

# Comparison of Sevoflurane-Nitrous Oxide and Target-Controlled Propofol with Fentanyl Anesthesia for Hysteroscopy

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A randomized prospective study was performed on the anesthetic induction, maintenance, and recovery characteristics of sevoflurane-nitrous oxide, compared to that of target-controlled propofol and fentanyl anesthesia, for forty day-case hysteroscopic surgery.

The patients in the sevoflurane group (n = 20) received sevoflurane-nitrous oxide for both induction (8%) and maintenance (1 - 2%) of anesthesia, while the patients in the propofol group (n = 20) received target-controlled propofol (4  $\mu$ g/ml, 3-6  $\mu$ g/ml as occasion demanded) with fentanyl (1  $\mu$ g/kg). In both groups, the airway was maintained by a facemask with the patient breathing spontaneously during the surgery. The mean times to unconsciousness and readiness for surgery were similar in both groups, with those for the sevoflurane group, compared to the propofol group being 80.4  $\pm$  18.9 vs. 83.6  $\pm$  38.8 sec, and 220.1  $\pm$  76.9 vs. 231.0  $\pm$  95.4 sec, respectively. Propofol was associated with significantly higher incidences of involuntary movement (30% vs. 5%) and apnea (35% vs. 0%) during the induction period than with sevoflurane. Hemodynamic variables were similar with the exception of significantly lower blood pressures during the first 5 minutes of induction with propofol. Emergence times to eye opening, hand squeezing and orientation for sevoflurane compared to propofol were: 316.6  $\pm$  79.3 vs. 507.4  $\pm$  218.8 sec, 390.0  $\pm$  69.3 vs. 653.1  $\pm$  201.6 sec and 380.6  $\pm$  80.8 vs. 666.3  $\pm$  208.7 sec, respectively, all of these being significantly faster for sevoflurane than propofol. The postanesthetic Aldrete's recovery scores of the patients immediately after surgery were higher in the sevoflurane group. Propofol was associated with more drowsiness, with sevoflurane being associated with more nausea, in the recovery period; however, neither delayed the time to discharge (103.7  $\pm$  28.1 vs. 99.0  $\pm$  36.2 min). In

conclusion, sevoflurane-nitrous oxide appears to be superior for day-case hysteroscopic surgery, than target-controlled propofol with fentanyl, with regards to the speed of recovery from anesthesia and the return to hemodynamic stability.

**Key Words:** Anesthetics, volatile; sevoflurane. anesthetics, intravenous; target-controlled; propofol. surgery; ambulatory; hysteroscopy.

## INTRODUCTION

Hysteroscopy is becoming a much more widely used technique, with diagnostic hysteroscopy replacing conventional dilatational curettage in the diagnosis of intrauterine pathologies.<sup>1</sup> Surgical hysteroscopy can also be used in the treatment of a septate uterus, uterine adhesions, and even in the resection of symptomatic submucous fibroids.<sup>2</sup>

Overall, this technique is short, easy and safe, and the need for tracheal intubation, using muscle relaxants, is unnecessary. As little postoperative pain is experienced the technique lends itself well to performance on a day-case basis.

Regional or general anesthetic techniques can be used and in day-cases or in an office based setting, where these procedures are increasingly being performed, but the requirement of "fit for discharge" can influence the choice of the agents used.

Sevoflurane and propofol share many properties that make them nearly ideal for outpatient anesthesia: both provide a rapid, smooth induction, allow for easy alteration of anesthetic depth during the maintenance period, and have fast emergence and recovery without serious side effects.<sup>3,4</sup>

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There have been several studies comparing propofol with sevoflurane for the induction and maintenance of, and recovery from, anesthesia in various settings with similar, but not identical, results.<sup>5-9</sup>

Despite the increasing clinical value of hysteroscopy, anesthesia for this is still controversial. There have been no reports comparing the use of sevoflurane-nitrous oxide with total intravenous propofol anesthesia by target-controlled infusion systems for the induction and maintenance of anesthesia during the procedure.

The objectives of our study were to evaluate the speed of induction and recovery, and the hemodynamic differences between the two techniques for day-case hysteroscopic surgery.

## MATERIALS AND METHODS

Institutional ethical approval and written informed consent were obtained from all patients. Forty females, ASA physical status 1, undergoing day-case hysteroscopic surgery were recruited. Contraindications to the use of spontaneously breathing general anesthesia techniques or the need for tracheal intubation were excluded.

No patient was premedicated. Shortly before anesthesia, base-line visual analogue scales (VAS) for pain, nausea, and drowsiness were assessed with 0 = minimal effect and 10 = maximal effect. Base-line cognitive function was evaluated with the mini-mental state test.<sup>10</sup> Computer-generated numbers randomly divided the patients into two groups.

All patients received 100% oxygen via a face-mask for 2 minutes prior to induction. For patients in the sevoflurane group (n = 20), a circle CO<sub>2</sub> absorber circuit with a 5 L reservoir bag was used. The circuit was primed with sevoflurane 8% in a 1 : 1 ratio of nitrous oxide to oxygen at a fresh gas flow of 8 L/min for 1 minute. Sevoflurane was administered with a Sigma Delta vaporizer (Penlon Ltd., Abingdon, England). Anesthesia was induced using the single-breath inhalation technique. The patients were asked to exhale fully, to take a deep breath with a primed face mask placed firmly over the nose and mouth, and then to hold their breath for as long as possible.

Thereafter, the patients were asked to breathe normally. After the loss of verbal command and eyelash reflex, the concentration of sevoflurane was decreased to 1% for maintenance because this surgery is generally short, easy, and nominal pain. The patients in the propofol group (n = 20) received bolus doses of 1 µg/kg fentanyl 2 minutes prior to the induction of anesthesia. The patient's ages and weights were entered into the TCI system (Master TCI UK, Fresenius Vial S.A., Le Grand Chemin, France). The target propofol was started at a concentration of 4 µg/ml, and if unconsciousness was not achieved within 3 minutes, was increased to 6 µg/ml. The infusion rate was set to flash mode, and the infusion line attached to the 20 gauge intravenous cannula on the patient's basilic or cephalic vein without an extension tube or three-way cobe. The patients received oxygen via a mask at 5 L/min during the anesthesia.

During the induction of anesthesia, when the patients stopped responding to the verbal commands to open their eyes, their eyelash reflex was tested. The disappearance of this reflex was interpreted as unconsciousness. The patient's times to unconsciousness and readiness for surgery (i.e. the time when the anesthesiologist considered that the anesthetic depth was adequate) were recorded.

The systolic and diastolic blood pressures and the heart rate were observed intraoperatively. Pulse oximetry, ECG, inspiratory nitrous oxide and oxygen concentration, as well as end-tidal CO<sub>2</sub> and sevoflurane were monitored continuously. Anesthesia was maintained and adjusted according to physiological parameters (movement, swallowing, tearing, sweating, tachycardia, and mean arterial pressure increases > 20% of base-line value) such that the target level of the propofol was within the range 3 - 6 µg/ml, and for the sevoflurane the end-expiratory sevoflurane level was within the range 1 - 2%.

Directly following surgery, the nitrous oxide and the anesthetic maintenance agents were stopped abruptly without tapering, with the patients then receiving 100% oxygen at the same flow rate (8 L/min).

Emergence from anesthesia was evaluated by recording the time from the end of surgery until

the patient was able to open their eyes, squeeze the observer's hand on command and be fully oriented as to the time and place. Time to sitting and walking without support was also recorded. VAS for pain, nausea, drowsiness, and minimal state scores were completed at 15, 30, 60, and 120 minutes following surgery. During the first hour of the recovery period, postanesthetic Aldrete recovery scores<sup>11</sup> were checked at equal time intervals. Postoperative pain, indicated by a score of more than 5 on the 0-10 VAS scale, was treated with i.m. ketorolac and emesis with metoclopramide. The patients were assessed regularly to establish their readiness for discharge, stable vital sign, pain controllability, level of nausea, ability to walk without dizziness, and ability to retain oral fluids. VAS, for satisfaction about anesthesia, was assessed before discharge. An independent observer, blinded to the anesthetic technique, collected the data in the recovery area.

All results are expressed as the mean  $\pm$  SD or as group percentages. Student t-tests, with Bonferroni corrections where appropriate, were used for the patients' variables and hemodynamic changes. Chi-square and Fisher's exact tests were applied to the variables of induction, complications, and postoperative assessment. A *p* value  $< 0.05$  was considered statistically significant. Statistical calculations were performed using SPSS 7.5.

## RESULTS

There were no significant differences between the two groups regarding their demographic data, operation times, times to unconsciousness, or times to readiness for surgery (Table 1).

The mean dose of anesthetic administered to the propofol group, including that used for induction, was  $272.2 \pm 79.2$  mg. The mean exposure to anesthetic in the sevoflurane group, expressed in MAC hours, was  $1.46 \pm 0.4$ .

There were more frequent incidences of apnea; defined as failure to maintain spontaneous ventilation for more than 30 sec (35% vs. 0%; *p*  $< 0.05$ ) in the propofol group. Of these patients, two experienced SpO<sub>2</sub> of  $< 90\%$ , as measured by pulse oximeter, which required immediate intervention with positive pressure ventilation, probably due to a problem in the upper airway, but without any serious events. Two patients receiving propofol complained of pain on injection. Two of the sevoflurane patients, during their inhaled induction, experienced slight airway irritation, eliciting coughing, but these were not serious. Following administration of induction agents, involuntary movements were more common in the propofol group than in the sevoflurane group (30% vs. 5%; *p*  $< 0.05$ ).

Induction was associated with a significant decrease in systolic and diastolic blood pressures,

**Table 1.** Patient's Characteristics and Speed of Induction and Recovery from Anesthesia

	Sevoflurane Group (n = 20)	Propofol Group (n = 20)
Age (yr)	36.9 $\pm$ 7.2	33.6 $\pm$ 5.1
Weight (kg)	55.9 $\pm$ 7.7	54.8 $\pm$ 9.0
Height (cm)	158.8 $\pm$ 5.2	160.1 $\pm$ 3.7
Vaginal prostaglandin (PGE1) given	16/20	15/20
Duration of surgery (min)	23.0 $\pm$ 8.4	19.3 $\pm$ 6.0
Time to unconsciousness (sec)	80.4 $\pm$ 18.9	83.6 $\pm$ 38.8
Time to ready for surgery (sec)	220.1 $\pm$ 76.9	231.0 $\pm$ 95.4
Open eyes to commands (sec)	316.6 $\pm$ 79.3*	507.4 $\pm$ 218.8
Orientation in time and place (sec)	380.6 $\pm$ 80.8*	666.3 $\pm$ 208.7
Able to squeeze a hand (sec)	390.0 $\pm$ 69.3*	653.1 $\pm$ 201.6
Able to sit unsupported (min)	63.9 $\pm$ 21.5	62.5 $\pm$ 32.2
Able to walk (min)	83.2 $\pm$ 22.7	91.9 $\pm$ 32.8
Home readiness (min)	103.7 $\pm$ 28.1	99.0 $\pm$ 36.2

Data are mean  $\pm$  SD.

\**p*  $< 0.05$  compared with the propofol group.

at a maximum after 3 minutes, in both groups (21% in the propofol group, 17% in the sevoflurane group). However, 1, 3, and 5 minutes following the induction of anesthesia, systolic and diastolic blood pressures in the propofol group were significantly lower than in the sevoflurane group (Fig. 1). During the remainder of the procedure, sevoflurane produced similar changes in blood pressures to propofol. Heart rate values also decreased after the induction of anesthesia, but showed similar trends in the both groups during the procedures, with no significant differences.

Emergence from anesthesia was briefer in the

sevoflurane group significantly (Table 1). The emergence time from discontinuation of the maintenance anesthetics, to eye opening and squeezing of hand on verbal command, and correctly stating name, age, date, and place, were shorter in sevoflurane group than the propofol group. However, the average time following surgery until the patients were able to sit and to walk, without support, and were judged "fit for discharge", were similar in both groups. The postoperative Aldrete scores were significantly better, at 15 and 30 minutes after surgery, in the sevoflurane group than the propofol group (Fig. 2). There

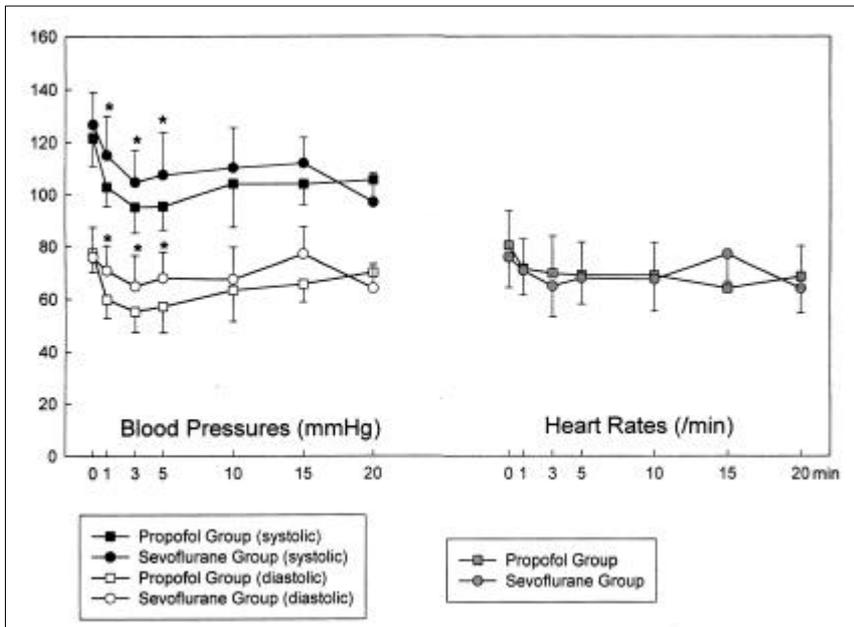


Fig. 1. Systolic (left upper panel), diastolic (left lower panel) blood pressures and heart rate (right panel) plotted at the base-line (0), 1, 3, 5, 10, 15, and 20 minutes after induction of anesthesia. Values are mean  $\pm$  SD. \*: significantly different from propofol group,  $p < 0.05$ .

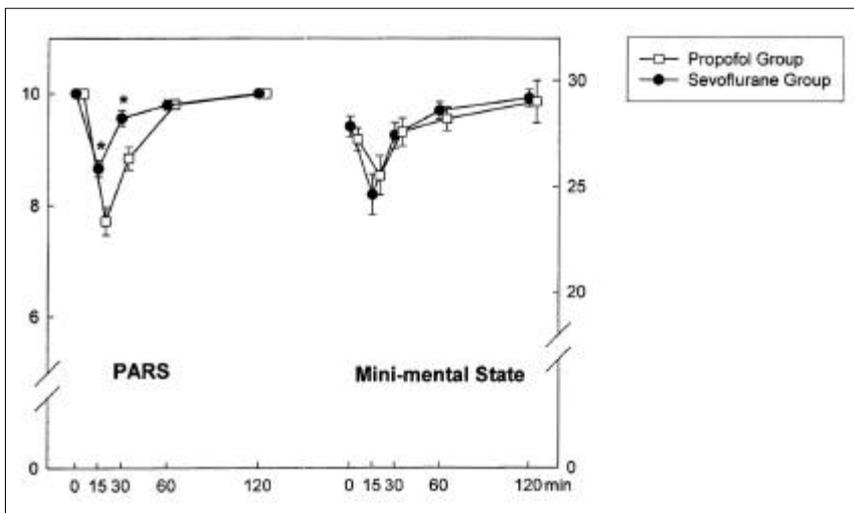


Fig. 2. Postanesthetic Aldrete scores (PARS) and mini-mental state after surgery plotted at the base-line (0), 15, 30, 60, and 120 minutes after surgery. Values are mean  $\pm$  SD. \*: significantly different from propofol group,  $p < 0.05$ .

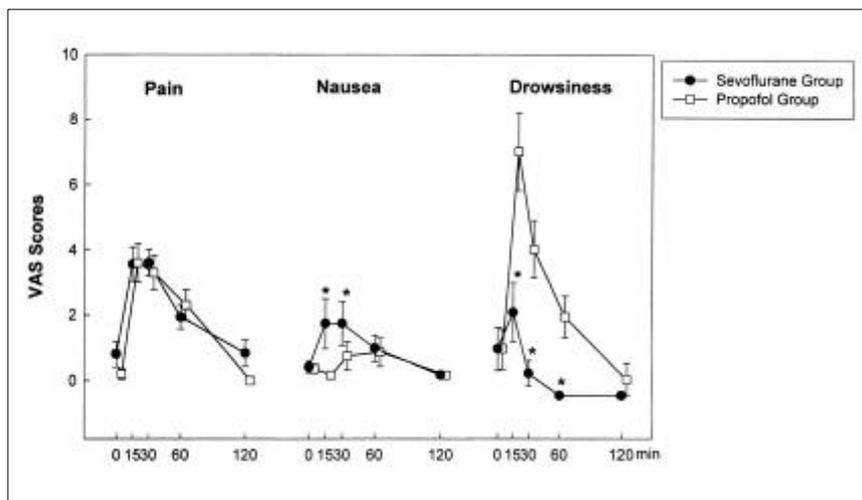


Fig. 3. Plots of the visual analogue scale scores for pain, nausea, and drowsiness after surgery plotted at the base-line (0), 15, 30, 60, and 120 minutes after surgery. Values are mean  $\pm$  SD. \*: significantly different from propofol group,  $p < 0.05$ .

were no significant differences between the two groups for minimal state scores at all time intervals.

The postoperative VAS scores for wound pain, nausea, drowsiness are presented in Fig. 3. No statistically significant difference was found between the two groups in the VAS pain scores. Of the patients in the sevoflurane group, 25% received postoperative i.m. ketorolac compared to only 15% in the propofol group ( $p > 0.05$ ). With the VAS for nausea, statistically differences were found between the two groups at 15 and 30 minutes, with more nausea reported for the sevoflurane group than the propofol group. The overall incidences of nausea, during the recovery period, were higher in the sevoflurane group than in the propofol group (40% vs. 10%;  $p < 0.05$ ). Antiemetics were only required for patients anesthetized with sevoflurane group (15% vs. 0%;  $p < 0.05$ ). The patients in the propofol group had significantly higher VAS for drowsiness than those in the sevoflurane group during the first 60 minutes following the end of anesthesia.

Other adverse events seen during the anesthesia recovery period for the sevoflurane group were shivering (10%) and headache (15%), but with none being reported for the propofol group ( $p > 0.05$ ). There was no significant difference in patient satisfaction scores ( $7.8 \pm 0.4$  vs.  $8.5 \pm 1.1$ ) between the two groups, with the majority of the patients saying they would request the same anesthetic for a similar procedure in the future.

## DISCUSSION

From this study our most important finding was that the times needed for induction of anesthesia were similar for both groups, but the emergence time from anesthesia was faster following anesthetization with sevoflurane than with propofol. Previous studies have shown that sevoflurane tended to need a significantly longer induction time than propofol.<sup>8,12</sup> The average induction time in our sevoflurane group was similar to those published by Smith and Twaites. However, they initially chose to select a target concentration of  $8 \mu\text{g/ml}$  for their propofol patient group, causing a rapid rise in the effective site concentration, resulting in a faster induction than with concentration used by ourselves. Nelskyla et al.,<sup>12</sup> in their study used 0.5 mg alfentanil as an analgesic adjuvant for induction with propofol. Their induction time for the propofol group was slightly faster than with ours where we used fentanyl. However, their induction time for the sevoflurane group was much slower than in ours as they defined unconsciousness as the disappearance of trapezius squeezing reflex. Fish et al.<sup>13</sup> used similar infusion rate for propofol and vol% of sevoflurane for induction in their study, with their results indicating there was no difference between the two anesthetic methods in the time to readiness for surgery.

The use of sevoflurane allowed a smoother transition to the maintenance phase without a period of apnea. Apnea occurred in 35% of the

patients in the propofol group, but did not occur at all in the sevoflurane group. There were two cases of temporary hypoxemia as monitored by pulse oximetry in the propofol group. They were ventilated manually until the return of spontaneous ventilation, but the smooth induction was still attained without prolonged induction. The increased incidence of involuntary movement due to excitatory phenomenon with propofol, and pain on injection, may discourage the selection of propofol for induction, despite its similar rapidity. However, according to the meta-analysis of Joo et al.,<sup>14</sup> propofol is still the preferred induction agent for general anesthesia of routine outpatient surgery due to its similar rapidity and antiemetic effect as sevoflurane.

Intraoperative hemodynamic variables showed similar trends with the two agents, with the exception of the first few minutes. We observed a decrease in mean arterial pressure after induction in both groups compared with the baseline, but a greater decrease with propofol during the first 5 minutes. This shows that both agents decrease systemic vascular resistance through endothelium mediated vasodilation,<sup>15</sup> which is further augmented when administered in conjunction with an opioid.<sup>16</sup> Previous investigations have shown higher incidences of bradycardia in patients anesthetized with sevoflurane.<sup>1,5</sup> These reports explained that this could be caused by the direct sevoflurane-induced inhibition of the beta-adrenoreceptor system,<sup>17</sup> and by the more profound analgesia provided by sevoflurane. In our study there were no significant differences in heart rates between the two groups during the whole procedure, possible due to: i) propofol and fentanyl are also known to cause bradycardia; ii) the average end-expired sevoflurane concentration of 1.46%, throughout the procedure, is relatively low due to the less invasive and less painful characteristics of hysteroscopic surgery with this agent.

A limitation of this study was that no comparisons were made on the depths of anesthesia between the two groups, but this was due to the difficulty of comparing depths of anesthesia between an inhaled and an intravenous anesthetic. The use of electroencephalographic (EEG)-related technology may provide some answers, as it has

been shown to correlate with propofol-induced sedation.<sup>18</sup> Blake et al.<sup>19</sup> observed that an EEG bispectral index suggested a greater depth of anesthesia for laryngeal mask insertion in the inhalational induction than in intravenous induction. However, there is no reference to adequate anesthesia for preventing movement using electroencephalographic derivatives, and in particular single breath induction of sevoflurane has not been evaluated.

In this study, we found that emergence from anesthesia (e.g., eye opening, orientation, and hand squeezing) was more rapid with sevoflurane compared to propofol, which is in accordance with the findings of the majority of other studies. The larger standard deviations support the clinical impression that a more accurate prediction of emergence times was possible following anesthesia with sevoflurane than with propofol. However, the times required for the patients to be able to "sit and walk unassisted" and be judged "fit for discharge" were similar in the two groups. Therefore, a difference in emergence of less than 10 minutes may be difficult to convert into economic benefits. The bolus dose of fentanyl might have influenced both induction and perioperative side effects. Given the short duration of anesthesia, fentanyl administered during the induction may have slightly lengthened the recovery times in the propofol group. It is also probable that it provided some pain relief and drowsiness during the recovery period. Interestingly, VAS scores for pain were not significantly different, but considerably more patients anesthetized using propofol with fentanyl complained of being sleepy.

Although the initial postoperative Aldrete scores were significantly lower in the propofol group, the scores returned to > 8 in both groups within 30 minutes. Recoveries of cognitive function (ability to perform the minimal state test) were similar between the two groups. There are conflicting reports on this point, as some agree with our findings,<sup>5</sup> although others have reported no differences between anesthetics at all.<sup>9</sup> The discrepancy between reports, on cognitive recovery, may be due to variations in protocol or different surgery duration.

We noticed an increased incidence and higher scores for postoperative emesis, but discharge

times with the use of sevoflurane compared to propofol, which is in accordance with most previous studies. Although the scores for nausea were mostly of a mild degree, 15% of the patients in the sevoflurane group required treatment for nausea or vomiting, whereas no treatment for this was required in the propofol group. Even if postoperative nausea is an unpleasant side effect complicating recovery after anesthesia, it is not a great inconvenience to patients receiving sevoflurane, since most expressed a willingness to receive the same anesthetic.

In summary, inhalation induced anesthesia with sevoflurane-nitrous oxide demonstrated excellent qualities compared to the intravenous induction using target-controlled propofol with fentanyl despite their similar speed. We also found that sevoflurane-nitrous oxide gave faster recovery profile than propofol-fentanyl. Although there was a greater incidence of nausea, sevoflurane-nitrous oxide appears to be superior to target-controlled propofol with fentanyl for day-case hysteroscopic surgery with regard to speed of recovery from anesthesia and the recovery of hemodynamic stability.

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