Original Research Article

Comparative study of Intraoperative Haemodynamics and recovery characteristics of desflurane and sevoflurane in patients receiving General Anaesthesia

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Abstract

Background: Inhaled anesthetics used for general anaesthesia have a rapid onset and offset of action. The Induction and recovery depends on anaesthetic drug solubility, cardiac output and minute ventilation. Sevoflurane and desflurane have low blood gas partition coefficients, and therefore share the advantage of faster onset and recovery from anaesthesia when compared to other inhaled anesthetics. Hence, we designed this prospective randomized study to compare the intraoperative haemodynamic parameters and recovery characteristics of desflurane and sevoflurane. **Methods:** Sixty patients aged between 18-50 years belonging to ASA I and II scheduled for elective general anaesthesia were enrolled in the study and randomly divided into two groups to receive desflurane(group D) and sevoflurane(group S) for the maintenance of anaesthesia. Both groups were premedicated, pre oxygenated and induced with propofol. Muscle relaxation maintained with vecuronium. Desflurane and sevoflurane concentrations were adjusted according to entropy parameters and clinical variables like HR, NIBP, MAP and SPO2. Neuromuscular blockade reversed with neostigmine and glycopyrrolate. Recovery characteristics assessed using modified Aldrete scoring. **Results:** The intraoperative haemodynamics was similar with both desflurane and sevoflurane, and was maintained within 20% of baseline values. However, early recovery characteristics were significantly better in group D. Time to eye opening was 6.63 $\pm$ 2.17 min in group S versus 4.77 $\pm$ 1.41 min in group D ($P < 0.001$). Time to Extubation was 8.03 $\pm$ 2.54 min in group S and 5.93 $\pm$ 1.44 min in group D ($P < 0.001$). Response to verbal commands was 8.77 $\pm$ 3.01 min in group S and 6.97 $\pm$ 1.67 min in group D ($P < 0.001$). Modified Aldrete score were significantly better in group D than group S at 1st min, 2nd min and 3rd min. Thereafter, modified Aldrete score assessed at 5, 10, 15, 30 and 60 min were similar in both groups. **Conclusion:** Both desflurane and sevoflurane produce similar stable haemodynamic profile. Despite the faster early recovery with desflurane, no significant differences were found between the two volatile anaesthetics after 5 minutes during intermediate recovery period.

Keywords: Desflurane, Sevoflurane, Entropy, Depth of Anaesthesia.

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INTRODUCTION

The search for an ideal inhalational general anesthetic agent continues. Inhaled anaesthetics allow rapid emergence from anaesthesia because of easy titrability with inherent neuromuscular blocking effects.[1] The low solubility in blood of the newest anesthetics facilitate rapid induction of anaesthesia, permit precise control of anesthetic concentrations during maintenance of anaesthesia, and favor prompt recovery at the end of anaesthesia independent of the duration of administration. The challenge to the anesthesiologist is to exploit the

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pharmacokinetic advantages of these drugs while minimizing the risks and increased expense associated with the manufacture and increased cost of administration of these new drugs.[2] Desflurane offers the advantage of precise control over depth of anaesthesia along with a rapid, predictable, and clear-headed recovery with minimal postoperative sequelae, making it a valuable anaesthetic agent for maintenance in adults and paediatric patients in surgeries of all durations. The agent has advantages when used in extremes of age and in the obese.[3] Many studies have compared recovery characteristics of Desflurane and Sevoflurane. Some have found early recovery with desflurane while others have not.[6, 12] Instead of MAC equivalent doses of desflurane or sevoflurane, we used entropy as a guide, which is quantifiable measure of sedative and hypnotic effects of inhaled anaesthetics as an indicator of adequate anaesthesia. Hence, we designed this study to compare the intraoperative haemodynamic characteristics of desflurane and sevoflurane in patients receiving entropy guided general anaesthesia.

MATERIALS AND METHODS

A prospective randomized study was conducted on 60 patients aged between 18-50 years, belonging to ASA I and II, undergoing elective surgery of less than 2 hours under general anaesthesia after obtaining informed written consent. Patients with cardiopulmonary, hepatic, renal and central nervous system dysfunction, inadequately controlled hypertension, Chronic alcohol or narcotic abuse were excluded from the study. A detailed history and Pre anaesthetic examination was done one day prior to surgery. All the patients were advised overnight fasting for 8 hours prior to surgery. Premedication with oral ranitidine hydrochloride 150 mg and alprazolam 0.25 mg were given the night before surgery. The patients were randomly allocated into two groups of 30 each (group S-sevoflurane and group D desflurane) using computer generated randomization. After shifting the patient to operating room, IV access was obtained with 18G IV cannula and ringer lactate started. Electrocardiogram, pulse oximetry, non invasive blood pressure, entropy and neuromuscular monitors (entropy and NMT module of Datex Ohmeda Avance S/5™) were connected. Baseline vitals – heart rate, systolic BP, diastolic BP, MAP, SpO_2 were recorded. State entropy and response entropy were noted. All patients were Premedicated with injection glycopyrrolate 0.01mg/kg, midazolam 0.03mg/kg and inj. fentanyl 2mcg/kg. After preoxygenation with 100% oxygen for 3 minutes, patients were induced with injection propofol 30mg boluses every 30 seconds till entropy reached 50 and intubation was facilitated with IV vecuronium 0.1mg/kg bolus dose. Intraoperative Monitoring of electrocardiography (ECG), oxygen saturation (SpO2), non-invasive blood pressure (NIBP), end tidal carbon dioxide (EtCO2), train of four (TOF) and entropy were continued. Anaesthesia was maintained with either desflurane (group D) or sevoflurane (group S) in combination with N2O 40% in O2. All patients were mechanically ventilated with a tidal volume of 6-8 ml/kg and respiratory rate of 12 – 14 breaths/ min, to maintain the end tidal CO2 between 35-40 mmHg. The initial dial concentration was set at 2% for sevoflurane and 6% for desflurane and adjusted subsequently to maintain the Response entropy in the range of 40-60, and also based on haemodynamic parameters. Muscle relaxation was maintained with inj. vecuronium IV top up doses with the aid of train of four (TOF) Monitoring. The fresh gas flow rate kept at 6litres/min until the difference between the set dial concentration and inspiratory inhaled anaesthetic concentration became less than 0.1% and then reduced to 2litres/min. Tachycardia and hypertension was defined as increase in heart rate and mean arterial pressures more than 20% from baseline and managed by increasing inspired concentration of volatile agents and inj. Fentanyl 1 mcg/ kg bolus if required, and the dose of supplemental fentanyl required was noted. Persistent tachycardia and hypertension resistant to above measures inspite of entropy less than 60 was managed with vasodilators and the case excluded from the study. Bradycardia was defined as heart rate less than 50 beats/ min and hypotension as more than 20% decrease in mean arterial pressure from baseline and treated with Inj. Atropine 0.6 mg iv and fluid boluses respectively. Desflurane/Sevoflurane and N2O was turned off after the last skin suture and fresh gas flow increased to 6litres/min of 100% oxygen. Residual neuromuscular blockade reversed with Inj. Neostigmine 0.05 mg/kg and Inj. glycopyrrolate 0.01 mg/kg. Early recovery was assessed by recording the time to spontaneous eye opening, time to extubation, time of response to verbal commands from the time of stopping volatile anesthetic agents. In the post-anesthesia care unit (PACU), intermediate recovery was assessed with the help of modified Aldrete Score.

Statistical methods

Based on the previous studies, by keeping the power of study as 80% and confidence limit at 95%, to detect a 10% difference in Mean arterial pressure between the two groups, the minimum sample size required was 29 in each group and to detect 15% difference in time to extubation between the two groups, the minimum sample required was 20 in each group. For a better validation of results we have included 30 patients in each group. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to

find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data. Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Patients in group S and group D had unequal gender distribution with a significant p value of 0.024. Other demographic profile, intubating conditions, duration of surgery, duration of anesthesia and duration of anesthetic agents used were comparable. There was decrease in heart rate following induction in both groups compared to baseline. However, there was no increase in heart rate above baseline in both groups after intubation and throughout intraoperative period. There was no clinically or statistically significant difference in the heart rate between the two groups. The systolic blood pressure, the diastolic blood pressures and mean arterial blood pressures were well maintained in the two groups and there was no significant difference both statistically and clinically. Time to eye opening, time to extubation and response to verbal commands were shorter in the Desflurane group which was statistically and clinically significant. Time to eye opening was 6.63 ± 2.17 min in group S versus 4.77 ± 1.41 min in group D (P< 0.001). Time to Extubation was 8.03 ± 2.54 min in group S and 5.93 ± 1.44 min in group D (P < 0.001). Response to verbal commands was 8.77 ± 3.01 min in group S and 6.97 ± 1.67 min in group D (P < 0.001). Recovery characteristics as assessed by modified Aldrete score were better in group D and clinically and statistically significant at 1,2 and 3 mins. At 1 min total modified Aldrete score was 12.63 ± 1.06 min in group D and 11.96 ± 1.03 min in group S (P= 0.017). At 2 min, it was 13.13 ± 0.93 min in group D and 12.46 ± 0.89 min in group S (P = 0.007). At 3 min, it was 13.86 ± 0.34 min in group D and 13.36 ± 0.71 min (P = 0.001). Since the gender distribution was unequal with a significant p value of 0.024, haemodynamic parameters and recovery characteristics were compared between the female patients in both the groups and between the male and female patients in the same group.

Table 1: Demographic data and duration

Parameters	Group S	Group D	P value
Age, years(mean±SD)	39.23±8.76	39.23±7.20	
Weight, kg (mean+ SD)	54.5±5.4	52.8±6.31	0.267
Duration of surgery ,min	63.43±12.34	64.09±13.77	0.767
Duration of anaesthesia,min	73.33±23.43	73.17±26.05	0.979
Duration of anaesthetic used	64.57±21.46	66.20±25.95	0.791

Table 2: Comparison of score on eye opening, time to extubation and response to verbal commands

Recovery parameters in min	Group S	Group D	P value
Eye Opening	6.63±2.17	4.77±1.41	<0.001**
Time to Extubation	8.03±2.54	5.93±1.44	<0.001**
Response to verbal commands	8.77±3.01	6.97±1.67	<0.001**

Table 3: Comparison of Modified Aldrete score in both groups

TOTAL SCORE	Group S	Group D	p- value
1 min	11.96±1.03	12.63±1.06	0.017*
2 min	12.46±0.89	13.13±0.93	0.007*
3 min	13.36±0.71	13.86±0.34	0.001*
5 min	13.76±0.43	13.86±0.50	0.414
10 min	14.00±0.00	13.90±0.30	0.078
15 min	13.93±0.25	13.90±0.40	0.703
30 min	13.90±0.30	13.86±0.43	0.732
60 min	13.86±0.34	13.76±0.56	0.414

DISCUSSION

Inhalational anaesthesia remains by far the most commonly used technique for general anaesthesia.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. In this study, we compared the haemodynamic changes and recovery characteristics following entropy guided anaesthesia with

sevoflurane and desflurane, in patients who were undergoing surgeries under general anaesthesia. There was no differences in the total dose of propofol, premedicants and vecuronium between the two groups. Duration of surgery and anaesthesia, $EtCO_2$ concentrations were comparable between the two groups. Anaesthetic agents were administered at equiMAC concentrations to maintain uniformity and the average MAC values were comparable in both groups. In our study, intraoperative haemodynamic parameters including Heart rate, SBP, DBP and MAP , did not differ in the two groups during the course of anaesthesia and were maintained within 20% of baseline values with both anaesthetics. Similar findings were noted in studies conducted by Kaur A *et al.* [4] and Wilhelm W *et al.*[5]. In anoter study by Nathason MH *et al.*[6] it was noted that Heart rate values were lower in the sevoflurane group during the induction-to-incision period.

Modified Aldrete Score

Consciousness	**Physical activity**
Awake and oriented 2	Able to move all extremities on Command 2
Arousable with minimal stimulation 1	Some weakness in movement of extremities 1
Responsive only to tactile stimulation 0	Unable to voluntarily move extremities 0
Haemodynamic stability	**Respiratory stability**
Blood pressure, 15% of baseline MAP value 2	Able to breathe deeply 2
Blood pressure 15%–30%of baseline MAP value 1	Tachypnea with good coughs 1
Blood pressure .30% below baseline MAP value 0	Dyspneic with weak cough 0
Oxygen saturation status	**Postoperative emetic symptoms**
Maintains value 90% on room air 2	None or mild nausea with no active vomiting 2
Requires supplemental oxygen (nasal prongs) 1	Transient vomiting or retching 1
Saturation, 90% with supplemental oxygen 0	Persistent moderate to severe nausea and 0 vomiting
Postoperative pain assessment	
None or mild discomfort 2	
Moderate to severe pain controlled 1 with IV analgesics 0	TOTAL SCORE 14
Persistent severe pain	

However, HR and MAP were otherwise similar during the maintenance and recovery periods. Recovery is a continual and ongoing process and is divided into three phases. Early recovery, as the patients emerges from anaesthesia and regains vital reflexes; intermediate recovery, when the patient achieves criteria for discharge from the PACU; and late recovery, when the patient returns to his or her preoperative physiological state. Early and complete recovery are desirable in all patients undergoing general anaesthesia without any side effects in order for patients to resume their normal activities of daily living. The pharmacokinetic properties of desflurane and sevoflurane favor better intraoperative control of anaesthesia and a rapid postoperative recovery. They have significantly lower blood/gas partition coefficients (0.45 and 0.65 respectively) than Isoflurane(1.4) or halothane(2.4). The lower fat/blood partition coefficient of desflurane, 27 vs 48 for sevoflurane, should favor its early elimination from the body resulting in early recovery. In our study ,eye opening was earlier in the desfurane group(4.77$\pm$ 1.41 min) when compared to sevofurane group(6.63$\pm$2.17 min) , which was statistically significant(P <0.001). Similar observations were made by Kaur A *et al.*[4] Eger *et al.*[7] and Tercan E *et al.*[8] in their study. However, in a study conducted by Tarazi *et al.*[9], they found that recovery indices like time to eye opening, command response, orientation, sitting in bed, sitting with legs dangling, standing, walking, discharge, and departure were marginally but not significantly better with sevoflurane than desflurane. Time to extubation in the desflurane group was 5.93$\pm$1.44 min and in sevoflurane group was 8.03$\pm$2.54 min, in our study. Hence, use of desfurane led to a shorter time to extubation than sevoflurane (P <0.001).This observation was similar to the observation made by Nathason *et al.*(5.1+2.2 desfurane vs 8.2+4.2 min).[6] Response to Verbal commands was faster in the desflurane group(6.97$\pm$ 1.67 min)than sevoflurane(8.77$\pm$ 3.01 min) in our study which was statistically significant(P <0.001). A study conducted by Mc kay *et al.* also show similar results(3.4$\pm$ 1.9 for desflurane vs 5.5$\pm$3.1 min; p < 0.01).[10]

Modified aldrete score[11] was comparatively higher in the desflurane group at 1,2 and 3 minutes which was clinically and statistically significant in our study. In the 1st minute total modified Aldrete score in the desflurane group was 12.63$\pm$1.06 whereas, in the sevoflurane group it was 11.96$\pm$1.03 (P =0.017). 2nd minute modified Aldrete score was 13.13$\pm$0.93 in the desflurane group and 12.46$\pm$0.89 in the sevoflurane group (P= 0.007). 3rd minute modified Aldrete score was 13.86$\pm$0.34 in desflurane group and 13.36$\pm$0.71 in sevoflurane group(P= 0.001). Total score observed at 5, 10, 15, 30 and 60 minutes were comparable in both the groups and statistically not significant. Despite

the faster initial recovery with desflurane, no significant differences were found between the two volatile anaesthetics after 5 minutes during intermediate recovery period. These results were consistent with studies conducted by Strum EM *et al.*[12]. on admission to PACU. Kaur A *et al.*[4] noted that although the intermediate recovery, as assessed by the modified Aldrete score was comparable between the desflurane and sevoflurane groups on arrival at the PACU and at 10 minutes, the score at 5 minutes was significantly higher in the desflurane group($p < 0.05$). Welborn *et al.*[13] reported that mean times to awakening (4.7 vs 8.0 minutes) and early recovery (9.3 vs 17.1 minutes) were more rapid with desflurane than with sevoflurane, respectively. However, they also found that later recovery times did not differ between the 2 groups. Overall incidence of side effects like PONV did not differ between the two anaesthetic groups in our study during the 60 minutes stay at PACU.These findings were consistent with the studies conducted by Nathason MH *et al.*, Strum EM *et al.*, and Macario A *et al.*[6,12,14] In our study we did not observe cough in either groups. In studies conducted by White PF *et al.*[15]and Lema FE *et al.*[16] evaluating the incidence of cough on the Shahbaz scale, they found that the overall incidence of coughing during the perioperative period was higher in the desflurane group (60% versus 32% in the sevoflurane group, $P < 0.05$. In a study conducted by De Oliveira GS *et al.*[17], to compare time to awakening and upper airway morbidity between desflurane and sevoflurane using balanced anaesthetic regimen inclusive of opioids concluded that desflurane retains faster awakening properties than does sevoflurane when used in combination with fentanyl as part of anaesthetic maintenance. The balanced anaesthetic maintenance regimen seems to reduce the potential airway reactivity properties of desflurane. In a study conducted by Takeda J *et al.* comparing the efficacy and safety of desflurane and sevoflurane, there was no statistically significant difference in the incidence of total adverse reactions between the desflurane and sevoflurane group. The results indicated that desflurane is an effective and safe inhalation anaesthetic.[18] In a study conducted by Lanuzzi E *et al.*, the quality of recovery from anaesthesia in elderly patients were analysed and concluded that VAS was higher in the Desflurane group as well as the need for postoperative analgesia.[19] In our study All patients either had no or mild- moderate pain and none required rescue analgesics.

Mahmoud *et al.* concluded that the faster emergence after discontinuation of desflurane led to an earlier discharge and more rapid resumption of normal activities.[20] We did not assess time to discharge from PACU in our study. Our results show a statistical and clinical difference between the early recovery profiles of patients who received desflurane versus sevoflurane. These findings are consistent with the faster kinetic profile and washout period of desflurane. However, the intermediate recovery profile was similar in both desflurane and sevoflurane. The limitation of our study was that, the recovery profile was assesed for only 60 minutes in PACU after cutting the inhalational agent. We did not assess the time to discharge from PACU, 24 hour analgesic requirements. Other tests to assess cognitive recovery such as DSST, MMS and other tests were not done in the present study. Another limitation of our study was a lack of investigator blinding to the use of study drugs. The use of entropy to titrate volatile anaesthetic concentration and discontinuation of all volatile anaesthetics at skin closure however, minimized the investigator bias.

CONCLUSION

Both desflurane and sevoflurane produce similar stable haemodynamic profile. Despite the faster early recovery with desflurane, no significant differences were found between the two volatile anaesthetics after 5 minutes during intermediate recovery period.

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