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Obstetric Anesthesia

Combined spinal and epidural anaesthesia and maternal intrapartum temperature during vaginal delivery: A randomized clinical trial

Br J Anaesth 2011;107:762-8
de Orange FA, Passini R, Amorim MMR, Almeida T, Barros A

Abstract

Purpose The purpose of this study was to compare the incidence of intrapartum fever in women who received combined spinal-epidural analgesia (CSE group) for labor to women who received only non-pharmacologic methods of analgesia (control group).

Background Epidural analgesia during labor has been reported to be associated with intrapartum maternal fever. The exact mechanism is unclear; however, epidural analgesia may contribute to changes in maternal thermoregulation. The problem with increased maternal temperature secondary to epidural analgesia is that this may result in unnecessary maternal and neonatal evaluation to eliminate the possibility of infection. CSE has become a popular technique for labor analgesia; however, the relationship between CSE use and maternal fever has not been evaluated. The investigators of this study wanted to determine if there was a relationship between CSE and increased maternal intrapartum temperature and fever.

Methodology This was a prospective, randomized, clinical trial of 70 parturients undergoing vaginal delivery to examine the incidence of intrapartum fever. Inclusion criteria included singleton pregnancy, full-term fetus, and cervical dilation of 3-6 cm. High risk pregnancies and women with a preexisting fever or who were on antibiotics were excluded.

Parturients were randomized to receive either Combined Spinal Epidural analgesia or no neuraxial or intravenous analgesia. The CSE group received 2.5 mg of 0.5% hyperbaric bupivacaine with sufentanil 5 µg, followed 30 minutes later with a 5 mL bolus of bupivacaine 0.05% with sufentanil 0.2 µg/mL, then intermittent boluses every 30 minutes as needed.

Women in the control group received no neuraxial or intravenous analgesia.

All women were monitored hourly and their temperature, blood pressure, heart rate and respiratory rate were recorded. Temperature was measured in the axilla on all patients. The primary outcome was the incidence of maternal fever between the two groups, which was defined as temperature ≥38°C. Secondary outcomes included maternal and neonatal temperature, cesarean delivery rate, instrumental delivery rate, use of oxytocin, duration of the first and second stage of labor, maternal or neonatal infection, need for maternal or neonatal antibiotic therapy, Apgar scores and umbilical cord blood pH. Sample size calculations and statistical
A P < 0.05 was considered significant.

**Result** A total of 68 subjects completed the study (N = 34 each group). There were no significant differences in demographics between groups. The average age was 22 with 69% being primaparas at an average 39.2 weeks gestation. The instrumental delivery rate was 11.4% in the CSE group and 0% in the control group (P = NS). The cesarean delivery rate was 11.4% in the CSE group and 20.6% in the control group (P = NS). The duration of the first stage of labor was 85 minutes longer in the control group (P = 0.01).

Subjects in the CSE group had a significantly higher incidence of fever (14.3% vs. 0%, P = 0.027). In the CSE group the temperature was significantly higher starting the first hour after CSE placement and continuing until the sixth hour (P < 0.05; Figure 1). There were no cases of chorioamnionitis or signs of maternal infection in either group. No parturient required antibiotic therapy. Apgar scores and cord gases were similar in both groups, and no neonate born to a mother with fever developed neonatal sepsis or required antibiotic therapy.

**Conclusion** The use of CSE was associated with a significant increase in maternal temperature and fever. However, this increase was not associated with complications in the mother or neonate.

**Comment** This is the second study recently to evaluate the relationship between neuraxial analgesia and maternal fever / neonatal outcomes. In a retrospective study, Greenwell et al (1) reported that women who received epidural analgesia and had a temperature >38.3°C (101°F) had a 2 to 6 fold increase in neonatal adverse events. In contrast, this randomized clinical trial found no adverse events in any neonate. However, it must be pointed out that the current study sample size was too small to evaluate differences in neonatal outcomes in women who received CSE. A much larger, multi-center, clinical trial would be needed to truly determine if neuraxial analgesia is associated with serious neonatal adverse outcomes.

Overall, this was a well-designed clinical trial. It is the first study to examine maternal fever in association with CSE rather than epidural analgesia for labor. The mechanism is most likely similar, and some authors suggest neuraxial analgesia is associated with an inflammatory response with subsequent release of cytokines which
contribute to maternal fever. (1) It may be that with CSE the onset of temperature elevation is earlier than with epidural analgesia. The authors of this study report previous investigations have found delayed onset of temperature elevation and fever in women undergoing epidural analgesia for labor.

I would have liked to have seen an epidural analgesia group included in this study because it would have helped determine how soon the temperature elevation occurs with these two techniques (CSE vs. epidural). Also I believe a limitation of this study is that temperatures were taken in the axilla as opposed to orally. Nonetheless, I found this to be a good start investigating this phenomenon … but only a start. At this point we are beginning to accumulate data that neuraxial analgesia during labor is somehow associated with maternal fever. We do not yet know if it is the cause of fever and we don’t know if the increase in maternal temperature is harmful in any way.

**Dennis Spence, PhD, CRNA**


The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.
WHAT FACTORS AFFECT INTRAPARTUM MATERNAL TEMPERATURE? A PROSPECTIVE COHORT STUDY: MATERNAL INTRAPARTUM TEMPERATURE

Anesthesiology 2012;117:302-8
Frölich MA, Esame A, Zhang K, Wu J, Owen J

Abstract

Purpose The purpose of this study was to identify factors associated with noninfectious maternal temperature elevation during active labor.

Background Maternal infections are the most common cause of intrapartum temperature elevation. Recent research has suggested an association between epidural analgesia and temperature elevation during active labor. Additionally, some reports suggest intrapartum temperature elevation may be associated with poor neonatal outcomes. There are conflicting results in the literature; some suggesting epidural analgesia may be the cause of maternal fever, while others have not reported this finding.

The theories suggested explaining the association between maternal fever and epidural analgesia are based on the concept that epidural analgesia may suppress heat-dissipating mechanisms such as pain-associated hyperventilation, or that epidural analgesia may promote placental inflammatory processes which in turn trigger maternal fever. However, sympathetic blockade from epidural analgesia should result in hypothermia secondary to redistribution of heat from the core to the periphery. Furthermore, other factors besides epidural use may influence temperature changes during labor. For example, prolonged labor in patients receiving oxytocin who have a long time from rupture of membranes to delivery may result in an inflammatory process. This could explain the temperature elevation seen in some parturients.

This study sought to evaluate the time course of maternal temperature changes and examine whether or not duration of labor, epidural analgesia, oxytocin dose, body mass index (BMI), or length of time from rupture of membranes where associated with maternal temperature elevation.

Methodology This was a prospective cohort study of 81 women scheduled for induction of labor. Patients were excluded if they had conditions that would affect normal temperature regulation, such as chorioamnionitis, or received medications such as acetaminophen, prostaglandins, or ibuprofen; had active cardiac disease, pulmonary disease, or neurologic disease. Epidural analgesia consisted of bupivacaine 0.1% with 2 µg/mL fentanyl administered via patient controlled epidural analgesia using a basal rate of 8 mL/hr and a demand bolus of 4 mL every 20 minutes. Oxytocin was titrated by nurses based on a standard protocol. After rupture of membranes, an intrauterine pressure catheter was placed in all patients. Temperature was measured
orally every hour. Statistical analysis and sample size calculation were appropriate.

Result  A total of 81 patients completed the study. Average labor duration was 14 ± 7 hours, length of rupture of membranes was 8 ± 5.6 hours, and BMI was 34.6 ± 9 kg/m². Median duration of labor was 8 hours. The majority of patients were white (47%) and then African American (40%). Approximately 56% of patients were GBS positive (Group B Streptococcus). The most common parity (number of vaginal births) was 0 (40%) and next most common was 1 (31%).

A mixed linear regression model was used to estimate the temperature slope, or change in temperature per hour. The temperature increased 0.017°C per hour which indicated the temperature increased significantly over time (P = 0.009). Fifty-four percent (54%) of patients had a positive temperature slope (increasing temperature over time) and 46% had a negative temperature slope. Patients with increased BMI had a larger increase in temperature over time (P = 0.0008). Similarly, in patients whose temperatures increased, time from rupture of membranes was associated with a much larger temperature change over time (slope). Total oxytocin dose was not associated with temperature change over time.

In patients who received epidural analgesia, temperature slopes were compared for the four hours before and after epidural initiation. No significant difference was found in the temperature slope before or after initiation of epidural analgesia. Epidural analgesia had no effect on the change in temperature over time.

Conclusion  In this study, induced labor was associated with a small temperature increase over time. Patients with a higher BMI and longer duration from rupture of membranes to delivery were more likely to experience temperature elevations during labor. Epidural analgesia had no effect on maternal temperature.

Comment  I thought this was a well done cohort study. Temperature studies are difficult to conduct, and the investigators did a good job of controlling for many of the factors that may confound their results (i.e., excluded patients with chorioamnionitis or those who received prostaglandins or acetaminophen; measured temperature orally). Therefore, this study provides some reassuring evidence to anesthesia providers that epidural analgesia use is NOT associated with increasing temperature during labor.

It is probably not surprising that prolonged rupture of membranes was associated with a more pronounced temperature elevation. Prolonged rupture of membranes may trigger an inflammatory response or subclinical infection that probably contributes to the temperature elevation seen. The finding of an association between increasing BMI and temperature elevation is interesting, and it may be that obesity as well contributes to an inflammatory response and secondary temperature elevation, as previous research
on obesity has found a link between obesity and inflammation.

One limitation of this study was that the investigators did not report the total amount of local anesthetic administered, or whether or not patients required additional top-up boluses of stronger concentrations of local anesthesia for labor analgesia. This could have potentially influenced the results. I also would have liked to have known about the neonatal outcomes. However, this would have required a much larger sample size. Nonetheless, I still think this was a good study that provides us some evidence demonstrating epidural analgesia has no effect on maternal temperature.

Dennis Spence, PhD, CRNA

The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.
Pediatric Anesthesia

Surgical Outcome in Children Undergoing Hypospadias Repair Under Caudal Epidural vs Penile Block

Kundra P, Yuvaraj K, Agrawal K, Kishnappa S, Kumar LT

Abstract

Purpose  The purpose of this study was to compare the success, quality, and complication rate of caudal epidural and penile block when used for postoperative pain relief in children undergoing hypospadias repair.

Background  Both caudal epidural and penile blocks are common anesthetic techniques used for postoperative pain relief in children undergoing hypospadias repair. Caudal anesthesia continues to be preferred over penile block by most anesthesia providers even though previous studies have indicated that penile block is superior to caudal anesthesia for the following reasons:

› lower complication rate
› improved analgesia
› longer duration of block
› less peripheral venous engorgement

This study sought to clarify previous studies on the subject.

Methodology  This was a randomized, double blind study on healthy children ages 4 to 12 undergoing primary hypospadias repair. Children were allocated to one of two groups. Group P contained 27 subjects who received penile blocks for postoperative pain relief. Group C contained 27 subjects who received caudal anesthesia for postoperative pain relief. Both groups received the same preoperative sedation and general anesthesia technique for the surgical procedure. After induction of general anesthesia, the penile block or caudal anesthesia was administered according to the randomization protocol. Penile blocks were administered at the dorsal root nerve with 0.5 mg/kg of 0.25% bupivacaine. The caudal epidurals were administered with the same dose of bupivacaine. In the first 48 hours of the postoperative period, nurses who were blinded to the type of postoperative pain block given to each patient administered intravenous morphine 0.1 mg/kg to patients that reported a visual analog scale (VAS) pain score greater than 5 on a 0 to 10 scale. After 48 hours, patients were given acetaminophen on demand. The differences between groups were analyzed with a two way repeated measure analysis of variance (ANOVA) with significance considered at P < 0.05.

Result  VAS scores demonstrated that penile blocks provided better postoperative analgesia than caudal epidurals, and this conclusion was supported by less morphine consumption in the penile block group. In addition, the penile blocks lasted significantly longer on average than the caudal epidurals. Penile blocks provided 5-6 hours of postoperative pain relief while the caudal epidurals provided 4 hours. Acetaminophen consumption was similar in both
groups for the period 48 hours after surgery. In addition, while there were no failures in the penile block group, there was one block failure in the caudal epidural group. Five patients developed postoperative urethral fistulas, and all of those patients were in the caudal epidural group.

**Conclusion**  This study of children undergoing hypospadias repair demonstrated that penile blocks provided superior and longer lasting postoperative pain relief compared to caudal epidural blocks. All patients who developed postoperative urethral fistula were in the caudal epidural group.

**Comment**  This study asks an interesting question about an issue that occurs in anesthesia as well as other health care settings. Why do we continue to use a particular technique when evidence suggests that there is a better technique available? In this case, it appears that using a caudal anesthetic for hypospadias repair is less effective and has greater risk of complications than using a penile block. Other studies have supported this conclusion as well. It is not so much the marginal benefit of pain relief one technique has over the other (6 hours for penile blocks vs 4 hours for caudal epidurals), but the significant postoperative complication of urethral fistula developed by those patients who received a caudal anesthetic. Venous engorgement from peripheral dilatation caused by caudal anesthesia is suggested to contribute to this complication. So why, as the article indicates, do anesthesia providers prefer to use caudal anesthesia for this procedure? This may be an example of providers not keeping up with evidence based practice. This also may be an example of providers using techniques that they are most comfortable with, even though there are other techniques that might have greater benefits with less risk. Regardless of the reason, it is important to periodically evaluate one’s techniques and make an effort to acquire new skills; choosing those that are best suited for the patient instead of clinging to “routine” techniques.

*Steven Wooden, DNP, CRNA*
Pharmacology

**INTRAOPERATIVE METHADONE IMPROVES POSTOPERATIVE PAIN CONTROL IN PATIENTS UNDERGOING COMPLEX SPINE SURGERY**

Anesth Analg 2011;112:218-223
Gottschalk A, Durieux ME, Nemergut EC

**Abstract**

**Purpose** The purpose of this study was to determine if a single bolus dose of methadone 0.2 mg/kg before incision for complex thoraco-lumbar spine surgery in adults improves pain control. A secondary purpose was to assess methadone side effects in this setting.

**Background** Severe postoperative pain is common after major spine surgery. Total intravenous anesthesia with propofol and sufentanil is commonly used to maintain anesthesia in these cases when neurophysiologic monitoring is used. Methadone is a long-acting opioid frequently administered to those with chronic pain. It is an opioid receptor agonist and NMDA receptor noncompetitive antagonist with a mean elimination half-life of 22 hours (range 15-60 hours), which may be beneficial after major spine surgery. Methadone has been limited in its use in the surgical setting as it has great potential to cause unwanted post-operative side effects which include prolonged sedation, respiratory depression, nausea, and vomiting. However, this patient population typically requires large doses of opioids for an extended period of time following surgery. Some researchers suggest that methadone, with its long duration of action, may be an alternative to sufentanil.

**Methodology** This was a prospective, randomized, single blind investigation of 30 patients, aged 18-75 years old, scheduled for elective multilevel thoracolumbar spine surgery with instrumentation and fusion. Exclusion criteria included preoperative methadone use, morbid obesity (BMI >36 kg/m²), history of substance abuse, history of myocardial infarction or heart failure, chronic renal failure, or liver failure or cirrhosis. Patients were randomized into one of two groups:

- **Sufentanil Group:** received 0.75 µg/kg initial loading dose of sufentanil before surgical incision followed by sufentanil infusion of 0.25 µg/kg/h
- **Methadone Group:** received 0.2 mg/kg subsequent to intubation

Anesthesia was maintained with propofol 50-150 µg/kg/min.; no potent inhalation agent was used. Inadequate intraoperative anesthesia (i.e., hypertension, tachycardia, patient movement) was treated with a bolus of 0.1 µg/kg of sufentanil every 2.5 minutes at the discretion of the anesthesia provider. When surgical wound closure was begun, the sufentanil was turned off and the patient extubated in the operating room or intensive care unit. Patients who remained intubated postoperatively did not receive any opioids as part of their sedation. All patients received postoperative PCA with either
fentanyl, hydromorphone, or morphine. Postoperative analgesia was managed by the neurosurgeon. All opioids were recorded as morphine equivalents.

The following parameters were measured:

- Pain rating via visual analogue scale
- Preoperative opioid consumption (in morphine equivalents)
- Time after surgery to first pain medication
- Cumulative opioid requirement at 24, 48 and 72 hours postoperatively (in morphine equivalents)
- Complications defined as:
  - hypotension (MAP < 50 mm Hg)
  - need for vasopressors
  - incidence of respiratory depression
  - respiratory arrest
  - need for naloxone
- The incidence of hypoxemia or desaturation or the need for supplemental oxygen
- The incidence of cardiac arrhythmias, MI, PONV and any treatment that was given

Student t tests or Mann-Whitney U tests were used to make group comparisons. Results are presented as the mean ± SD or median (25-75% interquartile range). A P < 0.05 was considered significant.

**Result**

A total of n= 29 subjects (methadone n = 13; sufentanil n = 16 completed the study). The mean age in the methadone group was 62.9 ± 9.5 as compared to 53.1 ± 15 in the sufentanil group (P = 0.051).

There were no differences in BMI (methadone group: 26.3 ± 4.6 vs. sufentanil 28.1 ± 4.7; P = 0.323), male gender (methadone group: 45.5% vs. sufentanil group 36.5%; P = 0.466), and ASA status (P = 0.448).

Median preoperative opioid consumption (morphine equivalents) was 8.0 (0-16) mg in the methadone group as compared to 7.5 (0-21.6) mg in the sufentanil group (P =0.771). Median surgical duration was 285 (248-467) minutes in the methadone group and 329 (283-475) minutes in the sufentanil group (P = 0.313). Median time to extubation was similar between the two groups (methadone group: 15 (13.5-18.25) minutes vs. sufentanil group 11.5 (5-33) minutes, P = 0.58).

The time from the end of surgery to first request of pain medications was longer in the methadone group; however, the difference was not statistically significant. The methadone group had significantly less pain at 48 hours compared to the sufentanil group (Figure 1; P < 0.05). However pain scores were similar at 24 and 72 hours (P = NS). Median opioid consumption at 24, 48 and 72 h was over twice as great in the sufentanil group when compared to the methadone group at each time point. However, the difference was only significant at 48 and 72 hours (Table 1). There was no significant difference in side effects between the two groups. No serious complications occurred in either group.

**Conclusion**

Postoperative pain control after a single 0.2 mg/kg pre-induction bolus of methadone improves pain control significantly at 48 hours.

### Table 1. Postoperative Opioid Consumption

<table>
<thead>
<tr>
<th>Time</th>
<th>Methadone group n = 13</th>
<th>Sufentanil group n = 16</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 h</td>
<td>50 (5, 390)</td>
<td>110 (10, 455)</td>
<td>ns</td>
</tr>
<tr>
<td>48 h</td>
<td>25 (5, 175)</td>
<td>63 (10, 230)</td>
<td>0.023</td>
</tr>
<tr>
<td>72 h</td>
<td>15 (0,80)</td>
<td>34 (10, 195)</td>
<td>0.024</td>
</tr>
</tbody>
</table>

**Note.** Results are median (min, max) morphine equivalents in mg.
Methadone has a median half-life of 22 hours, however there is significant variability in metabolism rates among individuals. The investigators hypothesized they would see differences in opioid consumption at 24 hours given methadone’s half-life. The sufentanil group consumed twice as much opioid at all time points, however the difference was only statistically significant at 48 and 72 hours. The authors suggested in their discussion this finding of significantly less opioid consumption at 48 and 72 hours, which is long past the median-half life of methadone, may be due to methadone’s ability to attenuate opioid tolerance and hyperalgesia. This theory is speculative, and this difference at 24 hours may be because the study was underpowered. If they would have had a larger sample size they may have seen differences at all time points.

There were some weaknesses to this study. Patients in the methadone group were almost 10 years older than those in the sufentanil group. However, it may be clinically relevant as older patients may require less opioids, and may have lower methadone metabolism, which may explain the difference. Therefore, this age difference could partially explain the differences seen. Additionally, the investigators do not describe the number of levels fused or the specific procedures performed for each group. This would have helped in the interpretation of their results. The investigators did not report if the patients were taking any adjunct

**Comments**

Multilevel thoracolumbar spine surgery with instrumentation and fusion is associated with significant postoperative pain. Furthermore, many of these patients may present with a history of chronic back pain which may increase their postoperative opioid requirements. In this study the investigators demonstrated that a single preoperative dose of methadone resulted in significantly less pain at 48 hours, and significantly less opioid requirements at 48 and 72 hours. These results are not surprising given the long duration of action of methadone.
pain medications (i.e., gabapentin, NSAIDS) preoperatively or postoperatively. Patients also received different types of PCA opioid agents (i.e., fentanyl, hydromorphone and morphine), and it is not known if a basal rate was used in either group, which may have influenced the results. Finally, the investigators used t-tests to compare pain and opioid consumption for each of the three days analyzed. A more appropriate analysis would have been to use a repeated measures analysis of variance or a nonparametric equivalent and used a more conservative P value to be considered significant (i.e., P <0.01) since they were making multiple comparisons.

Given these limitations, results of this study should be considered preliminary. If anesthesia providers choose to use methadone they need to ensure that the surgeons and nurses know the patient received a long acting opioid and that they should avoid or cautiously prescribe other sedatives and hypnotics. If a PCA is ordered I would not recommend a basal rate. Anesthesia providers may want to consider having an anesthesia “pain service” manage these patients to minimize the risks. Finally, as continuous end-tidal carbon dioxide becomes more readily available, patients administered long acting opioids might benefit from this monitor.

**Dennis Spence, PhD, CRNA**

The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.
WHO IS AT RISK FOR POSTDISCHARGE NAUSEA AND VOMITING AFTER AMBULATORY SURGERY?

Anesthesiology 2012;117:475-86

Abstract

Purpose   The purpose of this study was to identify risk factors and develop a risk score for postDischarge nausea and vomiting (PDNV) after ambulatory surgery.

Background   Approximately 25% of all surgical patients will develop postoperative nausea and vomiting (PONV). While there are published consensus guidelines to help identify and treat patients at risk for PONV, further research is needed to identify risk factors for the development of postDischarge nausea and vomiting. This is especially important given that more than 60% of surgeries in the United States are now performed on an ambulatory basis. Having a simplified risk score would help anesthesia providers tailor prophylactic regimens to prevent PDNV in at-risk patients.

In this study the investigators examined the incidence of PONV and PDNV. They also identified risk factors and a risk score for the development of PDNV in a group of ambulatory surgery patients. PONV was defined to include the time period from PACU admission until discharge home. PDNV was defined to include the time period from discharge home until 48 hours after emergence from anesthesia.

Methodology   This was a multicenter study conducted on 2,493 adults at 12 ambulatory surgery centers in academic centers around the United States. All patients were scheduled for outpatient surgery in which general anesthesia with intubation or laryngeal mask airway placement was anticipated. Anesthetic agents/techniques and PONV antiemetic prophylactic regimens used were based on local institution standards. Nausea and/or vomiting were evaluated in the PACU at 30, 60 and 120 min after surgery using an 11-point verbal numeric rating scale. Severe nausea was defined as a score of 7 or greater on the scale, and severe vomiting as three or more emetic episodes during any given time interval. Patients were provided with a diary and they recorded the severity and incidence of nausea and/or vomiting after discharge home for 48 hours after emergence from anesthesia.

The primary outcome was the percentage of patients with PDNV until 48 hours after emergence from anesthesia. Secondary outcomes included:
1. percentage of patients with vomiting after discharge
2. percentage of patients with nausea after discharge
3. percentage of patients with PONV in PACU
4. PONV and PDNV severity incidence

Multiple logistic regression was used to identify risk factors and develop a risk score for postDischarge. Sample size calculation was appropriate.
Result  A total of 2,170 patients were included in the analysis. The average age of patients was 50 yrs. A majority of patients were nonsmoking (85%), Caucasian (74%), female (65%) with 30% having a history of PONV. The four most common surgical procedure types included:

1. general surgery (20%) (41% of general surgery = laparoscopic cholecystectomy)
2. gynecological surgery (11%)
3. arthroscopic knee surgery (11%)
4. breast surgery (10%)

Laparoscopic approaches were used in 38% of all surgeries. A majority of patients (66%) received sevoflurane. A prophylactic serotonin receptor antagonist antiemetic was administered to 77% of patients, 48% received dexamethasone, 13% a dopamine antagonist, and 2.5% a histamine antagonist. Total intravenous anesthesia was not used, although 752 patients (35%) received additional boluses or infusions of propofol. There were 35% who received two intraoperative antiemetics and 12% who received three intraoperative antiemetics.

The overall incidence of postDischarge nausea and vomiting was 37%. The overall incidence of PONV was 21%. (See Figure 1). During both time periods the following factors were independent predictors of PONV and PDNV (Table 1):

1. female gender
2. age < 50
3. history of PONV
4. opioid use in the PACU

Additional predictors that increased the risk of PONV included >125 mcg of fentanyl intraoperatively, and arthroscopic and laparoscopic surgical approaches. Ondansetron administration intraoperatively decreased PONV incidence.

The only additional predictor of PDNV was nausea in the PACU. Patients who experienced nausea in the PACU had a 3-fold increased risk for PDNV.

Risk factors that were not independent predictors of PONV or PDNV included a history of motion sickness or migraines, ASA physical status, drinking status, and adjuvant peripheral nerve blocks.

A simplified risk score for PDNV in ambulatory surgery patients demonstrated that when zero, one, two, three, four, and five risk factors were present the incidence of PDNV was 11%, 18%, 31%, 49%, 59%, and 80% respectively.

Conclusion  Almost 40% of patients experienced PDNV. Anesthesia providers can use the simplified risk score developed in this study to identify patients who may be at risk for PDNV and thus benefit from prophylactic long-acting antiemetics.

Comment  PDNV is not a new problem, however it is a less well understood phenomenon compared to PONV. In this study, 37% of patients experienced PDNV, with over
13% experiencing severe nausea. These results tell me that we need to do a better job of identifying and prophylactically treating patients with long-acting antiemetics (e.g., aprepitant, scopolamine) using evidence-based guidelines.

The use of simplified risk scores, where each risk factor is given one point, make it easy for anesthesia providers to quantify a given patient’s risk of PONV or PDNV. However, these risk scores do not tell us which factors are most significant. For example, the strongest risk factor for PONV was a laparoscopic procedure (i.e., cholecystectomy). These patients had a 2.4-fold increased risk of PONV. For PDNV, nausea in the PACU was the strongest predictor, which increased the risk 3-fold. I think anesthesia providers should keep these factors in mind when deciding which patients should receive prophylaxis.

It is not surprising that ondansetron and dexamethasone did not reduce the incidence of PDNV up to 48 hours after emergence from anesthesia. These medications have a relatively short half-life when compared to long acting agents such as apreptinant or scopolamine. I think this brings home the point that we should start thinking more about utilizing some of these long acting antiemetic agents in high-risk patients. Anesthesia providers should use the risk factors and risk scoring system to help in the prevention of PDNV.

Dennis Spence, PhD, CRNA

The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.

### Table 1. Independent Predictors of PONV and PDNV

<table>
<thead>
<tr>
<th></th>
<th>PONV Period</th>
<th>Adjusted OR</th>
<th>PDNV Period</th>
<th>Adjusted OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>2.19</td>
<td>Female gender</td>
<td>1.54</td>
<td></td>
</tr>
<tr>
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<td>Age &lt; 50 yrs</td>
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<td>PONV hx</td>
<td>1.43</td>
<td>PONV hx</td>
<td>1.50</td>
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<td><strong>Intraoperative Variables</strong></td>
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<td>&gt;125 µg fentanyl in surgery</td>
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<tr>
<td>Opioids in PACU</td>
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<td>Opioids in PACU</td>
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<tr>
<td></td>
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<td>Nausea in PACU</td>
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**Note:** OR = odds ratio
**The 50% and 95% Effective Doses of Desflurane for Removal of the Classic Laryngeal Mask Airway in Spontaneously Breathing Anaesthetized Adults**

Anesthesia 2011;66:274-277
Hui MT, Subash S, Wang CY

**Abstract**

**Purpose**  
The purpose of this study was to determine the 50% and 95% effective dose (ED) at which the classic LMA could safely be removed in anesthetized adults who were spontaneously breathing desflurane.

**Background**  
LMAs are used extensively for airway management in patients presenting for outpatient surgery requiring general anesthesia. Some recommend removing the LMA when the patient is still deeply anesthetized, while others only recommend removal after the patient is awake. The rationale for removing the LMA when the patient is still deeply anesthetized is that this minimizes the incidence of coughing, bucking, breath holding, biting on the tube, bronchospasm, and laryngospasm. Desflurane has a rapid recovery profile for return of upper airway reflexes, and some investigators recommend removing the LMA when the patient is still deeply anesthetized because airway reflexes return quickly.

**Methodology**  
This was a prospective, descriptive study of 38 adult (18-44 years) ASA I or II patients presenting for elective minor surgery under general anesthesia with an LMA. Patients with a history of GERD, substance abuse, neck pathology, reactive airway disease, suspected difficult airway or BMI > 35 kg/m² were excluded. After informed consent was obtained, unsedated patients were transported to the operating room for induction of anesthesia.

Anesthesia was induced with propofol 3.5 mg/kg, then an LMA size 4 for males and size 3 for females was placed according to the manufactures recommendations. Anesthesia was maintained with 50% nitrous oxide and 50% oxygen at 2 LPM and desflurane. Paracetamol 40 mg was given after induction. Local anesthesia or regional blockade was performed on all patients. No opioids were administered.

At the end of the surgery the nitrous oxide was discontinued and oxygen increased to 6 LPM. The end-tidal desflurane concentration for patient number one was set to 6% for 10 minutes before removal of the LMA. All LMAs were removed after suctioning and lifting the jaw (authors did not state if cuff was deflated). The patient was then given oxygen via face mask at 10 LPM.

Using the Dixon up-down method, each subsequent patient had the desflurane concentration increased or decreased in increments of 0.1%, depending on the previous patient’s response. Successful removal of the LMA was defined as: absence of coughing, gagging, clenched teeth, biting on tube, airway obstruction, body movement within 1 minute of removal, breath holding, laryngospasm or desaturation to SPO₂ <90%, and bronchospasm. If removal was successful the next patient had their end-tidal concentration decreased by 0.1%, if removal was unsuccessful the concentration was increased by 0.1%. This continued until at least 6
crossover pairs occurred. The ED$_{50}$ and ED$_{95}$ were determined using Probit analysis.

**Result** A total of $n = 38$ subjects completed the study. Three were excluded; 1 had a severe laryngospasm on induction and the other 2 required opioids to facilitate LMA placement. This left $n = 35$ for the analysis. Seventy-one percent of subjects were female with a mean age of 27 ± 6 years, weight of 56 ± 12 kg, and height of 161 ± 0.1 cm. Surgical duration was 49 ± 26 minutes. The most common surgical procedure was breast biopsy (66%), followed by minor orthopedic procedures (28%),inguinal hernia repair (13%), and lipoma excision (3%). None of the patients reported pain after completion of the surgeries.

There were 13 subjects who had failed LMA removal. The reasons for failed LMA removal are listed in Table 1. The desflurane ED$_{50}$ for smooth LMA removal was 5.29% (95% CI: 5.13-5.38%) and the desflurane ED$_{95}$ for smooth LMA removal was 5.55% (95% CI: 5.43-6.39%) (Figure 1). The MAC ratio for the ED$_{50}$ was 0.88 and for the ED$_{95}$ was 0.93.

**Conclusion** In unpremedicated ASA I and II patients who received desflurane and no opioid for maintenance, the effective concentration for safe LMA removal in 50% and 95% of patients was 5.29% and 5.55%, respectively.

**Comment** This is the second study this year published on the safe removal of the classic LMA when desflurane was used. This study was conducted in Malaysia and the previous study by Sahiner et al in Turkey. In both studies nitrous oxide was used but turned off 10 minutes before beginning to change the desflurane concentration. The major differences I see between the studies are that the desflurane concentration started at 6% in this current study and was titrated down in 0.1% increments. Whereas in the Sahiner et al study the desflurane concentration was set at 4% and titrated up or down in 0.5% increments. Additionally, in this current study more events were used to classify “LMA removal failure.” In the Sahiner et al study unsuccessful LMA removal was defined as the occurrence of the following complications: coughing, teeth clenching, gross purposeful movements, breath holding, laryngospasm, or desaturation <90% within 1 minute of LMA removal.

In the Sahiner et al study the ED$_{50}$ and ED$_{95}$ were 2.1% (95% CI: 1.1-2.9%) and 3.9% (95% CI: 3.1-7.9%), respectively. The ED$_{50}$ and ED$_{95}$ to the MAC ratio of desflurane were 0.4 and 0.7, respectively. However, in this current study the ED$_{50}$

<table>
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<tr>
<th>Table 1. Causes of Failed LMA Removal in n = 13 Subjects</th>
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<td>------------</td>
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<tr>
<td>Gross purposeful movement</td>
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<td>Airway obstruction</td>
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<tr>
<td>Clenching of teeth</td>
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<td>Coughing</td>
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<td>Biting on LMA</td>
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<td>Breath holding</td>
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<td>Gagging</td>
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<td>Laryngospasm</td>
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<tr>
<td>Bronchospasm</td>
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<td>Desaturation &lt; 90%</td>
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**Note.** Data is n (%). Some subjects experienced more than one event.
and ED_{95} were considerably higher at 5.29% and 5.55%, respectively. These results make me scratch my head as to why one would see such dramatic differences. I think the broader list of events defined as LMA failure is probably the most likely explanation for the higher ED_{50} and ED_{95} found in this current study. This would result in more events being defined as a failure unless anesthetic depth was increased. The higher desflurane concentration at which the first patient started may have influenced the results in some way as well.

Limitations to this study include that the investigators did not report the frequency of smoking in their sample. Additionally, the investigators did not state if the LMA was removed inflated or deflated. If the LMA was removed deflated, it is possible this could have contributed to the higher MAC ratios as compared to the Sahiner et al study. In the Sahiner et al\textsuperscript{1} study the LMA was removed inflated.

So at what desflurane concentration can one safely remove an LMA? Well, I think it is probably somewhere between 4%\textsuperscript{1} and 6%, which is the ED_{95} in both studies. It is important to point out that in both studies the patients did not receive any opioids. Given opioids blunt the airway response, I think if the patient has a good opioid load on board, one could safely remove the LMA when the patient is at a lower concentration. If minimal or no opioids are used then I would go at closer to 6%. Of course, one must consider the patient’s comorbidities and other surgical/anesthetic factors when deciding to remove the LMA deep. I tend to leave the LMA in until the patient is fully awake, however results of this study and the one by Sahiner et al\textsuperscript{1} at least provide me with some evidence to support removal of the LMA deep in a patient who received desflurane.

**Dennis Spence PhD, CRNA**


The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.