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ORIGINAL ARTICLE

A Prospective, Randomized Single-blind Study of Sevoflurane *vs* Desflurane, with Dexmedetomidine, on the Intraoperative Hemodynamics and Postoperative Recovery for Transsphenoidal Pituitary Surgery

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ABSTRACT

Introduction: The anesthesia goals for transsphenoidal pituitary surgeries include intraoperative hemodynamic stability and early postoperative recovery for cranial nerve evaluation. In this study, we aim to compare the intraoperative hemodynamics and postoperative recovery of sevoflurane with desflurane in a dexmedetomidine-based general anesthesia.

Materials and methods: Sixty patients, 18 to 65 years, American Society of Anesthesiologists (ASA) grades I and II, with Glasgow Coma Scale 15/15 were included. Thirty patients each were randomly divided into group S (sevoflurane) and group D (desflurane). The primary objective was to compare the intraoperative hemodynamics. Secondary objectives were to assess the total dose of dexmedetomidine, number of propofol doses, time to extubate, agitation score at emergence, and modified Aldrete score. The anesthesia management included an intravenous induction followed by maintenance with inhalational agent in oxygen: Nitrous oxide mixture (50%), dexmedetomidine infusion, and rescue doses of propofol.

Results: Heart rate (HR) and mean arterial pressure (MAP) were similar in both the groups except MAP just 5 minutes postincision, which was higher in group S ($p < 0.001$). There were no differences in intraoperative dexmedetomidine use, propofol bolus doses or time to extubate. But the agitation score was higher in group S ($p < 0.001$). The modified Aldrete score was higher in group D at 5, 15, 30, and 60 minutes ($p < 0.001$).

Conclusion: Both desflurane and sevoflurane produce a similar intraoperative hemodynamic response in a dexmedetomidine-based general anesthesia except sevoflurane, in the doses used in our study was insufficient to attenuate the hypertensive response to incision. With regard to emergence agitation and recovery profile, desflurane appears to be a superior agent.

Keywords: Desflurane, Dexmedetomidine, Sevoflurane, Transsphenoidal pituitary surgeries.

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INTRODUCTION

Transsphenoidal approach to pituitary is akin to a keyhole surgery. It requires both controlled hypotension during general anesthesia, which will reduce the bleeding and help in the surgical field exposure as well as early postoperative recovery for neurological evaluation of cranial nerves.[1] An ideal anesthetic agent must provide both intraoperative hemodynamic stability and rapid recovery. Dexmedetomidine, an $\alpha 2$ agonist, has substantially changed the practice of anesthesia by being an excellent sedative, analgesic, producing controlled hypotension with no postoperative respiratory depression. It acts as an excellent adjuvant in maintenance of general anesthesia, especially in neurosurgeries.[2] Both desflurane and sevoflurane, are recommended for use in neurosurgery because of their favorable recovery profile.[3,4]

In this prospective randomized study, we aim to compare the intraoperative hemodynamic parameters and postoperative recovery profile of sevoflurane with desflurane in a dexmedetomidine-based general anesthesia in patients undergoing transsphenoidal pituitary surgery.

MATERIALS AND METHODS

After obtaining Institutional Ethics committee approval and written informed consent from participants, 60 patients, aged 18 to 65 years, ASA grades I and II, scheduled for transsphenoidal pituitary surgery with preoperative Glasgow Coma Scale 15/15 were included in the study. We excluded all patients with surgical time more than 60 minutes, all emergency cases, patients with uncontrolled hypertension or preoperative bradycardia, ischemic heart disease, or cardiac arrhythmias, severe pulmonary, hepatic or renal disease, pregnancy, morbid obesity, history of allergy to study drugs, chronic alcoholism and drug abuse, serum potassium level >5.5 mEq/L and patients with raised intracranial pressure.

Thirty patients each were randomly (randomization table) divided into two intervention arms: Group S (sevoflurane) or group D (desflurane). The study was single-blinded. The anesthesiologist administering the anesthesia could not be blinded due to obvious difference in the shape of the desflurane vaporizer and the need for electrical connection. The primary objective was comparison of the intraoperative hemodynamics between both the groups. The secondary objectives were assessment of the total dose of dexmedetomidine required intraoperatively, number of intraoperative propofol doses required, the time to extubate, agitation score at emergence, and modified Aldrete score for postoperative recovery.

In the operating theater, standard monitors, which included electrocardiography, noninvasive blood pressure monitoring, pulse oximetry, end-tidal carbon dioxide ($EtCO_2$), and inhalational agent monitoring were applied to the patient and the baseline parameters were noted. Balanced salt solution at 4 mL/kg was started through an 18-G cannula on the upper limb. The patients were explained the presence of nasal packing after the surgery and the need for mouth breathing after waking up from anesthesia. All the patients were administered intravenous dexmedetomidine, loading dose 1 μg/kg over 10 minutes followed by 0.4 μg/kg/hour infusion, continued intraoperatively. The patients were further sedated with intravenous midazolam 0.03 mg/kg and fentanyl 2 μg/kg. Anesthesia was induced with lignocaine 1 mg/kg, propofol 2 mg/kg, and succinylcholine 2 mg/kg. The patients were intubated orally with cuffed endotracheal tubes size seven for females and eight for males. Throat packing was done with laryngoscopic guidance. Anesthesia was maintained with sevoflurane (1.5–2% end-tidal) or desflurane (3–4% end-tidal) adjusted to minimum alveolar concentration (MAC) 1.2 to 1.4 in an oxygen:nitrous oxide mixture of 50:50. Ventilation was adjusted to maintain $EtCO_2$ between 30 and 35 mm Hg. Fentanyl 1 μg/kg was repeated prior to surgical incision. Heart rate and MAP were noted preoperatively, at intubation, just before incision, and thereafter at every 5 minutes postincision up to 5 minutes after extubation. After the intubation dose of succinylcholine, no other neuromuscular blocking agent was administered. Propofol boluses of 0.5 mg/kg were administered in the event of return of spontaneous respiration or patient movement. All the patients received intravenous paracetamol 1 gm for postoperative analgesia and ondansetron 4 mg as antiemesis prophylaxis. The inhalational agent, nitrous oxide, and dexmedetomidine infusion were stopped at the end of surgery. From the time of shutting off the agent, time to extubation was noted. Patients were extubated when they achieved any three of the following criteria: Eye opening, sustained head lift, sustained hand grip, tongue protrusion. Agitation score at emergence according to Richmond agitation sedation scale was recorded. Postoperatively, modified Aldrete score was used to grade recovery at 5, 15, 30, and 60 minutes. Total doses of dexmedetomidine and propofol boluses given in intraoperative period were noted.

Adverse hemodynamic incidences, such as hypotension, hypertension, bradycardia, or tachycardia were noted. Fall or rise in MAP up to 30% of baseline was managed with adjusting the infusion rate of dexmedetomidine in the range of 0.2 to 0.7 μg/kg/hr. The fall in MAP > 30% was treated with intravenous fluid bolus followed by intravenous ephedrine 6 mg. The rise in MAP above 30% or tachycardia was treated with 0.5 mg/kg of esmolol. Bradycardia was treated with discontinuation of dexmedetomidine infusion followed by intravenous glycopyrrolate 0.004 μg/kg.

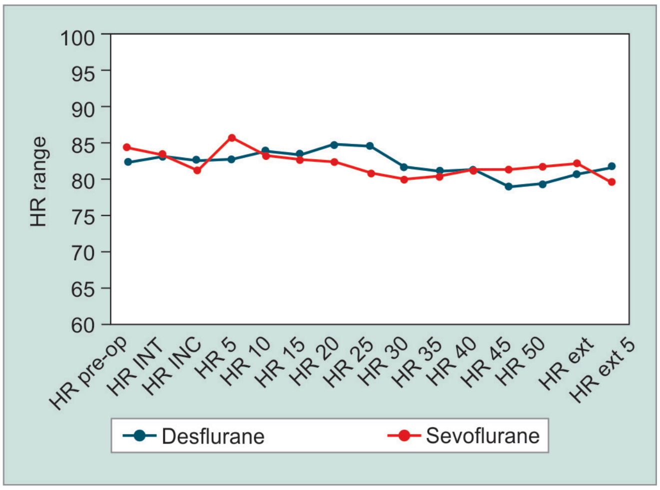
The sample size was calculated using nMaster 1.0. As per Magni et al,[4] the sample size was calculated for a mean change in MAP in group S as 7 mm Hg and group D as 7.5 mm Hg, to find a mean difference of 3 mm Hg between both the groups. This required a total of 24 patients to be enrolled in each treatment arm with alpha error at 5% and power of the study as 90%. Sixty patients were included in our study to improve the precision of the study. The data were analyzed using Statistical Package for the Social Sciences (version 21.0, SPSS Inc., Chicago Illinois, USA). Continuous data were presented as mean ± standard deviation and categorical data as proportions; 95% confidence limits were calculated. Hemodynamic parameters at different time points, dexmedetomidine dose, propofol bolus doses, time to extubate, and modified Aldrete score were compared by the unpaired t-test with $p < 0.05$ kept as significant for statistical analysis. Difference in agitation scores was assessed between both the groups by Mann–Whitney test.

RESULTS

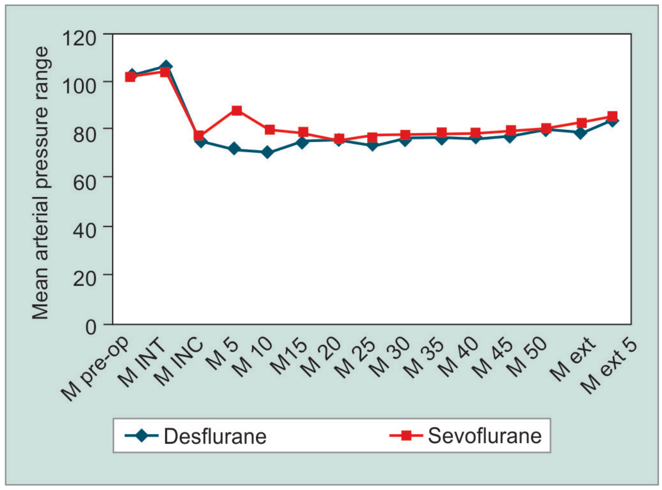
All 60 patients recruited for study successfully completed the required assessments as per the protocol. The demographic data are comparable in both groups as seen from Table 1.

Table 1: Demographics (data presented as mean/standard deviation)

	Group D	*Group S*
Age	43.30/13.08	37.87/11.01
Sex (F/M)	11/19	14/16
Weight	66.47/10.84	66/13.61
ASA status (I/II)	14/16	14/16
Surgical duration	29.07/8.90	31.60/7.35
Anesthesia duration	74.33/12.37	75/11.60



Graph 1: Comparison of HR between both the groups



Graph 2: Comparison of MAP between both the groups

Table 2: Intraoperative hemodynamic complications (data presented in number of patients)

	Group D	*Group S*
Tachycardia	2	3
Bradycardia	0	0
Hypotension	12	12
Hypertension	1	3

Table 3: Secondary outcomes (data presented in mean/standard deviation except propofol dose)

	Group D	*Group S*	*p-value*
Total dexmedetomidine dose	99.73/22.34	101.47/22.91	0.768
Single rescue dose of Propofol	9 patients	9 patients	–
Time to extubate	13.73/5.52	13.47/4.10	0.833
Agitation score	0.00/0.871	0.93/1.34	0.002
Modified Aldrete score 5 min	7.37/0.89	6.67/0.80	0.002
15 min	8.37/1.03	7.30/0.915	0.00
30 min	9.17/0.950	8.10/0.923	0.00
60 min	9.53/0.681	8.87/0.90	0.002

As seen from Graphs 1 and 2, intraoperative hemodynamics including HR and MAP were similar in both the study groups except MAP just 5 minutes after incision which was significantly higher in group S as compared with group D ($p < 0.001$, mean difference 17.133, 95% confidence interval 9.449–24.818).

The rate of hemodynamic complications was not statistically significant between both the groups (Table 2). Single hypotensive episode happened in 12 patients in both groups, observed commonly just prior to incision. None of them required treatment with ephedrine. We also observed three patients with intraoperative hypertension in group S *vs* 1 in group D. There were no episodes of bradycardia in either groups. We observed tachycardia in two patients belonging to group D as against three patients in group S.

Further analysis of the secondary outcomes revealed no differences in intraoperative dexmedetomidine use, propofol bolus doses, or time to extubate (Table 3). But the agitation score at emergence was significantly higher in group S as compared with group D ($p < 0.001$). The modified Aldrete score was significantly higher in group D as compared with group S at 5, 15, 30, and 60 minutes ($p < 0.001$).

DISCUSSION

The unique feature of transsphenoidal approach to pituitary surgeries is that it does not require craniotomy. It is a minimally invasive procedure, performed with the help of an endoscope, which is passed either through the nose or an upper alveolar incision, across the sphenoid sinus to reach the sella turcica.[1] This necessitates the requirement of a good surgical field with excellent visibility. Controlled hypotension during general anesthesia helps to provide the same. Also, the cranial nerves II, III, IV, and V are situated in close proximity to the sphenoid sinus and may be injured during the surgery. Postoperative evaluation of these cranial nerves necessitates the use of anesthesia agents with a rapid recovery profile.[5]

Dexmedetomidine, an $\alpha 2$ agonist, has proven to be an efficacious agent for producing a bloodless surgical field by virtue of its properties, such as controlled hypotension and bradycardia. It has been found to be a valuable adjunct during general anesthesia in various surgeries, such as otorhinolaryngology, orthopedic, spine, and neurosurgeries.[2] It is an excellent sedative, analgesic and helps to maintain adequate depth of anesthesia, improves surgical field visibility, and also produces a rapid postoperative recovery without respiratory depression which is required in transsphenoidal pituitary surgeries.

After intravenous induction, inhalational agents are commonly used for maintenance. The end-tidal concentration of desflurane (3–4%) and sevoflurane (1.5–2%) used along with fentanyl (3 µ/kg) and nitrous oxide (50%) can be considered to be equipotent.[6] Although in our study the dexmedetomidine dose varied within the given range, there was no difference in the total dose required in both groups. Also, the surgeries with duration of more than 60 minutes and patients with raised intracranial pressure were excluded. In this scenario, succinylcholine was used for intubation and thereafter, the required depth of anesthesia was maintained with only dexmedetomidine and the inhalational agent with propofol as the rescue agent. Jain et al[2] found that balanced anesthesia without the use of neuromuscular blocking agents produces similar recovery profiles with no difference in perioperative hemodynamic stability in neurosurgeries. Equipotent doses of the inhalational agents were fixed with changes done only to dexmedetomidine infusion within the given range of 0.2 to 0.7 µg/kg/hour and with rescue doses of propofol boluses.

During maintenance of anesthesia, both desflurane and sevoflurane present a similar cardiovascular profile: Dose-dependent reduction in systolic, diastolic, and mean blood pressure.[6,7] Heart rate does not change significantly with sevoflurane, but desflurane exceeding 1 MAC is known to cause sympathetic stimulation and tachycardia.[8] We did not find any difference in rates of tachycardia in both intra- and intergroup in our study despite using MAC 1.2 to 1.4. This may be attributed to the simultaneous use of dexmedetomidine in our study, which is known to produce bradycardia due to its sympatholytic actions.

In our study, both desflurane and sevoflurane when combined with dexmedetomidine produced a similar intraoperative hemodynamic profile except MAP just 5 minutes after incision which was significantly higher in group S, but this MAP was still less than the baseline MAP for both the groups. A previous study has proved that 1.5 MAC sevoflurane in air is insufficient to attenuate the cardiovascular responses to surgical incision. The authors found an increase in both the HR and MAP just after incision.[9] In our study, use of dexmedetomidine may have helped to prevent a rise in HR, but was insufficient to prevent a hypertensive response after incision.

A study comparing desflurane *vs* sevoflurane found no differences in the hemodynamics during the anesthesia maintenance period, but found desflurane to have a faster recovery profile after laparoscopic bariatric surgery.[7] Another study conducted in outpatient surgeries also concluded that both the inhalational agents provided similar intraoperative hemodynamics, but early postoperative recovery was faster with desflurane as maintenance anesthetic.[6] Another study comparing the above agents for supratentorial craniotomies found a similar intraoperative hemodynamic and postoperative recovery profile with both the agents.[3] Another study concluded that intraoperative maintenance of anesthesia with desflurane produced faster recovery as compared with sevoflurane in neurosurgical patients.[4]

Desflurane as an anesthesia maintenance agent has proven to be superior to sevoflurane with regard to the early postoperative recovery profile, being especially useful in ambulatory surgeries, bariatric surgeries, and neurosurgeries with craniotomies.[3,4,6,7] We found a statistically significant difference in the recovery profile between both the groups in our study as well. The postoperative recovery in group D, as evaluated by modified Aldrete score at 5, 15, 30 and 60 minutes, was significantly faster. The lower blood–gas partition coefficient of desflurane (0.45) *vs* sevoflurane (0.65) and fat–blood partition coefficient of desflurane (27) *vs* sevoflurane (48) favor early recovery with desflurane over sevoflurane.[3,7] This pharmacokinetic profile of desflurane leads to faster washout from the body at the end of anesthesia and leads to rapid recovery.

We also found that the agitation score on emergence was significantly higher with sevoflurane. Emergence delirium or emergence agitation is a well-documented entity with sevoflurane.[10,11] It generally presents as agitation, confusion, disorientation, and violent behavior. After transsphenoidal surgeries, the presence of nasal pack and the requirement for mouth breathing may also agitate the patients.[10] Agitation, straining, and bucking are all undesirable after these surgeries to prevent cerebrospinal leakage, dislodgement of nasal pack, and epistaxis.[1] A study found that the use of dexmedetomidine as an adjunct to sevoflurane anesthesia ameliorated the risk of emergence agitation.[11]

One of the limitations of our study was that we did not have a depth of anesthesia monitor, such as bispectral index. We used nitrous oxide in our study due to unavailability of medical air.

CONCLUSION

In conclusion, both desflurane and sevoflurane produce an overall similar intraoperative hemodynamic response when used in a dexmedetomidine-based general anesthesia. But sevoflurane and dexmedetomidine, in the doses used in our study, are insufficient to attenuate the hypertensive response to incision. Since a hypertensive response to incision may be deleterious in patients, we recommend the use of additional agents, such as lignocaine or additional opioids or β-blockers prior to incision. Also with regard to emergence agitation and recovery profile, desflurane appears to be a superior agent to sevoflurane for such surgeries.

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