of local anesthetic and clonidine may be beneficial in patients with UCMD by eliminating the deleterious physiologic effects of pain as well as avoiding the need for agents which may potentially impair respiratory function.

Possible cardiac involvement posed an additional anesthetic concern in our patient. Although commonly associated with Duchenne and Becker muscular dystrophy, there does not seem to be a strong association between cardiac involvement and UCMD. Brockington et al. reviewed a case series of fifteen patients with UCMD patients. Both cardiac functional and electrical conduction were examined with echocardiogram and serial electrocardiograms. The entire study group had an unremarkable echocardiogram and all but one patient had normal electrocardiograms. Despite these findings, the possibility of cardiac involvement is raised by one child of the cohort who died suddenly from an arrhythmia.

In conclusion, we present a 4-year-old with UCMD who required operative intervention for a ruptured appendix. Anesthetic care implications included the need for a rapid airway control to limit the risks of aspiration due to the intra-abdominal process, choice of neuromuscular blocking agent for rapid sequence intubation, associated airway issues related to micrognathia and limited mouth opening, and the potential for involvement of the cardiovascular and respiratory systems. The use of propofol and remifentanil for rapid sequence intubation eliminated the need for neuromuscular blocking agents. However, some potential issues with airway management were noted including micrognathia and limited mouth opening. Additional involvement of respiratory or cardiovascular performance may impact the perioperative care of these patients.
References


LETTERS TO THE EDITOR

PRACTICE GUIDELINES AND PREVENTION OF OBSTETRIC ANESTHESIA-RELATED MATERNAL MORTALITY

KRZYSZTOF M. KUCZKOWSKI*

In the United States obstetric anesthesia has been a major subspecialty of anesthesiology for a long time and is now an integral part of practice of most anesthesiologists1. An obstetric anesthesiologist has become an essential member of the obstetric care team, who closely works with the obstetrician, family practitioner, midwife, neonatologist and Labor and Delivery nurse to ensure the highest quality care for the pregnant woman and her baby. The anesthesiologist’s (obstetric anesthesiologist’s) unique skills in acute resuscitation combined with experience in critical care, make members of our specialty (subspecialty) particularly valuable in the peripartum care of the high risk patients, extending our role well beyond the routine provision of intrapartum anesthesia or analgesia1.

It is with interest that I read the recent, and timely article by Siddik-Sayyid and Zbeidy discussing the practice guidelines for obstetric anesthesia. I wish to express my great appreciation to the authors for their thoughtful and valuable comments, recommendations, and conclusions. I also wish to add the following (brief) comments on this important subject.

1. Anesthesia-related complications are the sixth leading cause of pregnancy-related maternal mortality in the United States3. Difficult or failed intubation following induction of general anesthesia for Cesarean delivery remains the major contributory factor to anesthesia-related maternal complications. Although the use of general anesthesia has been declining in obstetric patients, it may still be required in selected cases. Since difficult intubation in obstetric anesthesia practice is frequently unexpected, careful and timely preanesthetic evaluation of all pregnant women should identify the majority of patients with difficult airway and avoid unexpected difficult airway management3,4.

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2. The American College of Obstetricians and Gynecologists (ACOG) recognizes hazards of general anesthesia (particularly if administered in emergency situation), and recommends early consultation with an obstetric anesthesiologist in all high-risk parturients. Such early communication should encourage timely decision-making and improve the cooperation between the obstetricians and obstetric anesthesiologists. ACOG also advocates early administration of epidural analgesia in all high-risk parturients, particularly the morbidly obese and those with a potentially difficult airway.

Keywords: Obstetric anesthesia, complications, difficult airway, pregnancy, labor analgesia, complications, maternal mortality, maternal morbidity.

References
Dear Editor;

Tongue swelling (TS) after surgery is a rare but potentially lethal postoperative complication\(^1\). TS causes include trauma, allergy, infection, bleeding, massive fluid overload and rarely ischemia and infarction of the tongue. In anesthesia practices, it is usually presented after long term oral intubations\(^2\).

In this report we present TS case which started immediately after operation and lasted 20 hours in child who had undergone a cleft palate repair.

A 3 years-old, 13 kg girl; Non premedicated, after sevoflurane induction, succinylcholine was administered. The trachea was intubated atraumatically, size 4 mm cuffed tracheal tube (Mallincrot\(^\circ\)). Anesthetic maintenance was with sevoflurane in nitrous oxide/oxygen (50/50\%).

After 155 minutes of uneventful cleft palate repair operation and trachea was extubated and taken into postanesthesia care unit (PACU). The patient was observed to have developed TS 20 minutes postoperatively (Fig. 1). It was thought to have been caused by the tongue depressor and the patient observed closely. Her hemodynamic status was normal, bilateral lung ventilation was good, arterial saturation was satisfactory and there was no inspiratory stridor. No ventilation difficulty developed. Methylprednisolon 20 mg was given intravenously. After 1 hour of observation in the PACU no further enlargement and deterioration was seen in the child and she was sent to reanimation care unit for close follow-up. Intubation preparations was made up. The patient was observed with

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Fig. 1
Tongue swelling after cleft palate repair
her head up and oxygen was given via face mask. With the help of her mother cold compression was applied with cold sticks. After her uneventful follow-up, the child’s tongue regressed to its normal size and she was sent to plastic surgery ward.

The congestion, caused by the deterioration of the venous drainage of the tongue lead to the swelling of tongue. Cyanosis usually accompanies swelling of the tongue if is an accompanying arterial obstruction (ischemia, infarct) it. The tongue depressor of the automatic ecartor which is used in cleft palate operations may have caused TS by the deterioration of the venous circulation and may have lead to respiratory difficulties and difficult airway. In our case TS was not complicated and remained limited, and because of that the follow up was limited to observation and symptomatic treatment. However, after that event we searched the published literature and found that airway patency and safety should be provided to the patients who developed TS, and extubation should only be done after resolving of the edema and the tongue regressed to its normal size.

References

Requested Change

Dr. Mehdi Trifa, the Corresponding Author, requests a change in the names of authors in the article:

THE ANALGESIC EFFECTS OF ILIOINGUINAL-ILIOHYPOGASTRIC NERVE BLOCK IN CHILDREN – Concentration or Volume?

Published in the Middle East Journal of Anesthesiology, Volume 20 (1), February 2009, page 83, to read as follows” TRIFA M, CHAABANE Z, DRIDI S, SEBAI B, MISSAOUI A, FEKIH HASSEN A AND BEN KHALIFA S
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