Comparison of intraoperative brain condition, hemodynamics and postoperative recovery between desflurane and sevoflurane in patients undergoing supratentorial craniotomy

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ABSTRACT

Background: Post operative recovery has been reported to be faster with desflurane than sevoflurane anesthesia in previous studies. The use of desflurane is often criticized in neurosurgery due to the concerns of cerebral vasodilation and increase in ICP and studies comparing desflurane and sevoflurane in neurosurgey are scarce. So we compared the intraoperative brain condition, hemodynamics and postoperative recovery in patients undergoing elective supratentorial craniotomy receiving either desflurane or sevoflurane. **Materials and Methods:** Fifty three patients between 18-60yr undergoing elective supratentorial craniotomy receiving N_2O and oxygen (60%:40%) and 0.8-1.2 MAC of either desflurane or sevoflurane were randomized to group S (Sevoflurane) or group D (Desflurane). Subdural intra cranial pressure (ICP) was measured and brain condition was assessed.. Emergence time, tracheal extubation time and recovery time were recorded. Cognitive behavior was evaluated with Short Orientation Memory Concentration Test (SOMCT) and neurological outcome (at the time of discharge) was assessed using Glasgow Outcome Score (GOS) between the two groups. **Results:** The emergence time [Group D 7.4 ± 2.7 minutes vs. Group S 7.8 ± 3.7 minutes; P = 0.65], extubation time [Group D 11.8 ± 2.8 minutes vs. Group S 12.9 ± 4.9 minutes; P = 0.28] and recovery time [Group D 16.4 ± 2.6 minutes vs. Group S 17.1 ± 4.8 minutes; P = 0.50] were comparable between the two groups. There was no difference in ICP [Group D; 9.1 ± 4.3 mmHg vs. Group S; 10.9 ± 4.2 mmHg; P = 0.14] and brain condition between the two groups. Both groups had similar post-operative complications, hospital and ICU stay and GOS. **Conclusion:** In patients undergoing elective supratentorial craniotomy both sevoflurane and desflurane had similar intra-operative brain condition, hemodynamics and post operative recovery profile.

Key words: *Desflurane, intracranial pressure, recovery, sevoflurane, supratentorial craniotomy*

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INTRODUCTION

Early recovery from anesthesia after intracranial procedures enables early postoperative neurological evaluation and helps further management of patients. Residual effects of inhalational anesthetics can contribute to delay in emergence from anesthesia and thereby preclude an early assessment of postoperative neurological functions. Both desflurane and sevoflurane has favorable recovery profile, but postoperative recovery is reported to be faster with desflurane than sevoflurane anesthesia due to the difference in blood: Gas (desflurane 0.45 vs. sevoflurane 0.65) and fat: Blood (desflurane 27 vs. sevoflurane 48) partition coefficients of the two agents.[1]

The use of desflurane is often criticized in neurosurgery due to its cerebral vasodilating property. Cerebral vasodilatation and increase in intracranial pressure (ICP) by desflurane has been reported in various animal and human studies.[2-4] However, it has been found to have little clinical significance.[5,6] In spite of the widespread

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use of desflurane and sevoflurane, studies directly comparing desflurane and sevoflurane anesthesia in patients undergoing supratentorial craniotomy are scarce. Therefore, we planned to conduct this study to compare postoperative recovery after desflurane and sevoflurane anesthesia in patients undergoing supratentorial surgeries. The intraoperative brain conditions, intraoperative and postoperative hemodynamics, postoperative complications, the duration of Intensive Care Unit (ICU) and hospital stay and the neurological outcome between the two agents were also compared.

MATERIALS AND METHODS

Study design

Prospective randomized study.

Ethics

After institutional ethics committee approval and written informed consent 107 patients undergoing nonemergent craniotomy for supratentorial lesions were enrolled in this study.

Patient selection

Patients of American Society of Anesthesiologist physical status I–III, aged 18-60 years having Glasgow Coma Scale (GCS) of 15, undergoing elective craniotomy for supratentorial lesions were included in this study. Patients with intracranial hypertension, gross cerebral edema on computed tomography scan, GCS <15, intracranial aneurysm or arteriovenous malformation, obesity, severe systemic disease, anemia (hematocrit <25%), history of craniotomy in past 30 days, pregnancy, history of psychiatric disorders/alcohol or substance abuse, allergy to any of the study drugs and patients who were planned for postoperative mechanical ventilation were excluded from the study. Patients were randomly allocated into two groups (group S; received sevoflurane + nitrous oxide [N_2O] and oxygen [60%:40%]) or (group D; received desflurane + N_2O and oxygen [60%:40%]). During the pre-anesthetic checkup the cognitive function was assessed with Short Orientation Memory Concentration Test (SOMCT).[7] In SOMCT patients were asked to recall the current year, month, time, a sentence (previously told to them), the sequence of months through the year and some numbers in reverse order.

All patients were premedicated with glycopyrrolate (0.2 mg) intramuscularly, before shifting to operating room. Standard monitors including electrocardiogram, noninvasive blood pressure, and pulse oximeter (SpO_2) were attached. General anesthesia was induced with fentanyl 2 mcg/kg and thiopentone till loss of eye lash reflex. Rocuronium 1 mg/kg was used to facilitate tracheal intubation. Central venous and arterial cannulation was performed following tracheal intubation. Mechanical ventilation was adjusted to achieve a $PaCO_2$ of 30 ± 2 mm Hg and the inhaled anesthetic concentration was adjusted to obtain a minimum alveolar concentration (MAC) between 0.8 and 1.2. After achieving a steady anesthetic state, fresh gas flow rate was maintained at 2 L/min. Intermittent blouses of vecuronium were given as and when required. Skull pin sites were infiltrated with 0.25% bupivacaine solution. Starting with skin incision, mannitol (1 g/kg) was administered over a period of 30 min. After dural exposure, a 20 gauge venous cannula was inserted into the subdural space along the surface of the brain and was connected to a calibrated pressure transducer via a length of polyethylene high pressure tubing filled with normal saline. The transducer was zeroed at the level of mastoid process. The cannula was positioned so that respiratory and arterial blood pressure fluctuations could be identified. After stabilization of reading, value of subdural pressure obtained was considered as ICP.[8] After dural opening the attending neurosurgeon, who was blinded to the study groups assessed the brain condition on a 4-point scale[9]:

1. Perfectly relaxed,
2. Satisfactory relaxation,
3. Firm brain, and
4. Tight brain.

Intervention like change in position, further reduction of $PaCO_2$, additional mannitol or furosemide was undertaken when brain condition was of grade 4.

Heart rate (HR) and mean arterial blood pressures were recorded as baseline (before anesthesia induction), after induction, at or immediately after intubation and subsequently at 1 min interval till 5 min of intubation, at the skull pin application and thereafter at 15 min interval till the time of tapering the inhalational agents. Thereafter, vitals were recorded at every 1 min interval till 10 min after tracheal extubation. Vitals were recorded at 15 min interval thereafter till 3 h following surgery. Mean arterial pressure (MAP) >20% above baseline and/or HR >100 or >20% above baseline was treated with increasing the inspired concentration of sevoflurane or desflurane upto 1.2 MAC, followed by fentanyl 0.5-1 mcg/kg bolus, propofol 0.5 mg/kg slow intravenous (IV) bolus and then labetalol (5 mg increments) if required. Decrease of MAP to <20% below the baseline value was treated by decreasing the inhaled anesthetic agents up to the level of 0.8 MAC and bolus of IV fluids. Failure of blood pressure response to those agents was managed with administration of mephentermine (5 mg increments). Bradycardia (as defined by HR <40 for >1 min) was managed with atropine. All patients received ondansetron (0.1 mg/kg) and paracetamol

(15 mg/kg) intravenously 30 min, before the end of surgery. Sevoflurane and desflurane were tapered at the beginning of skin suturing and stopped after skin dressing. The residual neuromusclular blockade was reversed with neostigmine and glycopyrollate. MAP >20% above baseline during emergence were treated with injection labetalol (5 mg increments). All patients were shifted to ICU after tracheal extubation.

Emergence time was defined as the time interval between discontinuation of anesthetics and eyes opening spontaneously or on verbal prompting. Tracheal extubation time was defined as the time between discontinuation of anesthetics and tracheal extubation (after fulfilling standard extubation criteria). Recovery time was defined as the time between discontinuation of anesthetics and the time when patients were able to recall their names and dates of birth.[5] The SOMCT was evaluated at ICU admission and at every 15 min interval thereafter, for the 1st h and then every half hourly for the following 2 h. Patients were observed for 3 h for monitoring of postoperative complications. Neurological outcome at the time of discharge from hospital was assessed using Glasgow outcome score (GOS).

Statistical analysis

We intended to include minimum 50 patients in our study as per study by Heavner *et al.* to have a statistical power of >80%.[1] The statistical analysis was carried out using stata 11.0 (College Stations, Texas, USA). Data were presented as number (%)/mean ± standard deviation/median (range). The difference in proportions was compared using Chi-square/Fisher's exact test. The difference in means/medians was compared using Student's *t*-test/ Wilcoxon's rank sum test. To compare the mean in >2 groups one way ANOVA, followed by Bonferroni test for multiple comparisons was used. For correlation between variables Pearson's Correlation Coefficient was used.

RESULTS

In this study, a total of 107 patients were assessed for eligibility, of which 54 patients were excluded. Of the remaining 53 eligible patients, 3 were excluded (2 in desflurane and 1 in the sevoflurane group) due to need for postoperative ventilation or reintubation in the postoperative period [Figure 1]. A total of 50 patients (Group D 24 patients and Group S 26 patients) were included in the final analysis.

The demographic characteristics of the two groups were comparable [Table 1]. The two groups had similar intracranial pathologies [Table 2]. Intraoperative and recovery characteristics of the patients are shown in Table 3. Subdural ICP could be measured in 47 (22 in group D and 25 in group S) out of the 50 patients. The reasons for inability to measure ICP were dural tear during craniotomy (2 patients) and failure to insert the cannula due to adherent duramater to the tumor (1 patient). The ICP in both the groups was comparable (Group D; 9.1 [±4.3] mmHg vs. Group S; 10.9 [±4.2] mmHg; *P* = 0.14). There was no difference in intraoperative brain condition (*P* = 0.62) between the two groups. Only 2 patients (4%) (one patient in each group) required additional therapeutic measures to reduce the intraoperative brain bulge. We observed a good

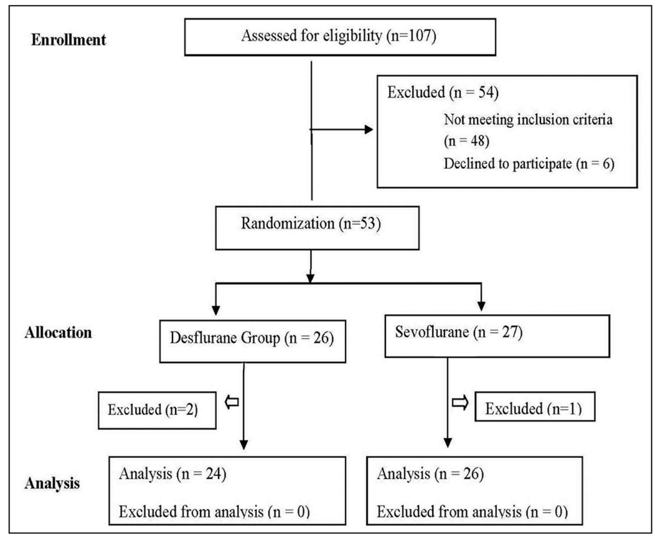

Figure 1: Consort flow diagram of the study

Table 1: Demographic characteristics of the two groups of patients*

Parameter	Group D (*n* = 24)	Group S (*n* = 26)	*P*
Age (years)	34.9 (11.7)	39.5 (12.0)	0.18
Weight (kg)	66 (12.3)	59.6 (10.6)	0.06
Male:female†	16 (66.7):8 (33.3)	15 (57.7):11 (42.3)	0.29
ASA status†			
I	18 (75)	20 (76.9)	0.92
II	6 (25)	6 (23.1)	
III/IV	0	0	
Baseline SOMCT	24 (2.8)	23.5 (1.9)	0.43

*Data shown a mean ± (SD) unless specified; †Data shown as number (percentage); SOMCT: Short orientation memory concentration test; ASA: American society of anesthesiologists; SD: Standard deviation

Table 2: Intracranial pathology*

Intracranial Lesion	Group D (*n* = 24)	Group S (*n* = 26)	*P*
Glioma	15 (62.5)	14 (53.8)	
Meningioma	5 (20.8)	8 (30.7)	0.12
Cystic lesion	1 (4.1)	2 (7.6)	
Others	3 (12)	2 (7.6)	
Tumor size (cm³)	23.9 (15.9)	25.7 (18.7)	0.70

*Data shown as number (%) of patients

correlation between the tumor size with brain condition grade (Pearson's Correlation Coefficient = 0.57) and ICP (Pearson's Correlation Coefficient = 0.61).

The duration of anesthesia and surgery, fentanyl consumption, and the interval between the last dose of muscle relaxant/fentanyl and tracheal extubation were comparable between the two groups [Table 3]. The incidence of hypertension and hypotension was also comparable between the two groups. The mean labetalol and mephentermine consumption was similar between the two groups [Table 3].

The emergence time, extubation time and recovery time were similar between the two groups [Table 3]. Postoperative complications like postoperative nausea vomiting, respiratory complications, shivering and emergence agitation were similar between the two groups [Table 4]. No patient in any group had any cardiovascular complication. There was no difference in the hospital and ICU stay and the GOS between the two groups [Table 4].

There was no significant difference of HR and MAP between the two groups at different time intervals [Figures 2-4]. The baseline and immediate postoperative SOMCT scores (on ICU admission) were comparable between the two groups. There was no significant difference in the SOMCT scores between the two groups at any time point in the postoperative period [Figure 5].

Table 3: Intraoperative operative and recovery characteristics of the patients*

Parameters	Group D (*n* = 24)	Group S (*n* = 26)	*P*
Subdural ICP (mmHg)	9.1 (4.3)	10. 9 (4.2)	0.14
Brain grade†			
1	41.7	26.9	0.62
2	29.2	46.1	
3	25.1	23.1	
4	4.2	3.8	
Duration of anesthesia (min)	311.2 (61.2)	331.3 (70.3)	0.28
Duration of surgery (min)	234.2 (54.4)	261.5 (68.4)	0.12
Emergence time (min)	7.4 (2.7)	7.8 (3.7)	0.65
Extubation time (min)	11.8 (2.8)	12.9 (4)	0.28
Recovery time (min)	16.4 (2.6)	17.1 (4.8)	0.50
Fentanyl consumption (mcg)	297.9 (47.7)	279.6 (49.5)	0.19
Vecuronium consumption (mg)	8.6 (1.8)	9.1 (2)	0.34
Duration between last dose of muscle relaxant and extubation (min)	58 (9.2)	61 (8)	0.21
Duration between last dose of fentanyl and extubation (min)	28.4 (6.3)	28.9 (7.4)	0.77
Labetalol consumption (mg)	13.7 (11.9)	8.5 (12.5)	0.13
Mephentrine consumption (mg)	3.7 (5.9)	1.9 (3.8)	0.19

*Data shown as mean ± (SD) unless specified; †Data shown as percentage; ICP: Intracranial pressure

Table 4: Postoperative complications, hospital and ICU stay and the GOS of the patients*

Complications	Group D (*n* = 24)	Group S (*n* = 26)	*P*
PONV	9 (37.5)	6 (23.1)	0.27
Emergence agitation	6 (25)	6 (23.1)	0.87
Shivering	1 (4.2)	1 (3.8)	0.43
Respiratory	1 (4.2)	2 (7.7)	0.60
Hospital stay (days)†	5 (3-18)	6 (3-10)	0.31
ICU stay (h)†	20.5 (11-129)	25.5 (10-60)	0.79
GOS‡	4.66 (0.5)	4.77 (0.4)	0.43

*Data shown as number (%) of patients unless specified; †Data shown as median (range); ‡Data shown as mean (±SD); PONV: Postoperative nausea vomiting; GOS: Glasgow outcome score; ICU: Intensive care unit

DISCUSSION

We observed similar ICP, intraoperative brain condition and recovery profile between sevoflurane and desflurane in patients undergoing nonemergent supratentorial craniotomy. Previous studies have shown faster postoperative recovery with desflurane than sevoflurane.[1,10,11] Heavner *et al.* observed a significantly faster time to extubation, eye opening and orientation with desflurane than sevoflurane after various surgeries.[1] Nathanson *et al.* reported the mean emergence time (4.8 ± 2.4 vs. 7.8 ± 3.8 min) and extubation time (5.1 ± 2.2 vs. 8.2 ± 4.2 min) to be significantly less with desflurane as compared to sevoflurane in outpatient surgeries but the recovery of cognitive function and discharge times from the hospital were similar between the two.[10] Dupont *et al.* reported a faster emergence time (7.2 ± 4.8 min vs.13.7 ± 8.6 min) and extubation time (8.9 ± 5 min vs. 18 ± 17 min) with desflurane than sevoflurane in patients undergoing pulmonary surgery. The return of cognitive function at 5 min was earlier with desflurane but there was no significant difference after 15 min of tracheal extubation.[12] In their study on neurosurgical patients, Magni *et al.* reported similar emergence time (12.2 ± 4.9 min vs. 10.8 ± 7.2 min) but longer tracheal extubation time (18.2 ± 2.3 min vs. 11.3 ± 3.9 min) and recovery time (12.4 ± 7.7 min vs. 1.3 ± 3.9 min) in the sevoflurane compared to the desflurane group.[5] Bertrand and associates reported the emergence time and full recovery time with desflurane to be 14.9 ± 2.4 min and 22.1 ± 3.1 min respectively in patients undergoing acustic neuroma surgery.[13] Gauthier *et al.* reported the emergence time, extubation

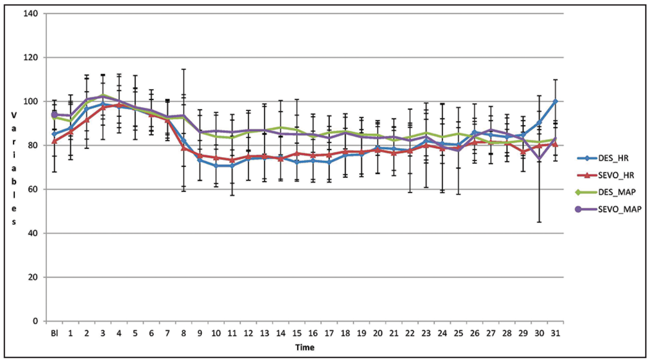

Figure 2: Figure showing heart rate and mean arterial pressure at baseline and at different intervals in the induction, intubation and maintenance phase. Bl: Base line; 1: Induction; 2: Intubation; 3-7: 5 min postintubation at 1 min interval; 8: Pin fixation; 9-31: After pin fixation at 15 min interval till tapering of inhalational agents

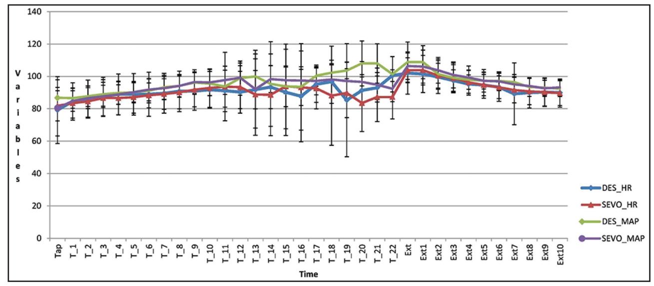

Figure 3: Figure showing heart rate and mean arterial pressure from tapering of inhalational agents till 10 min after extubation. Tap: Tapering of inhalational agents; T_1 to T_22: At 1 min interval from tapering of inhalational agents till extubation; Ext: At extubation; Ext1-Ext10: At 1 min interval from extubation till 10 min of extubation

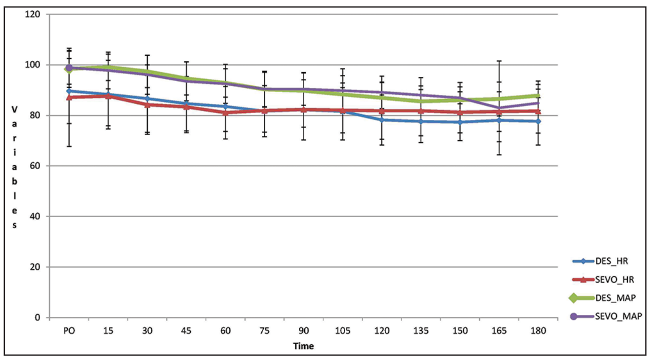

Figure 4: Figure showing heart rate and mean arterial pressure in the postoperative period. PO: Baseline postoperative on Intensive care unit (ICU) admission; 15-180: From 15 min of ICU admission to 180 min of ICU admission

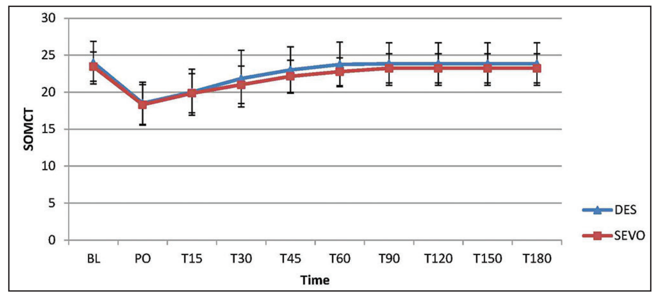

Figure 5: Short Orientation Memory Concentration Test score of the patients at different intervals. BL: Base line; PO: Baseline postoperative on Intensive care unit (ICU) admission; T15-T180: From 15 min of ICU admission to 180 min of ICU admission

time and orientation time in sevoflurane group to be 15.0 ± 8.7 min, 19.9 ± 12.7 min and 32.9 ± 26 min respectively in neurosurgical patients.[14]

Though direct comparisons cannot be made, the emergence/extubation/recovery time in the studies where N_2O was used were similar to our study results.[1,10,12,13] However, in studies where N_2O was not used the emergence/extubation/recovery times were longer than that of our study.[5,14] The difference in the recovery could be attributed to use of N_2O. The additive effect of N_2O on the anesthetic regimen would have reduced the requirement of inhalational agents and opioids resulting in a quicker recovery.

In our study we did not find any difference in the postoperative cognitive function between the two groups. Bilotta *et al*. compared the early postoperative recovery between sevoflurane and desflurane in obese patients undergoing craniotomies.[6] They observed a better early postoperative cognitive recovery in desflurane than sevoflurane group. In their study on patients undergoing supratentorial craniotomy Magni *et al*. observed a faster recovery of cognitive function (better SOMCT sore) in desflurane group than the sevoflurane group but only in initial 15 min of tracheal extubation.[5] Our findings on cognitive functions are different from these studies in terms of similar postoperative cognitive function at all-time intervals. These differences could be due to the difference in the study population (obese patients) or different anesthetic regime (no use of N_2O).[5,6] However, in more recent studies the authors couldn't detect any difference in postoperative cognitive function between desflurane and sevoflurane.[15,16]

Cerebral vasodilatation and raised ICP are concerns with the use of all inhalational anesthetics in patients with intracranial pathologies and desflurane is considered to have more cerebral vasodilation and ICP raising potential when compared to isoflurane and sevoflurane.[17] However, these concerns with the use of desflurane have been found to have little clinical significance.[5,6] Talke *et al*. studied the effect of sevoflurane on the lumbar cerebrospinal fluid pressure (LCSFP) in normocapnic patients scheduled for transsphenoidal pituitary surgery.[18] They found that the LCSFP increased by 2 ± 2 mmHg with 1 MAC of sevoflurane and concluded that the change produced by 1 MAC sevoflurane was not different from that produced by 1 MAC desflurane or isoflurane which was observed in their earlier study.[19] Kaye *et al*. compared the effect of 1.2 MAC of desflurane and isoflurane (in oxygen and air mixture) on LCSFP in normocapnic patients undergoing craniotomy for removal of supratentorial tumors.[20] They too observed that neither isoflurane nor desflurane caused significant increase in LCSFP from the baseline values.

However, the correlation between LCSFP and brain relaxation is not uniform.[21] In patients undergoing elective craniotomy for resection of supratentorial mass lesion, Turner *et al*. observed that brain relaxation is not predictive of LCSFP and LCSFP values only at the extremes of the observed distribution correlated with brain relaxation.[21] Moreover, in patients with supratentorial tumors, ICP is a strong predictor of intraoperative brain swelling.[22] In patients with supratentorial pathology ICP of >7 mmHg was associated with some degree of brain herniation and ICP of >11 mmHg was associated with pronounced brain herniation.[22] Hence in our study, we measured subdural ICP instead of LCSFP. The method of measurement of ICP in our study is a relatively simple and has been described previously in different studies.[8,22]

Fraga *et al*. compared the MAP, ICP, and cerebral perfusion pressure (CPP) using 1 MAC of either isoflurane or desflurane (with 60% N_2O) in normocapneic patients undergoing craniotomy for supratentorial brain tumors.[23] The ICP measurements throughout the study did not change within each group compared with baseline values and they did not find any significant difference of MAP, ICP, and CPP between the two groups. We measured the ICP intraoperatively and compared the hemodynamic parameters during the perioperative period between the two groups. Our study results have shown that the ICP and hemodynamic parameters in both the groups were comparable.

Ornstein and associates studied the cerebral blood flow and CO_2 reactivity in hypocapneic patients undergoing craniotomy using desflurane and isoflurane at 1 and 1.5 MAC.[24] The degree of cerebral vasodilatation was comparable at different MAC of both the agents. Sponheim *et al*. reported a dose-dependent and clinically similar increase ICP and reduced MAP and CPP at 0.5 and 1.0 MAC of isoflurane, sevoflurane and desflurane in N_2O (60%) in hypocapneic children.[25]

Magni *et al*.[5] compared the intraoperative brain condition between 1.2 MAC sevoflurane and desflurane in patients undergoing supratentorial craniotomy and reported identical brain condition between the two agents. They measured the brain condition subjectively, but we in addition to subjective brain condition grading measured the ICP also, both of which together reflect the brain condition better than subjective brain grading alone. They reported faster tracheal extubation, recovery and better early cognitive function (SOMCT score only at 15 min of tracheal extubation) with desflurane as compared to sevoflurane in neurosurgical patients.[5] But the emergence time and late cognitive function between the two groups were similar. The MAC hour in sevoflurane group was significantly higher than desflurane, which could have resulted in delayed tracheal extubation and recovery in sevoflurane group in their study.

In spite of theoretical concern of cerebral stimulation, use of N_2O is common in in many neurosurgical centers. In spite of use of N_2O in our study, we did not find high incidence of raised ICP or severe intraoperative brain bulge and the intraoperative brain condition/ICP between the two groups were similar.

We measured the hemodynamic parameters in the perioperative period. Considerable hemodynamic fluctuations can occur at various stages of surgery and in the postoperative period. The effect of anesthetic agents on hemodynamic parameters is important, because different agents can influence the morbidity and mortality of the patients by affecting the hemodynamic parameters. We did not find any difference in the length of hospital and ICU stay and also the GOS at hospital discharge between the two groups.

The present study is not without limitations. We included patients without evidence of intracranial hypertension and our results cannot be extrapolated to patients with evidence of intracranial hypertension. Our study was not blinded. But the brain condition was assessed by the attending neurosurgeons who were blinded to the groups and we measured the ICP which did not show any difference.

CONCLUSION

In patients undergoing elective supratentorial surgery, both sevoflurane and desflurane produce similar intraoperative brain condition, perioperative hemodynamics and postoperative recovery.

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