

## Post-Operative Effects: Comparison of Total Intravenous and Inhalational Anesthesia

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### Abstract

**Background:** Propofol is an intravenous anesthetic with known antiemetic properties. Less confirmed are its potential analgesic or antinociceptive postoperative effects when used as a maintenance anesthetic during surgery. We compared the postoperative effects of total intravenous anesthesia (TIVA) with propofol to those of inhalational anesthesia with sevoflurane and looked for differences in the quality of recovery of patients.

**Methods:** We studied 23 patients scheduled to undergo endoscopic sinus surgery (ESS). Using a double-blind experimental method, we randomly assigned patients to receive either TIVA with propofol/remifentanyl (PR) or inhalational anesthesia with sevoflurane/remifentanyl (SR). We measured degree of pain (per visual analog scale where 1=no pain and 10=worst pain imaginable), incidence of nausea and vomiting, and duration of recovery postoperatively.

**Results:** Mean pain rating was  $3.4 \pm 3.3$  in the PR group and  $5.3 \pm 2.8$  in the SR group. Median pain rating was  $3 \pm 3$  in the PR group and  $5.5 \pm 1.5$  in the SR group. In the PR group, 3 out of 12 patients reported a pain score  $> 4$ ; In the SR group, 6 out of 10 patients reported a pain score  $> 4$ . Only 1 incidence of nausea was reported per group. Narcotics administered were comparable between both groups. Mean recovery time was  $67 \pm 30$  minutes in the PR group and  $69 \pm 27$  minutes in the SR group.

**Conclusion:** We found no statistically significant difference between TIVA with propofol and inhalational anesthesia with sevoflurane as they relate to postoperative pain, nausea and vomiting, narcotic administration, and recovery time.

**Keywords:** Propofol; Sevoflurane; TIVA; PONV

### Introduction

Propofol is an intravenous hypnotic that is commonly used in total intravenous anesthesia (TIVA) because of its widely acknowledged antiemetic properties. However, it may be the better choice for induction and maintenance of anesthesia in patients due to a reported analgesic effect [1,2] that, combined with its antiemetic properties, provide patients with a better quality of recovery.

A recent editorial by White casts [3] doubt on whether or not propofol is indeed in possession of analgesic properties or if studies that discover that to be the case are merely a "statistical anomaly". Its post-operative effects must be verified and compared to those of a comparable maintenance anesthetic (i.e., sevoflurane) and found more favorable before a preference for propofol as a maintenance anesthetic can be justified.

The purpose of the present work was originally to compare the perioperative effect of TIVA with propofol and inhalational anesthesia with sevoflurane on blood loss and surgical field visualization in patients undergoing endoscopic sinus surgery (ESS). However, a secondary goal of this work was to compare the quality of recovery between patients anesthetized using TIVA (propofol/remifentanyl) to patients anesthetized using inhalational anesthesia (sevoflurane/remifentanyl) by evaluating post-operative nausea and vomiting (PONV), pain, administration of narcotics, and time to recovery. We hypothesized that patients anesthetized with TIVA using propofol would have less pain, PONV, and a faster recovery time post-operatively than those anesthetized with sevoflurane.

### Methods

This study was registered with the NIH and can be found at [http://](http://clinicaltrials.gov/ct2/show/NCT01214057)

[clinicaltrials.gov/ct2/show/NCT01214057](http://clinicaltrials.gov/ct2/show/NCT01214057). After obtaining approval from the Committee for the Protection of Human Subjects, twenty-three patients scheduled to undergo endoscopic sinus surgery (ESS) for chronic rhino sinusitis were consented and enrolled. Inclusion criteria were patient age between 18 and 80, chronic rhino sinusitis, American Society of Anesthesia (ASA) grade I or II, and indication of surgeon of need for ESS. Exclusion criteria included pregnancy, known coagulopathy, international normalized ratio greater than 1.3, partial thromboplastin time greater than 50 seconds, use of non-steroidal anti-inflammatory agents in the last 10 days (two or more doses), poorly controlled hypertension with a preoperative systolic blood pressure of 160 mm Hg or a diastolic blood pressure of 90 mm Hg, or taking more than two anti-hypertensives at the time of preoperative evaluation.

### Anesthetic protocol

Patients were randomly assigned using a blocked randomization method to receive either sevoflurane/remifentanyl (SR, n=11) or propofol/remifentanyl (PR, n=12) general anesthesia. Both patients

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and surgeons were blinded to the type of anesthetic used. Patients were premedicated in the holding area with dexamethasone and midazolam. The patients were monitored by American Society of Anesthesia (ASA) standards with ECG, non-invasive blood pressure, pulse oximetry and temperature probe. Their blood pressure was recorded every 2 minutes for the first 10 minutes, then every 5 minutes.

In order to reduce the visual bias of a propofol infusion, anesthesia was induced in both SR and PR groups with lidocaine 0.5 mg/kg, propofol infusion at 250 mcg/kg/min and total volume infused was adjusted for an induction dose of 2-3 mg/kg before bolus of muscle relaxant, rocuronium 0.5 mg/kg. Remifentanyl infusion was started at a rate of 0.4 mcg/kg/min one to two minutes before the propofol infusion and a 100 ml 0.9% normal saline bag was used to blind surgeons in the SR group. Sevoflurane 1-3% was administered to the SR group and the propofol infusion was stopped. After intubation the remifentanyl infusion was changed to 0.2 mcg/kg/min in both groups. In order to limit the amount of fluids administered, remifentanyl was diluted at a concentration of 4 mg in 100 ml.

The target mean arterial blood pressure (MAP) was maintained at 70-80 mm Hg by adjusting the propofol concentration within its range (100-150 mg) and the sevoflurane concentration within its range (1-3 vol%) according to the anaesthesiologist's judgement and by surgeon request. If this failed, the remifentanyl rate was adjusted by 0.05 mg/kg/min. The end-tidal CO<sub>2</sub> level was continuously monitored and adjusted to a concentration of 32-34 mm Hg.

### Surgery protocol

Patients were positioned in the reverse Trendelenburg position and four squeezed cottonoids soaked with a mixed solution of epinephrine and lidocaine (1:100000 epinephrine: lidocaine 2% at 1:1) were applied topically to each nasal cavity. The surgical procedures were performed by three fellowship-trained surgeons from the Department of Otorhinolaryngology at the University of Texas Health Science Center in Houston, TX with subspecialty training in endoscopic sinus surgery using a similar stepwise technique. The IV line and solutions were foiled to prevent the surgeon from seeing the color of the anesthetic agent used. All surgeries took place at Memorial Hermann Hospital – Texas Medical Center.

### Operative time

Surgical operating time (SOT) was defined as the time from the moment of injection of local anesthetic in the nasal cavity to the end of application of the local hemostatic agents. SOT was documented for each patient.

### Quality of recovery

The quality of recovery of patients was based on alertness and ventilator support/oxygenation at arrival to the post anesthesia recovery unit (PACU) from the time of extubation and again 30 minutes after arrival to the PACU, degree of pain reported by patient in PACU (as per a 10 point visual analog scale where 1= no pain and 10= worst pain imaginable), amount and type of opioid and non-opioid analgesic given at discharge (after second phase PACU or 23 hours day surgery), abnormal blood pressure or heart rate values that necessitated intervention after PACU transfer, incidence of nausea and vomiting, and delay in discharge (if patient was in day surgery unit).

### Postoperative analgesia

One microgram of fentanyl/kg was given if the patient's visual

analog scale (VAS) of pain was more than 6 before leaving OR. In the PACU, morphine 1-2 mg IV bolus every 5-10 minutes and ondansetron 4 mg IV bolus were administered if VAS > 4 and per patient request.

### Statistical Analysis

Intercooled Stata version 9.2 statistical software (Stata Corporation, College Station, TX) was used to perform data analysis. A p value of less than 0.05 was defined as statistically significant. Due to the pilot controlled nature of the study, a power analysis was deferred for the secondary aims of the study addressed in this paper. The study was powered only for the primary goal of blood loss assessment and it was determined that an N of 30 would be needed. A non-parametric analysis was conducted using the Wilcoxon–Mann–Whitney U test.

### Results

Twenty-three patients completed the study. No statistically significant differences were observed between the two groups with respect to age, gender, surgery duration, or duration of anesthesia (Table 1).

One subject's pain rating had to be excluded from the analysis due to incomplete documentation in the PACU. This exclusion reduced the number of subjects in the SR group to 10 for the pain rating analysis. In the PR group, patients' average VAS pain rating was 3.4 with a standard deviation of 3.3. The average patient rating of pain in the SR group was 5.3 with a standard deviation of 2.8. The median patient rating of pain in the PR group was 3 with a median absolute deviation of 3. In the SR group, patients' median pain rating was 5.5 with a median absolute deviation of 1.5. In the PR group 3 of the 12 subjects reported a VAS pain rating greater than 4, while 6 of the 10 subjects in the SR group reported a VAS pain rating of greater than 4 (Table 2). The Mann-Whitney U test was used to analyze the pain rating scores; a U of 82 resulted in no statistically significant difference between the two groups (two-tailed test).

In the PR group 2 subjects were treated with morphine post-operatively compared to 4 subjects in the SR group. In the PR group 3 patients received hydromorphone post-operatively compared to 1 patient in the SR group. In both groups 1 patient received midazolam post-operatively. The drug type and amount administered to subjects was comparable between the two groups except in the case of meperidine, which was administered to 2 subjects in the PR group to combat shivering.

Parameters	PR group (n=12)	SR group (n=11)	p-value
Age	51.3±16.2	50.3±16.0	0.89
Gender (male)	7 (58.3%)	6 (54.5%)	0.86
Duration of surgery (hours)	2.4±1.2	3.6±1.8	0.07
Duration of anesthesia (hours)	3.3±1.3	4.7±2.0	0.06

Data are presented as mean ± SD. There were no statistically significant differences between the two groups

**Table 1:** Patient demographics and total surgery and anesthesia time.

Group	Pain Rating Mean±SD	Pain Rating Median±MAD	Minimum	Maximum	VAS > 4 yes/no
PR (n=12)	3.4±3.3	3±3	0	9	3/9
SR (n=10)	5.3±2.8	5.5±1.5	0	10	6/4

There was no statistically significant difference between the two groups. VAS = visual analog scale for pain rating where 1= no pain and 10= worst imaginable pain. A non-parametric analysis was made using the Wilcoxon–Mann–

**Table 2:** Visual analog scale (VAS) pain ratings given by patients in the TIVA with propofol group (PR) and inhalational anesthesia with sevoflurane group (SR).

Only one incidence of nausea was reported per group (Table 3). The average length of recovery time in the PACU unit was 67 minutes for the PR group and 69 minutes for the SR group (Table 4). Student's t-test found the p-value to be a statistically insignificant 0.84.

## Discussion

The results of the study indicate no significant difference in the mean rating of pain between the two groups. While the means were not significantly different, it is of note that double the number of patients in the SR group reported a VAS pain rating of greater than 4 than patients in the PR group. This finding is consistent with Anker-Møller et al. [4]'s study which determined that propofol, in subhypnotic doses, reduces the amplitude of the pain-evoked potential while increasing the pain threshold. While our findings regarding a VAS pain rating greater than 4 between the two groups supports research that has found early post-operative pain to be less in patients anesthetized with TIVA using propofol [1,2], a lack of significant p-value between the means reported by both groups cannot conclusively refute studies that found there to be no difference in pain between patients anesthetized with TIVA using propofol and inhalational anesthesia using sevoflurane [5,6].

As this study looked at post-operative effects of anesthesia and surgeries were of duration longer than two hours, the use of propofol to induce anesthesia is not a confounding factor due to its half-life of 30 minutes [7]. Intravenously administered lidocaine also has the reported effect of reducing post-operative pain [8]. Although lidocaine was administered intravenously before the induction dose of propofol and locally to the sinuses, it was administered in both groups. Given the short half-life of lidocaine (approximately 10 minutes after initial parenteral administration and, after 30 minutes, a slower elimination phase of about 90 minutes) [9], the initial administration would have been metabolized by the end of surgery and it is unlikely that it had any effect post-operatively. Any molecular or chemical effects it may have had would have been present in both groups and therefore negligible.

The incidence of PONV in the PACU was the same in both groups with only one patient per group experiencing nausea. These results contradict studies that found the incidence of PONV to be significantly reduced in patients that received TIVA with propofol compared to patients that received inhalational anesthesia using sevoflurane [6,9,10] or inhalational anesthesia using other volatile anesthetics [11,12]. Although our study was limited by the number of patients enrolled (n=23), our findings are consistent with other larger studies that compared the incidence of PONV in patients anesthetized with TIVA using propofol and patients anesthetized with inhalational anesthesia using sevoflurane. Research by Watson and Shah [13] (n=40) and by Tan et al. [2] (n=80) found no difference in PONV between the two groups. While propofol was the induction agent used in both the PR

Group	Nausea	No Nausea
PR (n=12)	1 (8.33%)	11 (91.67%)
SR (n=11)	1 (9.09%)	10 (90.91%)

There was no statistically significant difference between the two groups

**Table 3:** Incidence of nausea in the PR group and in the SR group.

Group	Total time in PACU (mins)
PR (n=12)	67±30.41
SR (n=11)	69±27.04

Data are presented as mean ± SD. There was no statistically significant difference between the two groups

**Table 4:** Total recovery time of patients in both groups measured in minutes.

and SR group and research has found that it may have anti-emetic properties that may continue into the postoperative period even when used only as an induction agent [14], the average duration of surgery for both groups was well past the 30 minute half-life of propofol [7].

Recovery time between the PR and SR groups were comparable and no statistically significant difference was found. This finding confirms studies that indicate there is no difference in the total recovery time of patients anesthetized with TIVA using propofol and patients anesthetized with inhalational anesthesia using sevoflurane [6,12].

There are two limitations in this study that need to be acknowledged and addressed. The first is the pilot nature of the study; we were unable to recruit a sufficient number of patients to fulfill the requirements of the power analysis done for the primary goals of the study, much less for the secondary goals pertinent to this paper. The findings in this study must therefore be viewed cautiously due to the small sample size. A second limitation of the study is a lack of standardization in the management of patient pain post-operatively. In spite of this limitation, the variety and potency of the post-operative pain medication administered to patients does contribute to our evaluation of the post-operative analgesic effects of propofol and sevoflurane.

Due to the limitations of this pilot study, more research is needed to confirm the reported analgesic properties of TIVA using propofol [15]. The difference between the mean VAS pain ratings of the two groups followed in this study is not significant enough to warrant a change in protocol favoring TIVA using propofol as there was also no difference found in PONV or recovery time between the groups.

## Conclusions

This study found no statistically significant difference between TIVA with propofol and inhalational anesthesia with sevoflurane as they relate to postoperative pain, nausea and vomiting, narcotic administration, and recovery time.

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## Disclosure

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