

# Comparison of Recovery Profile of Propofol, Sevoflurane, and Desflurane Anesthesia in Transnasal Trans-sphenoidal Surgery for Pituitary Tumors: A Prospective Randomized Trial

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## Abstract

**Background** Smooth and early emergence is always a concern in neurosurgical patients as it prevents complication and facilitates neurological examination and immediate postoperative intervention, if necessary.

**Methods** A prospective randomized trial was conducted to evaluate the effects of propofol, sevoflurane, and desflurane used for maintenance of anesthesia at the time of emergence and recovery from anesthesia in 75 patients undergoing elective trans-sphenoidal surgery for pituitary tumors. We evaluated time for emergence and extubation, modified Short Orientation Memory Concentration Test (SOMCT) score, Aldrete's scores, pain score, and postoperative nausea and vomiting (PONV) score.

**Results** Emergence and extubation times were significantly shorter in patients receiving desflurane as compared with those receiving propofol or sevoflurane ( $p < 0.001$ ). Modified SOMCT and Aldrete's scores were comparable in all the three groups with better cognitive scores in patients who received desflurane. Heart rate and mean arterial pressure were comparable at emergence and extubation in all the three groups except mean airway pressure (MAP) at extubation that was higher in the desflurane group compared with propofol and sevoflurane groups ( $p = 0.02$ ), which was clinically comparable. Pain and PONV scores were also comparable between the groups.

**Conclusions** Desflurane had shorter time to emergence and time to extubation in comparison to propofol and sevoflurane. Thus, desflurane can be used as an alternative to propofol and sevoflurane for maintenance of anesthesia in patients undergoing transnasal trans-sphenoidal pituitary surgery for its excellent recovery profile after anesthesia.

## Keywords

- ▶ desflurane
- ▶ emergence
- ▶ propofol
- ▶ sevoflurane
- ▶ trans-sphenoidal pituitary surgery

## Introduction

Smooth and early emergence is a major concern in neurosurgical patients. Early emergence from anesthesia facilitates early neurological examination and immediate postoperative intervention, if necessary. It is especially important in patients undergoing transnasal trans-sphenoidal surgery (TSS) because straining or coughing during

emergence from anesthesia can precipitate hemorrhage, cerebrospinal fluid (CSF) leakage, and dislodgement of nasal pack.<sup>1</sup> These patients are extubated only when they are fully awake so as to prevent airway obstruction and restlessness in post extubation period. Anesthetic technique that facilitates early awakening with clear higher mental functions is highly desirable in these patients to avoid complications.

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Anesthetic agents are the major determinants of the time of emergence and extubation, thus making short-acting anesthetic agents preferable as maintenance agents in these cases.<sup>2</sup> Propofol, an intravenous (IV) anesthetic agent with short duration of clinical effects due to rapid distribution into peripheral tissues and minimal cumulative effect, has been used commonly to achieve the same. Sevoflurane and desflurane are third-generation volatile anesthetic agents, having property of rapid emergence from anesthesia due to low blood-gas partition coefficient of 0.65 and 0.42, respectively.<sup>3-5</sup>

Ali et al<sup>6</sup> compared propofol, sevoflurane, and isoflurane in patients undergoing TSS and observed that propofol and sevoflurane were better than isoflurane for emergence from anesthesia under bispectral index (BIS) guidance. There is little literature on comparing desflurane with other short-acting anesthetic agents on emergence from anesthesia in cases of TSS. We hypothesized that emergence from anesthesia will be faster with desflurane compared with propofol and sevoflurane in TSS. Therefore, we planned to evaluate the effect of three short-acting anesthetic agents, namely propofol, sevoflurane, and desflurane, used for the maintenance of anesthesia at the time of emergence and recovery from anesthesia as the primary outcome and quality of recovery as the secondary outcome in cases of TSS in this study.

## Methodology

This prospective randomized trial was conducted in 75 patients undergoing elective TSS surgery for pituitary tumors after getting approval from the institute ethics committee and informed consent from the patients. Patients aged 18 to 65 years, the American Society of Anesthesiologists (ASA) classes I and II were included while patients with pituitary apoplexy and redo surgery were excluded from the study.

Patients were randomly allocated by a computer-generated random number table and serially numbered opaque envelope technique into three groups—P, S, and D—according to the anesthetic agent they received (propofol, sevoflurane, or desflurane) for the maintenance of anesthesia, respectively.

A standardized anesthesia protocol was followed in all cases. Pre-induction monitoring included electrocardiogram (ECG), noninvasive blood pressure (NIBP), pulse oximetry (SpO<sub>2</sub>), neuromuscular transmission (NMT), and BIS using Aspect 2000 monitor with sensor Xp. Anesthesia was induced with fentanyl (2 µg/kg) followed by propofol (1–2 mg/kg) until loss of verbal response in all the three groups. Muscle relaxation was achieved with vecuronium (0.1 mg/kg), and trachea was intubated when train-of-four (TOF) count was zero in NMT. Anesthesia was maintained as per the group allocation and was titrated to maintain BIS in the range of 45 to 55. Intraoperative analgesia was maintained with fentanyl infusion (1 µg/kg/h), while muscle relaxation was maintained with intermittent doses of vecuronium (1 mg/dose) maintaining the TOF count less than 2 throughout the surgery. All patients received a mixture of oxygen and nitrous oxide (50:50) with gas flows at 2 L/min to keep end-tidal carbon dioxide (EtCO<sub>2</sub>) between

35 and 40 mm Hg during mechanical ventilation. Radial artery of nondominant hand was cannulated for continuous monitoring of invasive blood pressure. Posterior hypopharynx was packed with moist rolled gauze.

Patients in Group P received propofol infusion (3–8 mg/kg/h), while those in Groups S and D received sevoflurane and desflurane, respectively, for the maintenance of anesthesia titrated to keep BIS between 45 and 55 in all the three groups. Intranasal mucosa was prepared by instilling 20 mL of lignocaine containing adrenaline (1:400,000) into cotton pellets and packing the nose prior to surgery. Hemodynamic parameters were noted at regular interval. Blood pressure beyond 20% of the baseline value was treated with either esmolol (0.5 mg/kg) or mephenteramine (3 mg/dose).

At the end of the surgery, fentanyl infusion was stopped 30 minutes prior to emergence, and anesthetic agents used for maintenance were decreased to keep BIS around 60 and were finally discontinued immediately after nasal packing. Nitrous oxide was also stopped, and residual neuromuscular block was reversed. Trachea was extubated when the patient had adequate muscle power and regular respiration generating adequate tidal volume and was able to respond to verbal commands.

Emergence time was defined as the time interval between discontinuation of the anesthetic agent and the time to open eye on verbal commands. Extubation time was defined as the time interval between discontinuation of anesthetic agent and tracheal extubation.

Immediate postoperative cognitive function to assess clear higher mental function was evaluated at 5, 10, and 15 minutes after extubation using a modified Short Orientation Memory Concentration (SOMC) test. The questionnaire includes—where are you at present, which year is it now, which month is it now, count numbers from 1 to 10, and count reverse numbers from 10 to 1. If the patient was able to recall and count with minimal mistakes (1–3), it was regarded as good, with more than three errors as fair, and if he/she was not able to recall at all, it was regarded as poor. It was done to ensure complete awakening and orientation of the patient before proceeding for the neurological and visual field assessment. Recovery characteristics were assessed with a modified Aldrete's score at 10 and 15 minutes after extubation. Postoperative pain (by 11 points numeric rating scale [NRS]) and incidence of postoperative nausea and vomiting (PONV) (by number of patients having PONV) at 5, 10, and 60 minutes after extubation were also measured.

Duration of emergence and extubation was noted and analyzed as the primary outcome of the study. Hemodynamic parameters, rescue drugs to maintain hemodynamic stability, modified SOMC score, modified Aldrete's score, pain score, and PONV score were recorded to assess quality of recovery as the secondary outcome of the study.

## Sample Size Calculation

The sample size was estimated based on the study by Ali et al.<sup>6</sup> Twenty-four patients were needed in each group to

demonstrate a 40% improvement in emergence time with the new agent (desflurane) with respect to propofol with an  $\alpha$ -error of 0.05 and power of 80%. Considering 5% attrition of cases during the study, we included 25 patients in each group to ensure adequate power of the study for assessing emergence from anesthesia.

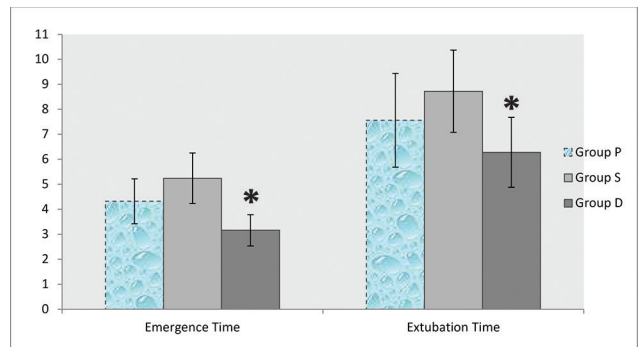
## Statistical Analysis

Demographic variables were presented as mean  $\pm$  standard deviation (SD) and were compared among the groups using one-way analysis of variance (ANOVA). Skewed data and ordinal distributed data were presented as median  $\pm$  quartiles (interquartile range) and were analyzed using repeated ANOVA or by using Kruskal–Wallis test or Mann–Whitney test as appropriate. Categorical variables were presented as frequency or percentage and were compared among the groups using chi-square test. Hemodynamic parameters were compared by two-way repeated measures ANOVA with Bonferroni correction. Emergence and extubation were compared among the groups using one-way ANOVA followed by Bonferroni correction. A  $p$ -value  $< 0.05$  was considered as significant.

## Results

All the patients included in the study completed it. Seventy-five patients included in the study were randomized into three groups of 25 each. The three groups were comparable with respect to the demographic parameters, pituitary pathology, duration of surgery, intraoperative fentanyl requirement, intraoperative IV fluids administered, and urine output (**Table 1**).

There was a statistically significant shorter emergence time in Group D ( $3.16 \pm 0.62$  min) as compared with group P ( $4.32 \pm 0.90$  min) and group S ( $5.24 \pm 1.01$  min) ( $p < 0.001$ ). Similarly, the extubation times were also significantly shorter statistically in the group D ( $6.28 \pm 1.40$  minutes) as compared with groups P ( $7.56 \pm 1.87$  min) and S ( $8.72 \pm 1.64$  min)



**Fig. 1** Recovery profile in minutes. \*Indicates  $p$ -value  $< 0.05$  on comparing among the groups.

(**Table 2**, **Fig. 1**). Modified SOMC test scores were comparable among all the three groups (**Table 2**).

The heart rate (HR) and mean arterial pressure was compared in all the three groups at the baseline, discontinuation of the anesthetic agents at the end of the surgery, discontinuation of nitrous oxide, at emergence (eye opening on command), and at the time of extubation. The mean baseline HR was comparable in all the three groups. There was an increase in HR at emergence and extubation in all the three groups compared with baseline value, but the difference in between the groups was not statistically significant (**Table 3**). Mean arterial pressure was comparable at baseline and at all other stages except for during the extubation when there was a rise in mean airway pressure (MAP) in the desflurane group as compared with propofol and sevoflurane group ( $p = 0.02$ ) (**Table 4**).

All the patients had hypertension during the emergence and extubation. The esmolol requirement in intraoperative period in all the three groups P, S, and D was found to be comparable ( $p = 0.131$ ).

Modified Aldrete's score measured in the post anesthesia care unit (PACU) at 10 and 15 minutes was also comparable in all the three groups. Pain and PONV scores were also similar among the groups (**Table 2**).

**Table 1** Demographic and intraoperative parameters

	Group P (n = 25)	Group S (n = 25)	Group D (n = 25)	$p$ -Value
Age (in years)	39.64 $\pm$ 12.24	39.92 $\pm$ 11.66	40.9 $\pm$ 13.5	0.935
BMI (kg/m <sup>2</sup> )	27.69 $\pm$ 3.30	25.74 $\pm$ 3.07	26.9 $\pm$ 3.0	0.095
Sex (M/F) (n)	15/10	7/18	15/10	0.074
ASA status (I/II) (n)	7/18	11/14	12/13	0.311
Pituitary pathology (acromegaly/Cushing's disease/NFPT) (n)	5/3/17	4/3/18	4/2/19	0.952
Duration of surgery (minutes)	101.28 $\pm$ 31.30	98.72 $\pm$ 31.47	95.8 $\pm$ 21.2	0.793
Intra-operative fentanyl ( $\mu$ g)	176.40 $\pm$ 18.68	168.40 $\pm$ 17.95	168.8 $\pm$ 20.5	0.254
Total intra-operative IV fluid (mL)	1226.00 $\pm$ 218.9	1204.00 $\pm$ 190.4	1168.0 $\pm$ 197.3	0.077
Total urine output (mL)	182.8 $\pm$ 27.7	166.4 $\pm$ 37.3	163.4 $\pm$ 27.3	0.067

Abbreviations: IV, intravenous; M/F, male/female; NFPT, nonfunctioning pituitary tumors; SD, standard deviation. Values expressed as mean  $\pm$  SD or n.

**Table 2** Parameters at emergence from anesthesia and postoperative period

	Group P (n = 25)	Group S (n = 25)	Group D (n = 25)	p-Value
Emergence time (minutes)	4.32 ± 0.90 <sup>a</sup>	5.24 ± 1.01 <sup>b</sup>	3.16 ± 0.62 <sup>c</sup>	0.00 <sup>d</sup>
Extubation time (minutes)	7.56 ± 1.87 <sup>a</sup>	8.72 ± 1.64 <sup>b</sup>	6.28 ± 1.40 <sup>c</sup>	0.00 <sup>d</sup>
Emergence agitation (calm/agitated)	23/2	22/3	23/2	0.13
<b>Postoperative Cognitive function (modified SOMC test)</b>				
At 5 minutes (good/fair/poor)	20/5/0	20/5/0	21/4/0	0.47
At 10 minutes (good/fair/poor)	23/2/0	20/5/0	24/1/0	0.16
At 15 minutes (good/fair/poor)	25/0/0	24/1/0	25/0/0	0.36
<b>Modified Aldrete's score</b>				
At 10 minutes	9.92 ± 0.40	9.76 ± 0.66	9.52 ± 0.87	0.12
At 15 minutes	10.00 ± 0.00	9.92 ± 0.40	9.92 ± 0.40	0.60
<b>Postoperative pain score (NRS)</b>				
At 5 minutes	2.40 ± 0.57	2.36 ± 0.57	2.36 ± 0.63	0.92
At 10 minutes	3.24 ± 0.52	3.56 ± 0.58	3.48 ± 0.71	0.06
At 60 minutes	4.40 ± 0.57	4.60 ± 0.50	4.20 ± 0.57	0.67
<b>Postoperative nausea and vomiting (number of patients)</b>				
At 5 minutes	0	2	3	0.22
At 10 minutes	0	3	1	0.16
At 60 minutes	0	0	0	1

Abbreviations: NRS, numeric rating scale; SOMC, Short Orientation Memory Concentration.

<sup>a</sup>Between group P and group S,  $p = 0.001$  for emergence and  $p = 0.04$  for extubation.

<sup>b</sup>Between group S and group D,  $p = 0.000$  for emergence and extubation.

<sup>c</sup>Between group P and group D,  $p = 0.000$  for emergence and  $p = 0.023$  for extubation.

<sup>d</sup> $p$ -Value < 0.05 on comparing among the three groups. Data were presented as number.

**Table 3** Mean heart rate at various stages (in beats/minute)

Events	GROUP P (n = 25)	GROUP S (n = 25)	GROUP D (n = 25)	p-Value
Baseline	75.36 ± 9.08	78.67 ± 5.68	79.05 ± 6.50	0.16
Discontinuation of test agent	81.08 ± 6.970	82.96 ± 3.900	82.96 ± 6.41	0.44
Discontinuation of N <sub>2</sub> O	82.52 ± 6.98	84.60 ± 3.72	84.68 ± 6.15	0.33
At emergence (eye opening)	86.40 ± 6.62	86.68 ± 3.90	87.68 ± 5.46	0.68
At extubation	94.280 ± 3.921	92.48 ± 4.788	94.52 ± 5.501	0.365

Abbreviations: N<sub>2</sub>O, nitrous oxide; SD, standard deviation.

Values expressed as mean ± SD.

**Table 4** Mean map at various stages (in mm Hg)

Events	Group P (n = 25)	Group S (n = 25)	Group D (n = 25)	p-Value
Baseline	89.22 ± 7.437	86.16 ± 5.853	86.49 ± 4.846	0.199
Discontinuation of test agent	87.08 ± 5.69	87.60 ± 4.65	87.72 ± 3.76	0.88
Discontinuation of N <sub>2</sub> O	89.92 ± 5.80	89.16 ± 4.70	89.68 ± 3.64	0.85
At emergence (eye opening)	92.44 ± 5.60	91.04 ± 5.47	92.08 ± 4.46	0.62
At extubation	99.48 ± 5.07	97.16 ± 5.41	100.32 ± 4.65	0.02 <sup>a</sup>

Abbreviations: N<sub>2</sub>O, nitrous oxide; SD, standard deviation.

<sup>a</sup> $p$ -Value < 0.05 on comparing among the groups. Values expressed as mean ± SD.

## Discussion

Emergence from anesthesia should be smooth and predictable with minimum hemodynamic and metabolic perturbations. Following TSS surgeries, the nose is packed, which makes these patients obligate mouth breathers in the early postoperative period.<sup>6</sup> It may cause restlessness and agitation in postoperative period if patient is not fully awake and able to understand the situation. The goal of anesthesia in neurosurgical patients in the immediate postoperative period is a fully awake and comfortable patient with adequate respiratory efforts and stable hemodynamics.

Desflurane due to lower blood-gas partition coefficient has the property of rapid recovery. No study till date has compared the effect of desflurane with other anesthetic agents in cases of TSS. In this study, we compared the three short-acting anesthetic agents (propofol, sevoflurane, and desflurane) used for maintenance of anesthesia and evaluated their effects on emergence from anesthesia. We observed a significant difference in the time of emergence and the time to extubation among the three anesthetic agents. The time to emergence and extubation was shortest in desflurane as compared with propofol and sevoflurane with sevoflurane having the longest time to emergence. Though the difference was statistically significant, its clinical significance is questionable.

Various studies have compared these three anesthetic agents in neurosurgical patients with contradictory results. Magni et al and Bilotta et al have reported shorter recovery with desflurane as compared with sevoflurane in supratentorial surgeries, similar to our observation.<sup>7,8</sup> On the other hand, Bastola et al<sup>9</sup> did not find a statistical difference in the time to emergence among propofol, sevoflurane, and desflurane, though they reported prolonged time to response to verbal commands with sevoflurane in patients undergoing surgery for supratentorial tumors similar to our results. Dube et al have reported a comparable recovery time between sevoflurane and desflurane in patients undergoing supratentorial craniotomy.<sup>10</sup> Our study was done in patients undergoing TSS in cases of pituitary adenoma in which early recovery from anesthesia is crucial. Our results were comparable to that of Magni et al and Billotta et al, with desflurane having the shortest recovery time as compared with sevoflurane.<sup>7,8</sup> The low blood-gas partition coefficient of desflurane (0.42) could account for the rapid emergence compared with sevoflurane (0.65).<sup>3,4</sup>

Ali et al observed shorter emergence time in propofol and sevoflurane groups (5 min) compared with isoflurane (9 min), while the duration was comparable for propofol and sevoflurane in patients undergoing TSS.<sup>6</sup> Cafiero et al reported faster recovery with sevoflurane-remifentanyl combination as compared to propofol with remifentanyl (7.4 vs. 12.8 min,  $p < 0.01$ ) in endonasal TSS while Citerio et al found no difference in time to eye opening with propofol and sevoflurane.<sup>11,12</sup> Several other authors have also reported no difference in time to recovery with inhalational anesthesia and total intravenous anesthesia (TIVA) in neurosurgical patients.<sup>13-16</sup> We observed a small, but statistically significant difference in time of emergence and extubation between

desflurane and sevoflurane groups (emergence time: Group D:  $3.16 \pm 0.62$  vs. Group S:  $5.24 \pm 1.01$  min,  $p = 0.000$ ; extubation time: Group D:  $6.28 \pm 1.40$  vs. Group S:  $8.72 \pm 1.64$  min,  $p = 0.000$ ). Emergence in desflurane group was even faster than in the propofol group (emergence time: Group D:  $3.16 \pm 0.62$  vs. Group P:  $4.32 \pm 0.90$  min,  $p = 0.000$ ; extubation time: Group D:  $6.28 \pm 1.40$  vs. Group P:  $7.56 \pm 1.87$  min,  $p = 0.023$ ). The small difference in duration observed between the groups may be of doubtful clinical significance.

Smooth emergence aims at preventing emergence hypertension and agitation. Hypertension is frequent during emergence with a reported incidence of 70 to 90%.<sup>17-19</sup> while 40 to 90% of patients require antihypertensive therapy during emergence.<sup>18-20</sup> The most common feared complication after neurosurgery is the development of intracranial hematoma (0.8-2.2%),<sup>21</sup> which has been associated with postoperative systemic hypertension, though a direct causal relationship could not be made.<sup>22</sup> Basali et al have described a link between perioperative hypertension and intracranial hemorrhage after craniotomy in a retrospective case control study and reported that patients with postoperative intracranial hemorrhage were 3.6 times more likely to be hypertensive. They observed a very strong association between intracranial hemorrhage and patients being normotensive intraoperatively, but hypertensive postoperatively.<sup>22</sup> In our study, we observed a statistically significant difference in the MAP only at the time of extubation with a rise observed in the desflurane group followed by propofol and sevoflurane. The difference among the groups is small, so again clinical significance of the difference in MAP is doubtful.

In contrast to our finding, Bastola et al had observed a comparable incidence of emergence hypertension among the three agents used for elective craniotomy.<sup>9</sup> Sevoflurane and desflurane have a dose-dependent systemic vasodilator effect, while propofol has both vasodilator and negative inotropic effects.<sup>23-25</sup> Hemodynamic parameters were comparable between the groups.

Modified SOMC test was done to assess cognition in the form of the clear higher mental function. It is used after the emergence from anesthesia to ensure complete awakening and orientation of the patient before proceeding for the neurological and visual field assessment. The modified SOMC scores achieved at 5, 10, and 15 minutes were comparable among the three groups with scores slightly better in desflurane and propofol groups as compared with the sevoflurane group, though the difference was statistically insignificant. Ali et al had also reported better cognitive scores in propofol group than in the sevoflurane group, while Billotta et al observed earlier postoperative cognitive recovery with desflurane-based anesthesia as compared with sevoflurane in overweight and obese patients.<sup>6,8</sup> In our observation, all the three agents are comparable in terms of immediate postoperative cognitive recovery with more number of patients having good scores in patients receiving desflurane. Modified Aldrete score was comparable in all the three groups at 10 and 15 minutes.

## Limitations of the Study

We have not measured serum catecholamine concentrations at emergence and extubation, which could have provided further valuable information related to anesthetic agent of choice in such situations.

## Conclusion

Desflurane had shorter emergence and extubation time in comparison to propofol and sevoflurane when used for maintenance of anesthesia under BIS guidance during TSS for pituitary adenoma without any significant side effects. Immediate postoperative cognitive functions were comparable in all three groups. As the difference in emergence criteria between the groups were small, the clinical significance of the difference is questionable.

We conclude that desflurane can be used as an alternative to propofol and sevoflurane for maintenance of anesthesia in patients undergoing transnasal trans-sphenoidal pituitary surgery for its excellent recovery profile after anesthesia.

### Conflict of Interest

None.

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