Clinical Investigation

Comparison between sevoflurane and desflurane on emergence and recovery characteristics of children undergoing surgery for spinal dysraphism

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ABSTRACT

Background and Aims: Rapid recovery is desirable after neurosurgery as it enables early post-operative neurological evaluation and prompt management of complications. Studies have been rare comparing the recovery characteristics in paediatric neurosurgical patients. Hence, this study was carried out to compare the effect of sevoflurane and desflurane anaesthesia on emergence and extubation in children undergoing spinal surgery. **Methods:** Sixty children, aged 1–12 years, undergoing elective surgery for lumbo-sacral spinal dysraphism were enrolled. Anaesthesia was induced with sevoflurane using a face mask. The children were then randomised to receive either sevoflurane or desflurane with oxygen and nitrous oxide, fentanyl (1 μg/kg/h) and rocuronium. The anaesthetic depth was guided by bispectral index (BIS®) monitoring with a target BIS® between 45 and 55. Perioperative data with regard to demographic profile, haemodynamics, emergence and extubation times, modified Aldrete score (MAS), pain (objective pain score), agitation (Cole's agitation score), time to first analgesic and complications, thereof, were recorded. Statistical analysis was done using STATA 11.2 (StataCorp., College Station, TX, USA) and data are presented as median (range) or mean ± standard deviation. **Results:** The demographic profile, haemodynamics, MAS, pain and agitation scores and time to first analgesic were comparable in between the two groups ($P > 0.05$). The emergence time was shorter in desflurane group (2.75 [0.85–12] min) as compared to sevoflurane (8 [2.5–14] min) ($P < 0.0001$). The extubation time was also shorter in desflurane group (3 [0.8–10] min) as compared to the sevoflurane group (5.5 [1.2–14] min) ($P = 0.0003$). **Conclusion:** Desflurane provided earlier tracheal extubation and emergence as compared to sevoflurane in children undergoing surgery for lumbo-sacral spinal dysraphism.

Key words: Children, desflurane, recovery, sevoflurane, spinal dysraphism

INTRODUCTION

Rapid recovery is desirable in neurosurgical patients to enable early post-operative neurological evaluation and prompt treatment of surgical complications. Residual effects of inhalational anaesthetic agents may contribute to delayed emergence from anaesthesia thereby precluding an early assessment of post-operative neurological function. Because of the low blood-gas partition coefficient of sevoflurane and desflurane (0.69 and 0.42, respectively), rapid emergence from anaesthesia is expected following their use, as compared to other inhalational agents. Sevoflurane is generally considered as a suitable inhalational agent in neuroanaesthesia practice. Desflurane is expected to provide earlier emergence from anaesthesia, and may be a preferred agent in neurosurgical patients. Previous studies comparing the emergence from sevoflurane and desflurane in

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children are scarce, and results are far from uniform.[1-3] Moreover, none of these earlier studies compared the effects of these two agents in paediatric neurosurgical practice. Hence, this study was carried out to compare the effect of sevoflurane and desflurane anaesthesia on emergence and extubation in children undergoing spinal surgery.

METHODS

The study protocol was approved by the Institute Ethics Committee. After written informed consent was obtained from parents or legal guardians, 60 children with American Society of Anesthesiologists grade I-II, aged between 1 and 12 years, undergoing elective surgery for spinal dysraphism, were enrolled for this investigator-initiated, prospective randomised controlled study. Children with cardiac, renal, hepatic and respiratory dysfunction; associated hydrocephalus, Arnold–Chiari malformation and history of seizures, were excluded from the study.

On the day of surgery, no sedative premedication was given. Routine monitors, including pulse oximeter (SpO_2), electrocardiogram and non-invasive blood pressure, were attached. Anaesthesia was induced with sevoflurane 8% in oxygen with a flow rate of 6 L/min. An intravenous (IV) access was secured once eyelash reflex was lost. Fentanyl (2 μg/kg), followed by rocuronium (1 mg/kg) was administered to facilitate endotracheal intubation. Anaesthesia was maintained with 60% nitrous oxide in oxygen and sevoflurane or desflurane at a fresh gas flow of 2 L/min and lungs were mechanically ventilated to maintain an end-tidal carbon dioxide ($EtCO_2$) of 35 to 40 mm Hg. A disposable paediatric bispectral index (BIS®) sensor was applied on the forehead of each patient and connected to BIS monitor. BIS values were recorded only when the signal quality index (SQI) was at least 90% and electromyogram (EMG) potential <30 dB. The patients were randomised according to the computer-generated chart and allocated to the groups using a sealed envelope technique into two groups (S and D). Group S received sevoflurane and Group D desflurane for maintenance of anaesthesia. BIS was targeted to a range of 45–55, to guide administration of anaesthetic agents. Body temperature was monitored with an oesophageal temperature probe, and normothermia (36–37°C) was maintained with the help of convective air warmer and warm IV fluids. Fentanyl (1 μg/kg) was given every hour, and rocuronium (0.2 mg/kg) was given to maintain single twitch using neuromuscular monitoring. Ringer lactate was given for intraoperative fluid replacement according to the formula of Holliday and Segar.[4] The haemodynamic parameters, including end-tidal concentration of the anaesthetic agents, were measured before induction, after induction, at skin incision, during laminectomy, during dural incision and stretching, at skin closure and at the time of discontinuation of anaesthetic agents. Intraoperatively, an increase in systolic blood pressure (SBP) or heart rate (HR) more than 20% above the pre-incisional value sustained for 3 min was managed with injection esmolol (0.5 mg/kg). Hypotension or bradycardia (decrease in SBP or HR more than 20% from baseline, respectively, sustained for 3 min) was managed first with fluid bolus followed by the IV mephentermine sulphate or atropine, if required. The last dose of fentanyl was administered at the beginning of dural closure if time lag with the previous dose was more than 30 min. About 15 min prior to the end of surgery, inhalational concentrations were adjusted in both groups to achieve BIS® in the range of 60–75. Inhalational agents and nitrous oxide were simultaneously turned off once the patient was positioned supine. Residual neuromuscular blockade was reversed with neostigmine (50 μg/kg) and glycopyrrolate (20 μg/kg). Trachea was extubated when patients met appropriate criteria such as resumption of regular respiratory pattern, adequate minute ventilation, oxygen saturation more than 95% and recovery of airway reflexes. Emergence time was measured as the time interval between discontinuation of anaesthetic agent and opening of eyes, spontaneously or on verbal commands, which were repeated every 30 s. Extubation time was measured as the time interval between anaesthetic agent discontinuation and tracheal extubation. At the end of procedure, duration of surgery (skin incision to skin closure) and anaesthesia (time of induction to time to discontinuation of anaesthetic agent), total intraoperative blood loss and total fentanyl consumption were noted. Patients were transported to post-anaesthesia care unit (PACU). Discharge readiness from PACU was assessed using modified Aldrete score (MAS).[5] Pain was evaluated using a modified objective pain score (OPS) based on objective pain score by Hannallah *et al*.[6] in the PACU on arrival, at 5 min, at 15 min and then, every 15 min for 120 min. The emergence agitation (EA) was assessed by using 5-point Cole's agitation score (ACS)[7] at similar intervals. The ready-to-discharge threshold for MAS was taken as a score of 9 or more (MAS = 10) and the

time to achieve it was noted. Fentanyl (0.5–1 μg/kg) was given for pain (OPS ≥4 or 5) or severe EA (ACS ≥4) lasting for more than 5 min. Total amount of post-operative fentanyl used and time of first analgesic administration were noted. HR, non-invasive blood pressure, respiratory rate and SpO_2 were recorded in the PACU every 5 min for first 15 min, and then at 15 min intervals for next 2 h. Post-operative complications such as nausea, vomiting, shivering and desaturation episodes (SpO_2 <95%) were noted. Ondansetron (0.1 mg/kg, maximum 4 mg) was given for post-operative nausea and vomiting (PONV).

The emergence time was taken as mean ± standard deviation (SD) for sevoflurane from the study by Singh et al.[8] for calculating the sample size for two groups, anticipating 20% change with desflurane. (SD of 3.4 with 5% level of significance and 90% power for sample size of 30 each).

Statistical analysis was done using STATA 11.2 (StataCorp., College Station, TX, USA). Data are represented as mean (±SD), median (range) and frequency (%). Within group categorical variables were compared using Chi-square test. In case of continuous variables, the parameters following a normal distribution were compared by using *t*-test, and changes were observed by repeated measure ANOVA (two-way ANOVA). For non-parametric continuous variables, within group, changes were evaluated by Freedman test followed by multiple comparisons using Wilcoxon sign rank test with Bonferroni correction and between groups changes were compared by using Wilcoxon rank sum test. A $P < 0.05$ was considered significant.

RESULTS

Sixty children participated in this study; however, one child was withdrawn from desflurane group, due to laryngospasm at extubation. The two groups were comparable with respect to demographic data and duration of anaesthesia [Table 1]. Haemodynamic parameters were comparable at all stages of surgery between the two groups, except during laminectomy and dural incision when the mean blood pressure (MBP) was lower in the sevoflurane group. None of the children demonstrated haemodynamic instability, requiring the use of rescue drugs. Tracheal extubation and emergence occurred earlier in desflurane group as compared to sevoflurane group [Table 2]. Total amount of intraoperative fentanyl and rocuronium consumption, fluid intake, output, blood loss and replacement were comparable between two groups [Table 2]. Two children of sevoflurane group and seven from desflurane group required a blood transfusion. BIS® values were comparable in both the groups at all measured time points [Figure 1] with steady-state end-tidal concentrations of both the agents [Table 3]. The time to achieve full MAS score [Table 4] and the MAS score at all-time point of measurements were comparable between the two groups. The post-operative haemodynamic variables were comparable at all-time intervals [Figure 2]. Time to first analgesic requirement was comparable between the two groups [Table 4]. The incidence of post-operative pain and EA were also comparable in both the groups ($P < 0.05$). There were no episode desaturations observed in the post-operative period and the rate of PONV was comparable.

Table 1: Demographic data

Parameters	Sevoflurane group (*n*=30)	Desflurane group (*n*=29)	*P*
Age (years)	5.8±3.5	5.9±3.3	
Weight (kg)	21.6±9.5	19.1±7.4	
Sex			
Male: female	14:16	14:15	
Duration of surgery (min)	168.1±76.3	188.2±97.1	0.44
Duration of anaesthesia (min)	213.5±69.3	236.5±89.3	0.33

Mean±SD or number. SD – Standard deviation

Table 2: Intraoperative data

Parameters	Sevoflurane group (*n*=30)	Desflurane group (*n*=29)	*P*
Total fentanyl (μg)	96.3±51.0	80.5±45.0	0.18
Total rocuronium (mg)	33.8±17.7	35.8±19.9	0.77
Total fluid administered (ml)	525 (210-3200)	600 (250-3000)	0.56
Urine output (ml)	150 (25-550)	150 (40-450)	0.90
Blood loss (ml)	50 (10-800)	60 (10-500)	0.61
Time to emergence (min)	8 (2.5-14)	2.5 (0.83-8)	0.0001
Time to extubation (min)	5.5 (1.2-14)	3 (0.8-10)	0.0003

Mean±SD/median (range). SD – Standard deviation

Table 3: Intraoperative end-tidal anaesthetic concentration (%)

Time intervals	Sevoflurane group (*n*=30)	Desflurane group D (*n*=29)
T_2	1.7±0.4	4.4±0.9
T_3	1.7±0.4	4.5±0.9
T_4	1.7±0.3	4.6±0.8
T_5	1.7±0.3	4.6±0.8
T_6	1.7±0.3	4.6±0.8
T_7	1.1±0.3	3.0±0.7
T_8	0.7±0.3	2.0±0.8

T_2 – After induction; T_3 – Skin incision; T_4 – Laminectomy; T_5 – Dural incision; T_6 – Dural stretching; T_7 – Skin closure; T_8 – Anaesthetic agent discontinuation

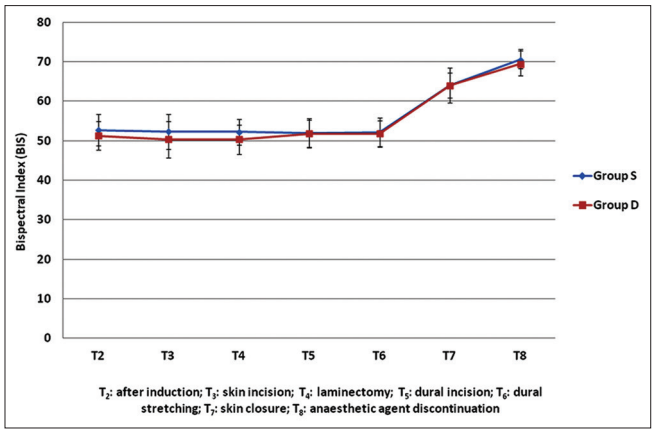

Figure 1: Intraoperative bispectral index monitoring. Comparable between the sevoflurane (S) and desflurane (D) groups during different stages of anaesthesia

Table 4: Post-operative data

Parameters	Sevoflurane group (*n*=30) (%)	Desflurane group (*n*=29) (%)	*P*
Time to attain full MAS (min)	0 (0-10)	0 (0-15)	0.22
Immediate post-operative pain (OPS ≥4)	20 (66.7)	16 (55.2)	0.26
Immediate severe EA (ACS 4/5)	13 (43.3)	6 (20.7)	0.06
Time to first analgesic (min)	10 (5-120)	10 (5-120)	0.28
Number of patients requiring fentanyl	21 (70)	19 (65.5)	0.71
Number of patients with PONV	2 (6.7)	2 (6.9)	0.99

Median (range)/*n* (%). ACS – Agitation Cole score; EA – Emergence agitation; MAS – modified Aldrete score; OPS – Objective pain score; PONV – Post-operative nausea and vomiting

DISCUSSION

Inhalational anaesthesia remains by far the most commonly used technique in paediatric patients. Whether they are used for induction or maintenance of anaesthesia, inhalational agents are pervasive because they are effective, reliable, safe, easy to deliver, stable and without major end-organ sequelae. Both sevoflurane and desflurane have a pharmacokinetic profile that results in relatively rapid emergence from anaesthesia. Because of relatively lower blood: Gas and fat: Blood partition coefficients of desflurane as compared to sevoflurane,[9,10] desflurane is expected to provide rapid, early and intermediate emergence and recovery from anaesthesia.

In this study, we compared the haemodynamic changes, timing and quality of recovery following BIS-guided anaesthesia with sevoflurane and desflurane, in children who were undergoing surgery for spinal dysraphism. Both the groups had stable and comparable haemodynamics at various stages of surgery, except during laminectomy and dural incision, when the MBP was significantly higher in desflurane group. This was possibly due to intense surgical stimulus and rapid rise in desflurane concentration to maintain prefixed BIS values during these potential painful stages of surgery. The rapid rise in the inspired concentration of desflurane might have associated sympathetic stimulation and consequent rise in MBP.[11,12] Similar observations were made by Kang *et al*.,[13] in their study, while changing anaesthetics from isoflurane to desflurane, where the HR and MB*P* values increased after 5 min.

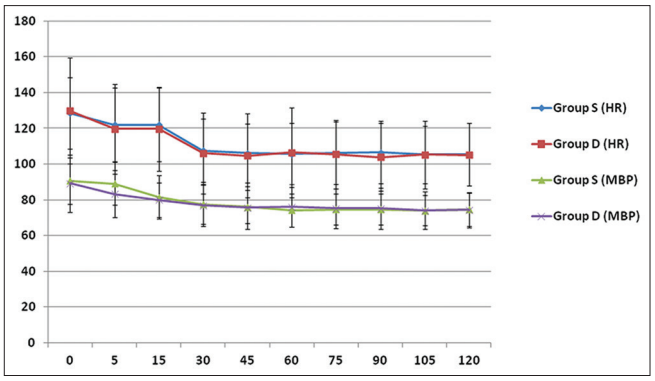

Figure 2: Post-operative haemodynamic parameters such as heart rate (HR) and mean blood pressure (MBP). No significant difference between the sevoflurane (s) and desflurane (d) groups

The time to extubation and emergence was significantly shorter in desflurane group. Numerous studies carried out in varied patient populations,[14,15] have demonstrated early recovery with desflurane as compared to sevoflurane. Cohen *et al*.[1] observed desflurane providing early emergence and recovery as compared to sevoflurane in children undergoing adenoidectomy. In children undergoing minor surgery, it was observed that the eye opening on verbal commands and tracheal extubation were earlier in desflurane group.[3] In adult patients undergoing ambulatory surgeries, recovery endpoints such as time to eye opening on verbal commands and regaining orientation were found to be significantly faster with desflurane.[16] Desflurane has also been demonstrated to reduce the average extubation time by 20–25% as compared to sevoflurane.[17] The quicker emergence with desflurane has been shown to be associated with more rapid recovery of protective reflexes.[18] In most of the studies mentioned here, the duration of anaesthesia was <1 h. In our study, the average duration of anaesthesia was about 4 h, and the results are consistent with the study carried out by other investigators[19] with duration of anaesthesia up to 3.1 h. They observed that patients receiving

desflurane exhibited a more rapid emergence, followed commands, were extubated early and gained orientation earlier than the patients receiving sevoflurane. In our study, the mean emergence and extubation times were shorter as compared to previous studies done by Cohen *et al*.[1] (eye opening time: 13.9 ± 8.3 vs. 10.7 ± 6.2 min and extubation time: 9.3 ± 3.3 vs. 6.5 ± 2.8 min, in sevoflurane vs. desflurane, respectively) and Kim *et al*.[3] (eye opening time: 9.2 ± 3.6 vs. 6.6 ± 3.0 min and extubation time: 9.3 ± 3.7 vs. 6.2 ± 2.7 min, in sevoflurane vs. desflurane, respectively). This difference is possibly due to the depth of anaesthesia being reduced at the time of skin closure, in our study.

It has been demonstrated that time for 'ready to discharge'status from PACU was significantly shorter in desflurane group as compared sevoflurane.[1] In our study, MAS and time to achieve full MAS were comparable between the two groups. Our results were similar to the meta-analysis done by Macario *et al*.[19] in varied patient population, where recovery from anaesthesia was earlier in desflurane group. However, there was no significant difference in intermediate recovery between sevoflurane and desflurane.

EA is a well-documented clinical phenomenon in children characterised by confusion, irritability, disorientation and inconsolable cry. The exact aetiology of EA is still unknown, although it is hypothesised to be due to rapid emergence following the use of the newer less soluble anaesthetic agents. The rapid emergence may create a dissociative state, and the children awaken with altered cognition.[20] Factors such as pre-operative anxiety and post-operative pain have also been implicated for the occurrence of EA. Few authors are of the opinion that sevoflurane causes less EA as compared to desflurane.[2,21] In our study, the EA was comparable between the two groups. This was in accordance with the observations made by different other authors.[1,22] In contrast Locatelli *et al*.[23] observed a comparable incidence of emergence delirium in children receiving either sevoflurane or desflurane, however, the duration of emergence delirium was significantly shorter with desflurane. The discrepancy in the occurrence of EA may possibly due to different scores utilised for the assessment and different premedication given to the patients those who were evaluated.[24] One child developed laryngospasm at extubation, which was treated with propofol and that lead to prolongation of the emergence time. The child was extubated 35 min later without any untoward event.

Post-operative pain scores (OPSs) at different time intervals and time of first analgesic requirement was comparable between the two groups. Although more patients required analgesia in sevoflurane group, it was not significantly different from desflurane group. Similar results have been reported,[25] in adult patients undergoing abdominal myomectomy and receiving anaesthesia with sevoflurane or desflurane. There was no significant difference in post-operative pain or analgesic requirement.

This study had certain limitations. There remained a possibility of bias as the study was not blinded, subjective nature of scoring systems and multiple observers in the PACU. Moreover, both modified OPS for assessment of pain and ACS for assessment of EA are not validated in children, which may possibly reduce the reliability of such scores. However, these scales are easy to use and have been used in many studies involving children. Although there was a statistically significant decrease in the time for extubation and emergence with the use of desflurane; its clinical significance is unknown as the difference was only a few minutes. While assessing EA, the contribution of post-operative pain remains an important confounding variable as a child who is in pain may also be agitated. Many of the children in our study were old enough to communicate about the presence or absence of pain; hence, this overlapping picture may be less limiting.

CONCLUSION

The use of desflurane for maintenance of anaesthesia resulted in the early emergence and tracheal extubation, as compared to sevoflurane, in children undergoing corrective surgery for spinal dysraphism. The incidence of severe EA was comparable with both the agents and their use was not associated with any untoward event.

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Conflicts of interest

There are no conflicts of interest.

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