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**Abstract**

**Purpose**  The purpose of this study was to compare success rates for advancement of an Eschmann stylet using a standard or modified (curved) Magill forceps in patients with difficult airways undergoing nasotracheal intubation using one of three indirect laryngoscopes (Airtraq, CMAC, or GlideScope).

**Background**  Nasotracheal intubation is required for many oral and maxillofacial surgeries. Patients with upper airway swelling, facial and pharyngeal deformities, and those with known difficult airways may be difficult to intubate by the nasal route. Some anesthesia providers use an Eschmann stylet with a straight Magill forceps and indirect video laryngoscope for nasal tracheal intubation. However, in a previous study, investigators found that the standard straight Magill forceps could not advance the endotracheal tube during nasotracheal intubation with indirect video laryngoscopy. The investigators hypothesize that the use of a modified pair of curved Magill forceps might be more effective for nasotracheal intubation with a video laryngoscope.

**Methodology**  This was a prospective study which randomized 150 subjects to one of six groups. (N = 25 in with each of 3 indirect laryngoscopes and each of those using 2 different Magill forceps, straight or curved.) After induction of anesthesia, subjects with an anticipated difficult airway were randomized to nasotracheal intubation with an Airtraq, C-MAC, or GlideScope and with either a straight or curved pair of Magill forceps. Difficult airway was defined as Mallampati score of 4; interincisor distance ≤2.5 cm, history of difficult intubation, or upper airway tumor or swelling. Subjects were intubated by one of nine anesthetists with at least 2 years experience who had performed more than 10 successful nasotracheal intubations with each laryngoscope. During laryngoscopy, the anesthetist used the forceps (straight or curved) to grasp the Eschmann stylet and advanced it into the larynx, then slide the endotracheal tube over the stylet into the glottis.

The primary outcome was the success rate of passing the Eschmann stylet into the glottis with either the straight or curved Magill forceps. The investigators also recorded the time to advance the stylet, time to intubation, and Cormack and Lehane grade view. Sample size calculation and statistical analysis were appropriate.

**Result**  There were no significant differences between the groups in demographics or predictors of...
difficult airway. Overall, 67% of subjects had more than one predictor of a difficult airway.

Use of the curved Magill forceps was associated with a higher likelihood of successful advancement of the Eschmann stylet into the glottis (93% vs. 65%, P < 0.0001; Figure 1). The time to advance the stylet into the glottis was significantly longer with the straight Magill forceps compared to the curved forceps (P = 0.0002; Figure 2). The Airtraq laryngoscope provided a significantly better glottic view compared to the C-MAC or GlideScope (Grade I view rate: 54% vs. 40% vs. 36%, P = 0.024). However, time to intubation was longer with the Airtraq compared to the C-MAC and GlideScope (113 sec vs. 86 sec vs. 88 sec, P = 0.01). The overall intubation failure rate was 11% and this was similar between the three different laryngoscopes. Nosebleeds occurred in 36% of patients. One laceration of the maxillary gingiva occurred during laryngoscopy with an Airtraq.

**Conclusion**

The curved forceps advanced the Eschmann stylet into the larynx 90% of the time with the Airtraq, C-MAC, or GlideScope indirect laryngoscopes. The reason for the higher success was that the curved forceps curved at an angle similar to that of the indirect laryngoscopes studied.

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**Figure 1. Success Advancing Eschmann Stylet Through Glottis**

![Graph showing success rate comparison between straight and curved forceps with Airtraq, C-MAC, and GlideScope.](image)

**Figure 2. Time to Advance Eschmann Stylet Through Glottis**

![Graph showing time to intubation comparison between straight and curved forceps with Airtraq, C-MAC, and GlideScope.](image)

*Note.* Airtraq vs. GlideScope P = 0.0053, Airtraq vs. C-MAC P = 0.0018, C-MAC vs. GlideScope P = NS.
**Comment**

Videolaryngoscopy has become the primary go-to device for difficult airway management by many anesthetists. Nasal intubation can be challenging in patients with predictors of a difficult airway and indirect videolaryngoscopy can help improve the glottic view; however, the problem with these devices is that a great view does not always mean an easy intubation. Navigating the endotracheal tube into the glottis can be challenging, especially during nasal intubation. Many times anesthesia providers need to use a pair of Magill forceps to help guide the endotracheal tube into the glottis.

I must admit, I have never used an Eschmann stylet for a nasal intubation, but it does seem like this would help with intubation because it is easier to grab with the forceps, and it does not cause the accidental rupture of the endotracheal tube cuff. The problem is that most Eschmann stylets are somewhat stiff and would be prone to cause a nosebleed. As we saw in this study, over a third of patients developed nosebleeds.

This study addressed a real clinical problem; that we need a pair of Magill forceps that match the curve of indirect devices that help with laryngoscopy without causing significant airway trauma. Unfortunately, I do not think my facility stocks the curved Magill forceps, but I think based on these results I may ask my supply personnel to order a pair. I encourage anesthesia providers to consider doing the same.

**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.
**Effect of Intraoperative High Inspired Oxygen Fraction on Surgical Site Infection, Postoperative Nausea and Vomiting, and Pulmonary Function**

Anesthesiology 2013;119:303-16

Hovaguimian F, Lysakowski C, Elia N, Tramèr MR

**Abstract**

**Purpose** The purpose of this study was to provide a current meta-analysis of the effects of a high F\textsubscript{I}O\textsubscript{2} on the incidence of wound infection, PONV, and pulmonary complications in patients receiving general anesthesia.

**Background** Some, but not all, studies examining the effects of 80% oxygen use during general anesthesia have reported lower rates of wound infections and PONV. Other studies have examined these effects and been unable to reproduce them. Furthermore, 100% oxygen has been reported to result in atelectasis after only a few minutes exposure during general anesthesia. These effects are important; wound infections increase health care costs dramatically. Previous meta-analyses of the effects of high F\textsubscript{I}O\textsubscript{2} have been equivocal. A number of additional clinical trials warrants a renewed meta-analysis.

**Methodology** This meta-analysis use PRISMA standards (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Randomized trials comparing “high” F\textsubscript{I}O\textsubscript{2} with a “normal” F\textsubscript{I}O\textsubscript{2} in adults throughout general anesthesia were selected for inclusion. (F\textsubscript{I}O\textsubscript{2} in the postoperative period was not studied.) In addition, all “high” F\textsubscript{I}O\textsubscript{2}s were at least 50% oxygen and “normal” F\textsubscript{I}O\textsubscript{2}s were less than 50% oxygen and half or less of the “high” F\textsubscript{I}O\textsubscript{2}. Thus, if the “high” F\textsubscript{I}O\textsubscript{2} was 80%, the “normal” F\textsubscript{I}O\textsubscript{2} it was compared against could be no more than 40%.

Original articles were searched for information about confounding factors, especially in regards to wound infections. Confounders were taken into consideration during meta-analysis. PONV results were divided into early PONV (0-6 hours postop) and late PONV (0-24 hours postop). Pulmonary complications included any adverse outcome either in the airways or alveoli or an alteration in alveolar to capillary oxygen transport.

**Result** The investigators examined 204 studies published between 2000 and 2012 and analyzed data from 26 studies that included 7,001 patients. Data from 900 of these patients had not been included in a previous meta-analysis. The median “high” F\textsubscript{I}O\textsubscript{2} was 80% (range 80% to 100%). Median “normal” F\textsubscript{I}O\textsubscript{2} was 30% (range 30% to 40%).

Wound infection information was included in 9 studies (5,103 patients). In 8 of these 9 studies ≥ 90% of patients received prophylactic antibiotics. Surgery types included: colorectal, appendectomy, abdominal, and gyn. Wound infection rates with “normal” F\textsubscript{I}O\textsubscript{2} averaged 14% (range 7% to 27%) vs. 11% in the “high” F\textsubscript{I}O\textsubscript{2} group (relative risk 0.77). Wound
infection rates were also analyzed separately in the colorectal surgery group which included 1,977 patients. Their average wound infection rate with a “normal” F$I$O$_2$ was 19% vs. 15% with a “high” F$I$O$_2$ (relative risk 0.78). Overall, the risk of wound infection decreased 23% in the “high” F$I$O$_2$ group.

PONV was evaluated in 2,293 patients. In “normal” F$I$O$_2$ patients, the rate of late nausea was 25% vs. 19.5% in the “high” F$I$O$_2$ group (relative risk 0.79). Early nausea was not affected by F$I$O$_2$. The effects of “high” F$I$O$_2$ were most noticeable in patients who had not received prophylactic antiemetics.

Pulmonary complications were evaluated in 3,698 patients. In “normal” F$I$O$_2$ patients the rate of atelectasis was 11% vs. 8% in the “high” F$I$O$_2$ group (relative risk 0.93). One study examined postoperative pulmonary function tests (PFTs). In this group, PFTs worsened as BMI increased in the “high” F$I$O$_2$ group.

**Conclusion**

Using an F$I$O$_2$ of 80% or greater during general anesthesia resulted in a modest reduction in the incidence of wound infection in patients who received prophylactic antibiotics compared to using 30% oxygen. A “high” F$I$O$_2$ reduced the risk of PONV slightly; primarily in patients who did not receive prophylactic antiemetics. Finally, a “high” F$I$O$_2$ did not increase the risk of atelectasis.

**Comment**

In recent years, there have been a number of studies that hinted at high F$I$O$_2$ during general anesthesia reducing the risk of PONV. None of them were really convincing. Similarly, we now know that wound infections are less likely when the tissue near the wound is well oxygenated and well perfused, so it makes some sense that higher F$I$O$_2$s might reduce the risk of wound infections. This meta-analysis shows pretty convincingly that a high F$I$O$_2$ reduces the risk of wound infection and PONV in at least some patients, though fairly modestly. Incidentally, this is a good example of why meta-analysis are important. Before reading this study, I would not have been willing to say that a high F$I$O$_2$ would reduce wound infections or PONV at all.

How do we use this information clinically? Since the positive effect of a high F$I$O$_2$ is quite weak, it is tempting not to worry about it at all. But in the case of wound infections I think we would be wise to consider the potential benefits of a high F$I$O$_2$. Here’s why: in 2011 Health Affairs reported that postoperative infections were the most common and most costly complication in all of healthcare. The average cost of a wound infection in adults was an additional $3,364 for over a quarter million patients a year amounting to a yearly cost to the healthcare system of over 13 Billion dollars. Even a 10% reduction would be over 25,000 fewer wound infections each year for a savings of 85 Million. At that scale, even a small decrease in wound infection rates becomes worth going after. (Health Aff 2011;30:596 or in Anesthesia Abstracts Volume 5 Number 6; June 2011.)

Michael A. Fiedler, PhD, CRNA
Leukocyte DNA damage and wound infection after nitrous oxide administration


Abstract

Purpose The purpose of this study was to compare white blood cell DNA damage in patients who had received nitrous oxide (N₂O) during major colorectal surgery with those who had not received N₂O. A secondary goal was to correlate leukocyte DNA damage with the incidence of postoperative wound infection.

Background Postoperative wound infections are a leading cause of surgical morbidity and mortality. Colorectal surgery patients have perhaps the highest rate of wound infections, up to 25% in the first week postop. Nitrous oxide is known to inhibit methionine synthase which plays a role in the process of DNA synthesis. Past studies have reported more DNA damage in OR personnel regularly exposed to N₂O than in personnel working outside the OR. Also, some studies suggest that 80% oxygen administered during general anesthesia reduced the wound infection rate. If a high F₁O₂ helps prevent wound infections, administering N₂O would be undesirable for this reason as well. Conversely, a high F₁O₂ may result in DNA damage due to free radical production.

Methodology This was a prospective, randomized, double-blind controlled trial. Lab personnel were also blinded to the group assignment of the blood they were testing for leukocyte DNA damage. Adults undergoing elective open colorectal surgery were included. Exclusion criteria included bowel obstruction, ongoing infection, fever within 24 hours preop, and those in whom nitrous oxide was contraindicated. All patients received antibiotics prophylactically before surgery and for 24 hours postop. Wounds were irrigated with povidone iodine solution.

Randomization was stratified to insure that factors other than N₂O administration that might affect the incidence of wound infections were equally distributed between groups. All anesthetics included propofol, sevoflurane, remifentanil, morphine, and rocuronium. Anesthesia machine flowmeters, vaporizers, and monitoring displays were shielded to prevent surgeons from knowing whether patients were in the N₂O group or not. Core temperature was kept above 35.5°C with forced air warming. One group received 30% oxygen, the second 80% oxygen, and the third 70% N₂O.

The presence of wound infections were assessed according to the ASEPSIS scale and the Centers for Disease Control and Prevention (CDC) criteria. Patients were followed for 30 days postop. Blood was taken to test for leukocyte DNA damage immediately before induction and 24 h postop.
**Result**  Data from 91 patients in three groups were analyzed. The median duration of general anesthesia was 2.8 hours, and the duration was not different between groups. Baseline DNA damage (measured before induction) was similar among groups. The presence of comorbidities, types of surgery, and preop lab values were also similar between groups. The lowest average core temperature was 36.3°C and did not differ between groups. Supplemental use of epidural analgesia ranged from 10% to 20% between groups but was not statistically significantly different.

Postoperatively, patients in the N₂O group had twice as great an increase in the percent leukocyte DNA damage as did the oxygen groups (P=0.0003). DNA damage was proportionate to the dose of N₂O received during anesthesia (r = 0.33, P=0.029). By ASEPSIS criteria the incidence of wound infections was higher in N₂O patients compared to 30% oxygen or 80% oxygen (odds ratio 4.29, P=0.036). By CDC criteria N₂O was not associated with an increase in wound infections (odds ratio 3.36, P=0.205). Patients who developed a wound infection spent over 12 days longer in the hospital (P=0.028).

**Conclusion**  An increase in leukocyte DNA damage postop was associated with a higher incidence of wound infections and 70% N₂O was associated with leukocyte DNA damage. The extent of the DNA damage was dependent upon the duration of N₂O exposure, and was most likely when N₂O was used for longer than 2 hours. The oxygen concentration, 30% vs. 80%, had no effect on leukocyte DNA damage.

**Comment**  For a long time the most critical thing we could say about N₂O was that it increased the risk of PONV moderately. Evidence over the last year has suggested that N₂O may increase the risk of postoperative cardiovascular morbidity in at least some patients when administered for 4 hours or longer (Anesth Analg 112:387-393 or Anesthesia Abstracts March, 2012, Volume 6 Number 3). Now comes a pretty solid study showing that 70% N₂O increases the risk of wound infections by 3x to 4x at least in high risk patients (colorectal surgery). This is a big deal. Postoperative infections are the most common and most costly complication in all of healthcare (average $3,364 for over 250,000 patients a year, Health Aff 2011;30:596 or in Anesthesia Abstracts Volume 5 Number 6; June 2011). At that rate, anesthesia could potentially make a huge dent in the rate of wound infections simply by ceasing to use N₂O. I’ve long been a defender of N₂O. By that I don’t mean I always used it, but that I defended it’s use in general; always considering it’s use in a specific patient by weighing the risks vs. benefits. I’m now finding N₂O harder and harder to defend. If the ENIGMA-II trial shows increased risk of cardiovascular morbidity after general anesthetics that include N₂O and this data showing increased infections is shown to apply to a wide range of patients and surgeries we will have to think hard about saying good-by to N₂O forever.

**Michael A. Fiedler, PhD, CRNA**

ASEPSIS = Additional treatment, Serous discharge, Erythema, Purulent exudate, Separation of deep tissues, Isolation of bacteria, and duration of inpatient Stay.
Effect of Preemptive and Preventive Acetaminophen on Postoperative Pain Score: A Randomized, Double-Blind Trial of Patients Undergoing Lower Extremity Surgery

Khalili G, Janghorbani M, Saryazdi H, Emaminejad A

Abstract

**Purpose**  The purpose of this study was to compare the effects of preemptive administration of intravenous acetaminophen vs. placebo on postoperative pain and total opioid consumption in patients undergoing elective lower extremity orthopedic surgery under spinal anesthesia.

**Background**  Preemptive analgesia is defined as the administration of analgesics prior to painful stimuli. Preventive analgesia is defined as administration of analgesics to block pain and afferent signals at the time of surgical incision closure while under anesthesia. Both techniques reduce or prevent central sensitization caused by incisional and inflammatory processes and thus decrease postoperative pain and analgesic requirements. However, there are conflicting results in the literature as to which antinociceptive technique is more effective.

Intravenous acetaminophen is believed to inhibit prostaglandin synthesis in the central nervous system and may block peripheral pain impulses by inhibiting activation of nociceptors. It is theorized to work centrally by preventing central sensitization. Intravenous acetaminophen has a peak onset of 15 minutes, a half-life of 2.4 hours, and an approximate duration of action of 6 hours. There have been no studies published which have compared preemptive to preventive administration of intravenous acetaminophen in patients undergoing elective lower extremity orthopedic surgery under spinal anesthesia.

**Methodology**  This was a prospective, double-blind, placebo controlled trial of 75 adults undergoing elective lower extremity orthopedic surgery. Patients were randomized to one of three groups:

1. Placebo: 100 mL normal saline 30 minutes prior to surgery and prior to skin closure.
2. Preemptive: 15 mg/kg acetaminophen 30 minutes prior to surgery and 100 mL normal saline prior to skin closure.
3. Preventive: 100 mL normal saline 30 minutes prior to surgery and 15 mg/kg acetaminophen before skin closure.

All patients received diazepam 0.2 mg/kg and a preload of 15 ml/kg lactated Ringer’s solution prior to spinal placement. Spinal anesthesia consisted of administration of 15 mg isobaric 0.5% bupivacaine. No analgesics were administered intraoperatively unless requested by the patient. Patients received as needed meperidine 0.05 mg/kg postoperatively. Pain scores were measured at 6, 12, 18, and 24 hours using a 0-10 verbal rating scale. Total meperidine...
administered during the first 24 hours was recorded. Sample size and statistical analysis was appropriate.

**Result**  A total of 75 subjects completed the study (25 in each group). No significant differences were found in demographic or surgical characteristics; however, patients in the preemptive group were approximately 8-9 years older than the other two groups (P = NS). Patients in the preemptive and preventive groups had approximately 40% lower pain scores compared to the placebo group at 6 hours (P <0.001). Pain scores were similar between the preemptive and preventive groups (P = NS). However, no significant differences were found at 12, 18, and 24 hours between the three groups (P = NS). Preemptive administration of intravenous acetaminophen reduced meperidine consumption by 45% compared to the placebo group (23 mg vs. 42 mg, P = 0.003). While preventive administration reduced pain scores by 29% compared to placebo, this difference was not significant. The preemptive group required 7 mg less meperidine during the first 24 hours compared to the preventive group; however, this difference was also not statistically significant. Time to first analgesic request was three minutes longer in the two treatment groups; however, this difference was not clinically relevant (preemptive = 10.8 ± 4.4 vs. preventive = 10.7 ± 4.3 vs. placebo = 7 ± 3.3, P = 0.008).

**Conclusion**  Preemptive and preventive administration of intravenous acetaminophen reduced postoperative pain and opioid consumption in patients undergoing elective lower extremity orthopedic surgery under spinal anesthesia. Results do not strongly support an early (prior to incision) or late (prior to skin closure) administration time.

**Comment**  I thought this was a simple, well-designed, clinically relevant study. The investigators wanted to see if giving intravenous acetaminophen before skin incision (preemptive) or prior to skin closure (preventive) were
both better than placebo in patients undergoing lower extremity surgery under spinal anesthesia. So what do the results tell us? That preemptive or preventive administration of intravenous acetaminophen in this population reduced pain scores at 6 hours by up to 40%. However, beyond that time it had no effect, which is not surprising given the duration of action of intravenous acetaminophen (6 hours). They both also decreased opioid consumption by between 29% - 45%.

The authors argued that acetaminophen blocks central sensitization, however, all patients probably had some degree of blockade of central sensitization development by administration of the spinal anesthetic. The intravenous acetaminophen worked most likely by decreasing prostaglandin release, and based on the results it appears this might favor preoperative administration (preemptive) given opioid consumption was slightly lower. However, this difference was not statistically significant.

Unfortunately, the study was underpowered to examine differences in opioid consumption between preemptive and preventive administration of intravenous acetaminophen. Additionally, I think the authors should have statistically controlled for age and gender in their analysis given the modest differences in demographics.

So based on these results, I agree with the authors that it does not make a major difference which technique you use. If the case is short, you might consider administration before skin incision or if the procedure is long consider administration prior to skin closure. Also, consider administration of peripheral nerve blocks or injection of local anesthetics by the surgeon into the skin incision, and consider giving non-steroidal anti-inflammatory agents.

**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.
Pharmacology

PROFOUND HYPOTENSION AFTER ANESTHETIC INDUCTION WITH PROPOFOL IN PATIENTS TREATED WITH RIFAMPIN

Anesth Analg 2013;117:61–4

Abstract
Purpose This is a case report of severe and persistent hypotension following propofol induction in a patient taking rifampin. It also includes a post hoc statistical analysis of similar cases found in the scientific literature.

Background Rifampin is an antibiotic that inhibits bacterial RNA polymerase. It is used to treat tuberculosis, methicillin-resistant and methicillin-sensitive staph infections, and as a prophylactic antibiotic to prevent postoperative heart valve and bone infections. Intravenous rifampin can cause hypotension via reduced systemic vascular resistance. Propofol causes hypotension largely via venous dilation.

Methodology A 64 y/o, 88 kg woman with a BMI of 33 kg/m² presented for elective surgery. Her history included symptomatic GI reflux and panic attacks. She had undergone a stress test three years earlier which showed no myocardial ischemia. Preoperative medications included atorvastatin, esomeprazole, naproxen, and PRN hydrocodone. Her surgeon prescribed rifampin 600 mg PO the night before surgery and 2 hours preop as prophylaxis against infection.

Before induction her HR was 102 bpm and BP was 150/90. She received 2 mg midazolam and 150 µg fentanyl IV. Seven minutes later general anesthesia was induced with 2.3 mg/kg propofol and 1.1 mg/kg succinylcholine followed by endotracheal intubation.

Three minutes after induction, her BP fell to 60/30 and HR was 112 bpm. No signs of allergic reaction were present. Phenylephrine IV bolus and 10 µg/mL infusion were administered along with 800 mL crystalloid IV fluid, 10 mg ephedrine but systolic BP remained 70 mm Hg or lower. Next, a total of 80 µg (0.08 mg) epinephrine and 320 µg phenylephrine was administered which increased BP to 92/53. The phenylephrine drip was continued to keep systolic BP above 90 mm Hg. Surgery then began 35 minutes after induction. Her postoperative course was routine.

Result Following this event the authors selected 25 medical records for each of three specific case scenarios:
1. Rifampin prophylaxis and propofol induction
2. No rifampin and propofol induction
3. Rifampin prophylaxis and thiopental induction

The induction drug was an independent predictor of hypotension (P<0.001). There was no association between preexisting hypertension or NPO deficit and subsequent hypotension after induction of anesthesia.
Following rifampin and a propofol induction, mean arterial pressure (MAP) fell an average of 38 mm Hg; far more than following propofol alone (down 22 mm Hg) or rifampin and thiopental (down 16 mm Hg, P<0.001). Furthermore, after rifampin and propofol, hypotension persisted for an average 33 minutes despite treatment with larger doses of phenylephrine. In excess of 2 L crystalloid IV fluid was frequently administered without significant improvement in MAP. The overall odds of hypotension following rifampin and propofol induction were 11 times higher even after adjustment for comorbidities.

**Conclusion**

Inducing general anesthesia with standard doses of propofol following rifampin prophylaxis was associated with prolonged, severe hypotension.

**Comment**

I’m guessing few anesthesia providers have encountered patients who were on rifampin prior to their general anesthetic. But it is still used and this report is a great example of learning from the experience and problem solving of others. It only takes a few minutes to read this report, but that one time your patient is on rifampin you’ll be glad you did. When that day comes, we won’t have the option to use pentothal any longer in the USA but I suspect Brevital or etomidate would be acceptable alternatives.

**Michael A. Fiedler, PhD, CRNA**
Recovery from Anesthesia after Craniotomy for Supratentorial Tumors: Comparison of Propofol-Remifentanil and Sevoflurane-Sufentanil (the PROMIFLUNIL Trial)

J Neurosurg Anesthesiol 2013 June 14, [Epub ahead of print]
Necib S, Tubach F, Peuch C, LeBihan E, Samain E, et al

Abstract
Purpose The purpose of this study was to compare 2 different anesthetic strategies for their respective effects on recovery profiles in the first 24 hours post craniotomy for supratentorial tumor excision: 1) target concentration infusion of propofol and remifentanil vs. 2) anesthesia protocol with sevoflurane and sufentanil.

Background Assessment of state of consciousness following craniotomy is an important and necessary component of care as alterations can be indicative of serious complications. A rapid recovery from neuroanesthesia is essential. The choice of anesthetic agents for craniotomy should allow for the fastest return to consciousness possible. Numerous clinical trials conducted to date have assessed anesthetic agents for rapid recovery. Controversial results have been reported regarding the quality and rapidity of postoperative recovery. Additionally, most of the studies that have been conducted to date did not extend the assessments to greater than 3 hours post procedure.

Methodology This was a randomized, double-blinded clinical trial. Patients having elective intracranial surgery for removal of supratentorial tumors were randomized and placed in one of two groups:

Group PR (Propofol Remifentanil) The “Primea Base” infusion device was used for anesthetic delivery. Propofol was administered to achieve an initial plasma concentration of 3 µg/mL (using the Marsh model) and increased by 1 µg/mL until the BIS value was between 45-55. Remifentanil was infused at an initial target plasma concentration of 4 ng/mL (using Minto’s model). Muscle relaxation was then administered and the trachea intubated. Propofol infusion during maintenance was adjusted by increasing or decreasing the target plasma concentration by 1 µg/mL according to BIS values. Remifentanil plasma concentrations were adjusted during maintenance according to HR and MAP by increasing or decreasing target plasma concentrations by 0.5 ng/mL.

Group SS (Sevoflurane Sufentanil) A bolus of 0.2 µg/kg of sufentanil was administered followed 1 minute later by 3 mg/kg of propofol. Muscle relaxant was administered and the trachea was intubated. After induction, sevoflurane end-tidal concentrations were adjusted according to BIS values. Sufentanil was
administered by bolus doses of 0.1µg/kg according to HR and MAP.

All patients received standardized preoperative care, standardized intraoperative monitoring, standardized maintenance (IV fluid therapy, mechanical ventilation, etc), and muscle relaxant reversal medications. Maintenance medications were adjusted to keep BIS values between 45 and 55. BIS monitoring was suspended after dura opening, however anesthetics were kept at the same level as during BIS monitoring. After the dura was closed, BIS monitoring was reinstituted. Management of hyper- or hypotension was also standardized. A provider not involved in the anesthetic and blinded to the group each patient was in, extubated the patient. In the PACU (24 hours) data was collected by a blinded observer at predefined intervals including:

- vital signs
- sedation scores
- glasgow coma scale scores (GCS)
- visual analogue pain scores
- MMS scores (mini mental assessment)
- Aldrete scores

Postoperative care was also standardized. The primary outcome variable was the time from discontinuation of anesthesia to extubation.

Secondary outcome variables included:

1. time from discontinuation of anesthesia to response to a simple command
2. time from discontinuation of anesthesia to recovery of spontaneous ventilation
3. agitation score at emergence
4. Aldrete, GCS, MMS (mini mental state) and pain scores
5. needed intra operative vasopressors or anti hypertensive agents

**Result**

A total of 35 patients were in the SS group and 31 in the PR group. No difference was noted in the time from discontinuation of anesthesia to extubation (12 min. vs. 13 min. in PR and SS groups respectively). Statistical significance was NOT achieved for any secondary outcome variables, however, statistically significant differences were found in several non-outcome variables:

- **Time to achieve Aldrete Score ≥ 10:** SS group 8 hours vs PR group 14 hours
- **Time to achieve MMS score ≥ 30:** SS group 12 hours vs PR group 17 hours
- **Time to achieve GCS score ≥ 15:** SS group 2.5 hours vs PR group 7 hours

Additionally, there were no differences between the two groups regarding postoperative complications.

**Conclusion**

This study failed to demonstrate that the time to extubation was different between two anesthetic protocols using target concentration administration of propofol-remifentanil versus manual administration of sevoflurane and sufentanil. Additionally, it failed to establish statistical significance in any of the secondary outcome variables measured. And while the time to achieve an Aldrete score of 10, an MMS score of 30, and a GCS score of 15 was significantly shorter in the sevoflurane - sufantinil group, these variables were not prospectively established as outcomes to study during the 24 hour postoperative period.

**Comment**

One of the most notable limitations of this study is related to the small sample size in each arm and the
inability to achieve necessary power. The investigators failed to enroll the 45 patients in each group required to determine if a difference exists in the outcome variables measured. Additionally, they did find significance when measuring the time to achieve three recovery room observation scores, yet time to achieve longer term indicators of CNS recovery (Aldrete score, Mini Mental Status, Glasgow Coma Scale) was not intended to be part of the outcome comparisons between groups; the scores were simply available! Nevertheless, even after noting these limitations, there was a degree of innovativeness illustrated in this methodology. Requiring an anesthesiologist not involved in the case to extubate/emerger the patient but with gas analysis shielded from his/her view, and infusion pumps, whether used or not, placed in each operating room to prevent him/her from knowing which group the patient was in, was a good way to prevent bias. It is, however, a shame that the study was not completed to achieve the needed sample size. It remains to be seen whether or not this would have changed the results.

I agree with the authors however, that a plausible explanation for the results they observed may have been related to the dose of propofol used (1,899 ± 837 mg). The differences seen in the recovery profile and return to consciousness following propofol remifentanil maintenance compared to a sevoflurane sufentanil technique may have been biased by dosing the anesthetics based upon BIS values. The BIS is a controversial “monitor” to start with, and it’s track record during propofol and opioid anesthetics is even poorer than during inhalation agent techniques.

Surgical time did not vary much between groups (mean 20 minutes) and while adequate depth of anesthesia was achieved with both techniques, the recovery profile based on our knowledge of pharmacokinetics and pharmacodynamics of both propofol and sevoflurane may be why recovery was so much faster with these doses in the sevoflurane sufentanil group.

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Marsh Model and Minto’s Model: Pharmacokinetic models that attempt to describe relationships between doses of drugs and plasma concentrations of drugs with respect to time. They are mathematical models used to predict the blood concentration profile of a drug after a bolus dose or after an infusion of varying duration. These models are typically derived from measuring arterial or venous plasma concentrations after a bolus or infusion in a group of volunteers, using standardized statistical approaches and computer software. The computations are then employed in infusion pump software programs.