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Advantages of Newer Inhalational Anesthetic Agents over the Older Agents

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Abstract

The objective of anesthesia is to facilitate surgery at minimal risk to the patient and to ensure optimal recovery following the procedure. Sevoflurane is a potent nonexplosive newer inhalational anesthetic agent that has several advantages. Various side effects like arrhythmia, hepatotoxicity, and delayed recovery limit the use of older agent halothane in many western countries. However, we do not have such studies done in our country. This prospective study was carried out in the Department of Anesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from September 2009 to June 2011, to analyze the advantages of newer inhalational agents over the older agents. A total of 60 patients were recruited in this study: 30 in Sevoflurane and 30 in Halothane group. We assessed hemodynamics and recovery after sevoflurane and halothane anesthesia. The mean arterial pressure (MAP) and the heart rate (HR) at 15 minutes interval were similar in both groups except at 75 minutes, when both MAP and HR were significantly higher in the halothane group as p=0.003 and p=0.001 respectively. Emergence time was 10.85 min. in the sevoflurane group and 15.13 min. in the halothane group (p<0.001). The mean BAMSE score and time to complete (TMT-A) at half an hour after recovery was significantly higher (29.3) (p=0.014) and significantly less (40.9 sec.) (p<0.001) in sevoflurane group. Our data suggests that sevoflurane is a better anesthetic agent than halothane in terms of balanced hemodynamics, shorter emergence time and early cognitive recovery.

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Introduction

Researchers are continually looking for safety in anesthesia by improving the quality of drugs, instruments and different procedures to provide a good recovery from anesthesia for better operative conditions.[1-3] In western countries, it is customary to use one of the five modern volatile anesthetic agents desflurane, sevoflurane, enflurane, isoflurane and halothane vaporized in a mixture of nitrous oxide in oxygen. In recent years, the use of halothane has declined because of medico legal pressure relating to hepatotoxicity and there has been a clear trend to avoidance of repeated halothane anesthesia.[4,5] Slow recovery compared with other new agent and sensitisation of the heart to catecholamine limits the use of halothane.[5,6] On the other hand sevoflurane with nitrous oxide provides satisfactory anesthetic

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induction and intubating conditions; however, induction using sevoflurane without nitrous oxide is associated with a high incidence of patient excitement and prolonged time to intubation. There were greater decreases in heart rate and systolic blood pressure during induction with halothane than with sevoflurane.[5] Sevoflurane has negligible airway irritant effects, which facilitates a 'smooth' induction, even in comparison with halothane in pediatric patients, and makes sevoflurane especially amenable to rapid induction of anesthesia in adults and children. Sevoflurane has a lower potential for hepatic injury than halothane.[5]

Unlike methoxyflurane, sevoflurane undergoes minimal intrarenal defluorination, which may account for the lack of fluoride ion-induced nephrotoxicity in humans, despite elevated plasma fluoride levels after its use.[5,6] Furthermore, earlier recovery with sevoflurane permits rapid patient assessment and improved potential for discharge from the operating room.[6,7]

Moreover, clinicians no longer commonly use halothane in today's operating rooms in developed countries. Apart from the liver dysfunction associated with obesity predisposing patients to halothane's adverse effects, halothane also accumulates in the adipose tissue. Delayed excretion and theoretically prolonged exposure to potentially reactive halothane metabolites are also thought to increase the obese patient's risk.[1,5]

Our study aims to see the advantages of newer inhalational anesthetic agents over the older agents by assessing the hemodynamics, emergence time and early complete recovery after sevoflurane and halothane anesthesia.

Methods

This prospective study was carried out in the Department of Anesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from September 2009 to June 2011. A total of 60 patients were recruited – 30 were assigned to Sevoflurane and 30 to Halothane groups.

Inclusion Criteria:

1) Adult patients of either sex aged between 18-50 years.
2) Patients with ASA-I and II physical states, scheduled for elective surgery under general anesthesia lasting approximately 1-2 hours and those remain admitted in the hospital for 24 hours after surgery
3) Patients who had given consent to participate in the study.

Exclusion Criteria:

1) Patients with a history of significant cardiac, pulmonary, hepatic, or renal diseases.
2) Patients having a chronic drug or alcohol abuse.
3) Patients with morbid obesity.
4) Patients with disabling neuropsychiatric disorders.
5) Hypersensitivity to anesthetics or family history of malignant hyperpyrexia.
6) Pregnant and breastfeeding women.
7) Patients who experienced hypo and hypertension, hypoxia, and severe blood loss during surgery.
8) Patients who needed narcotics as an analgesic in the first 3.5 hours in the post-operative ward.
9) Patients who did not give consent to participate in the study.

Data were collected using a pre-designed data collection sheet containing all the variables. All patients were examined 24 hours prior to surgery which was addressed as baseline values. Hemodynamic variables like mean arterial pressure (MAP), heart rate (HR), partial pressure of oxygen (SPO_2) and psychometric tests that assessed recovery of cognitive function (that restores in intermediate phase of recovery starting from 30 mins to 3 hours after anesthesia) were assessed using Bangla adaptation mini-mental state examination (BAMSE) and Trail making test part-A (TMT-A). Folistein *et al*.[8] developed a short simplified Mini Mental State Examination (MMSE). An adaptation of MMSE for the cultural context and for use of population, irrespective of literary skill was revised.[9] In the Bangla Adaptation mini mental state examination (BAMSE), MMSE items were changed in such a way that they would be applicable for illiterate individuals as well as culturally relevant in Bangladesh. The BAMSE contain 11 questions with total score of 30. Maximum score 30 and score lower than 21 are associated with cognitive impairment.[10] The Trail making test part-A (TMT-A) is a paper pencil test for assessment of cognitive function. In TMT-A, 25 circles are distributed over a sheet of paper and the circles are numbered as 1 to 25 and patient were asked to connect the circles without lifting the pencil as early as possible according to ascending order and the time required to complete the task was recorded in seconds. The TMT-A > 78 seconds considered as deficient.[15] We used in TMT-A the Bangla version of the digit 1-25. The BAMSE and TMT-A were repeated in the postoperative ward at ½ hour, 1½ hour, 2½ hours, and 3½ hours after recovery from anesthesia. Mean arterial pressure (MAP), heart rate (HR), partial pressure of oxygen (SPO_2) were measured before induction and every 15 minutes interval during surgery. The emergence time was counted from discontinuation of sevoflurane or halothane up to attainment of Aldrete recovery score >/= 9 in minutes and recorded.

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) version 20.0. Student's t-test (for comparison of data presented on a continuous scale), and Chi-square test (for comparison of categorical data between groups) were used. The level of significance was set at 0.05 and $p<0.05$ was considered significant.

This research was approved by the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Results

The age distribution of the patients between sevoflurane and halothane groups was almost identical with the mean ages of the former and the latter groups being 31.6±7.2 and 31.4±5.9 years respectively (p=0.938) (Table-I). Females were significantly higher in the sevoflurane group than that in the halothane group (p=0.02) (Table-I). Baseline values (24 hours before surgery) characteristics of the patients depict that the mean arterial pressure, heart rate, SPO_2, BAMSE score, and TMT-A were almost similar between Sevoflurane and Halothane groups (56.4±9.2 vs. 56.7±8.7 kg, p=0.886; 83±6 vs. 84±4 mmHg, p=0.668; 82±8 vs. 80±7 beats/min, p=0.292; 96.1±0.4 vs. 96.3±0.4%, p=0.356; 29.3±0.3 vs. 29.9±0.1, p=0.052 and 36.1±9.3 vs. 31.9±10.1 sec, p=0.103 respectively).

ASA grading was also found similar between halothane and sevoflurane groups (p=0.739) (Table-II). The mean arterial pressures at 15, 30, 45 and 60 minutes after induction were similar in both groups (p>0.05). However, at 75 minutes the mean arterial pressure was significantly higher in the halothane group than that in the sevoflurane group. In terms of heart rate as well, the groups were almost identical up to 60 minutes following induction, but it exceeds a significantly higher level in the halothane compared to the sevoflurane group at 75 minutes interval (p=0.001). Aldrete's recovery score was the same in both groups (p=0.986). Emergence time was 10.85 min in the sevoflurane group and 15.13min in the halothane group (p<0.001) (Table-III).

The mean BAMSE score at half an hour after recovery in the sevoflurane group was significantly higher (29.3). In contrast, in the halothane group mean score was (27.8) (p=0.014). But at 1.5 hours after recovery, the mean BAMSE score of the Sevoflurane and Halothane groups were 29.7 and 29.8 respectively (p=0.873). Thereafter no significant changes were evident throughout the whole period of observation of 3.5 hours (p>0.05) (Table-IV).

The mean time required by the patients of the sevoflurane group to complete trail making test part-A (TMT-A) at half an hour after recovery was significantly less (40.9 sec.) than the patients of the halothane group (55.8 sec. and p<0.001) However, no significant difference was observed between the groups in terms of TMT-A at 1.5, 2.5, and at 3.5 hours interval (p=0.219, p=0.279 and p=0.159 respectively) (Table-V).

Table-I. Distribution of respondents according to age in two groups (N=60)

Variables	**Group**		**p-value**
	Sevoflurane (n=30)	**Halothane (n=30)**	
Age group (years)			
<30	12(40.0%)	13(43.3%)	
30-40	13(43.3%)	15(50.0%)	
≥40	5(16.7%)	2(6.7%)	
Mean±SD	31.6 ± 7.2	31.4 ± 5.9	0.938
Sex			
Male	10	16	
Female	20	14	0.02

Table-II: Distribution of respondents according to baseline characteristics of two groups (N=60)

Baseline values 24 hours before surgery	**Group**		**p-value**
	Sevoflurane (n=30)	**Halothane (n=30)**	
Weight (kg)	56.4 ± 9.2	56.7 ± 8.7	0.886
ASA Grade-I Grade-II	24(80.0%) 6(20.0%)	25(83.3%) 5(16.7%)	0.739
Mean arterial pressure (mm Hg)	83±6	84±4	0.668
Heart rate (beat/min)	82±8	80±7	0.292
SPO_2	96.1±0.4	96.3±0.4	0.356
BAMSE score	29.3±0.3	29.9±0.1	0.052
Time required to complete TMT-A (sec.)	36.1±9.3	31.9±10.1	0.103

Table-III: Distribution of respondents according to per-operative findings of two groups (N=60)

Peroperative findings	Group		p-value
	Sevoflurane (n = 30)	Halothane (n = 30)	
Mean arterial pressure (mmHg)			
At 15 min	86 ± 7	88 ± 5	0.074
At 30 min	83 ± 11	86 ± 12	0.203
At 45 min	86 ± 9	82 ± 13	0.223
At 60 min	83 ± 8	84 ± 11	0.783
At 75 min	90 ± 6	95 ± 7	0.003
Heart rate (beats/min)			
At 15 min	85 ± 10	83 ± 9	0.505
At 30 min	73 ± 9	74 ± 12	0.902
At 45 min	70 ± 8	69 ± 12	0.681
At 60 min	68 ± 9	72 ± 11	0.100
At 75 min	84 ± 8	92 ± 13	0.001
SPO_2	99.8 ± 0.2	99.9 ± 0.1	0.326
Aldrete recovery score 9/10	9±1	9±1	0.986
Emergence time (min)	10.85+1.64	15.13±2.29	0.001

Table-IV: Distribution of subjects according to BAMSE score at different time intervals (N=60)

BAMSE score	Group		p-value
	Sevoflurane (n = 30)	Halothane (n = 30)	
Baseline values (24 hours before surgery)	29.3 ± 0.5	29.5 ± 0.5	0.452
Postoperative period 0.5 hours	29.3 ± 0.7	27.8 ± 1.0	0.014
1.5 hours	29.7 ± 0.2	29.8 ± 0.2	0.873
2.5 hours	29.8 ± 0.1	30.0 ± 0.0	0.624
3.5 hours	30.0 ± 0.0	29.9 ± 0.2	0.624

Table-V: Distribution of subjects according to the time required to complete TMT-A at a different time interval (N=60)

Time required to complete TMT-A (sec)	Group		p-value
	Sevoflurane (n=30)	Halothane (n=30)	
Baseline values (24 hours before surgery)	36.1 ± 9.3	31.9 ± 10.1	0.103
Postoperative period			
At 0.5 hours	40.9 ± 9.8	55.8 ± 11.4	<0.001
At 1.5 hours	37.6 ± 7.2	34.7 ± 10.3	0.219
At 2.5 hours	37.4 ± 6.9	35.1 ± 9.4	0.279
At 3.5 hours	37.5 ± 6.8	34.5 ± 8.9	0.152

Discussion

In this study, the mean arterial pressure and heart rates were observed to be almost homogeneous at 15, 30, 45, and at 60 minutes intervals following induction. At 75 minutes mean arterial pressure and heart rate were higher in the halothane group compared to the sevoflurane group. Epstein *et al.*[11] found hemodynamic status like mean arterial pressure, heart rate, oxygen saturation, end-tidal gas concentration and the temperature were stable with sevoflurane than halothane. Recently Kangralkar *et. al.*[12] conducted a study comparing sevoflurane and halothane in pediatric and adult patient & found mean heart rate, blood oxygen saturation level and mean arterial pressure were stable while maintenance of anesthesia sevoflurane than halothane. In our study it was demonstrated that hemodynamic stability was maintained with sevoflurane than halothane. The stability of heart rate in sevoflurane was desirable as it neither increased the myocardial oxygen consumption nor decrease the time available for myocardial perfusion.

In terms of cognitive recovery In this study we found the mean BAMSE score half an hour after recovery of patients from the sevoflurane group was 29 which was the same as the baseline value that is the preoperative value and demonstrated no change throughout the whole period of observation in postoperative ward, while the patients of the halothane group experienced a fall and rise in BAMSE score from recovery to the end of observation. The mean time required to complete TMT-A was identically distributed throughout the observation except at 0.5 hours after recovery when the sevoflurane group had a much lower score (40.9 sec.) and that is nearer to preoperative value (36.1 sec.) compared to their halothane counterpart (55.8 sec.).The pre-operative value of TMT-A of the halothane group was (31.9 sec.), more different than the post-operative value at 0.5 hrs. Philip *et al.*[13] demonstrated that significantly more patients were able to complete psychomotor recovery test during First 60 min post anesthesia. Redhu *et al.*[14] also concluded that psychomotor recovery was more rapid after sevoflurane anesthesia comparable to our study. The faster recovery of sevoflurane could be attributed to its lower blood and lipid solubility.

This study also revealed that emergence time from discontinuation of volatile agent up to the attainment of Aldrete recovery score >9 in the sevoflurane group was 10.85 min and in the halothane group was 15.13 min ($p<0.001$) demonstrated earlier emergence than halothane. Ravi *et al.*[15] also found that emergence time was 6.7 min in the sevoflurane group and 9.07 min in the halothane group. The time difference between two study might be: as Ravi and colleagues recorded their time from discontinuation of volatile agent till extubation and we counted the time from discontinuation of sevoflurane or halothane till attainment of Aldrete recovery score ≥9. Ravi and associates also concluded that sevoflurane provides rapid recovery from anesthesia due to its lower solubility comparable to our study.

However, the limitation of our study includes its single hospital trial with a small sample size. Hence, the results may not represent the whole community.

Conclusion

Our data suggests that advantages of sevoflurane include stable hemodynamics, shorter emergence time and early complete cognitive recovery that causes early mobilization of the patients, reduced postoperative complication and shorter hospital stay with reduced cost of the patients. On the other hand, halothane is a medication previously used for induction and maintenance of general anesthesia. After its large impact on medicine and anesthesia specifically, it has since fallen out of practice due to its side effect profile in many countries. Though sevoflurane is a costly drug, it should be considered instead of halothane, for more advantages and faster cognitive recovery which may reduce postoperative complications. Further studies are recommended involving multiple centers and with larger samples in this regard.

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