Original Article

Recovery of Cognitive Function in Adults: A Comparison of Sevoflurane And Halothane Anaesthesia

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Abstract:

Background: *Among the recovery phases, patient achieve their cognitive and psychomotor skills in intermediate phase. Rapid clearance drug like Sevoflurane has beneficial effect on early cognitive recovery which allows early mobilization and reduce post operative complication but Halothane with delayed recovery profile is still commonly used in our country.*

Objective: *So the study was done to compare the post operative cognitive recovery in adult patients receiving sevoflurane and halothane anaesthesia and with a view to increase the use of sevoflurane over halothane.*

Settings and study design: *This prospective randomized comparative study was done in Anaesthesia, analgesia and intensive care medicine department of BSMMU Hospital between September 2009 to June 2011. A total 60 patients[30 in sevoflurane group (Group-S) and 30 in halothane group(Group-H)]of either sex, 18-50 years, ASA-I and II, elective surgery under general anaesthesia, lasting more than 1 hour and remaining 24 hours after surgery were the study population. Cognitive recovery was assessed using Bangla adaptation mini-mental state examination (BAMSE) and paper pencil test-Trail making test part-A (TMT-A) one day prior to surgery (baseline value) and 30 minutes after recovery then at hourly interval up to 3.5 hours postoperatively and compared.*

Results: *Emergence time was significantly shorter in Group-S compared to Group-H (10.85 min & 15.13 min respectively, P<0.001). The mean BAMSE score Group-S was 29 at baseline and demonstrated no change at the end of the observation, while the Group-H experienced a fall and rise in BAMSE score. Time taken by the patients of Group-S to complete (TMT-A) at 30 minutes after recovery was significantly less (40.9 sec. Vs 55.8 sec, P <0.001) than patients of Group-H. And no significant difference was observed between groups at 1.5 hrs, 2.5 hrs and 3.5 hrs.*

Conclusion: *So the study concludes that adult patient of sevoflurane group experienced an early post operative cognitive recovery than halothane group. Though sevoflurane is costly, considering the benefits of patients in terms of early cognitive recovery that causes less postoperative complications and shorter hospital stay, sevoflurane should be used instead of halothane*

Key Words*: Cognitive Recovery, Adult patients, Abdominal Surgery, Sevoflurane, Halothane.*

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Introduction:

The objective of anaesthesia is to facilitate surgery at minimal risk to the patient and to ensure optimal recovery following the procedure. It is desirable that recovery from general anaesthesia should be safe, rapid, predictable and independent of any complications. Recovery has been considered in three phases: these include (A) immediate (B) intermediate (C) full recovery. Immediate recovery is the return of consciousness along with protective reflexes and

ability to take care of their own airway. The intermediate recovery phase lasts from 30 minutes to even 3 hours. During this period patients' cognitive and psychomotor skills are restored. Both anaesthesia and pre anaesthetic agents can affect the recovery phases. Drugs that are not accumulated in the body are usually beneficial for early recovery. These drugs do not cause any delayed or recurrent adverse effects even after prolonged administration.

Cognitive function of an individual is defined as the mental processes of perception, memory, and information processing, which allow the individual to acquire knowledge, solve problems and plan for the future action. Any delay or impairment of these processes following anaesthesia is considered as postoperative cognitive dysfunction or impairment.

Anaesthetics administered as part of a surgical procedure may alter the patient's behavioral state by influencing brain activity via at least two mechanisms: dose dependent global and regional specific suppression of neuronal activity and disruption of functional interactivity within distributed neural network. These alterations compromise recovery after surgery; mobilization of the patient is difficult and therefore hospital stay is extended. The resulting immobilization is associated with further complications e g, decubitus pneumonia or thrombosis.

The risk factors for postoperative cognitive disorders can be divided into age and co-morbidity- dependent, as well as related to surgery and anaesthesia. Substance abuse, preexisting psychiatric and neurological disorders, and conditions with high intracranial pressure represent some of the most common risk factors associated with co-morbidity. Another important risk factor for postoperative cognitive dysfunctions is type of surgery: very low incidence is associated with minor surgery while cardiovascular, orthopedic and urologic surgeries are characterized by high risk of postoperative cognitive disorders. Post operative factors (e.g., opioid analgesics) can also contribute to the development of cognitive impairment in the elderly. The most frequent symptoms of cognitive disorders are memory loss and lack of concentration, among these cognitive dysfunctions a state of delirium is developed which is associated with higher postoperative mortality and morbidity and with delayed functional recovery.

Researchers are continually looking for safety in anaesthesia by improving the quality of drugs

because delays in patient awakening can block an operating theater and incur costs in the form of cancelled operations and overtime pay.In western countries it is customary to use one of five modern volatile agents Desflurane, Sevoflurane, Enflurane, Isoflurane, 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 is a clear trend to avoid repeated halothane anaesthesia. Slow recovery compared with other new agent and sensitization of heart to catecholamine limits the use of halothane.in the other hand sevoflurane is considered the inhalational agent of choice because of its excellent recovery profile.

The relationship between postoperative cognitive recovery and the most common inhalational anaesthetic agents currently used in anaesthesia is not conclusive. Besides, most studies have been done comparing these agents in paediatric and elderly patients undergoing ambulatory surgery. But in developing country like Bangladesh halothane is still commonly used due to its low cost despite its disadvantages. Though sevoflurane is currently the inhalational agent of choice in most of the western countries but its use in our country is limited due to its high cost.

So the present study was undertaken to compare the characteristics of emergence and cognitive recovery of adult patients who received either sevoflurane or halothane for maintenance of anaesthesia. The data generated from the study might be helpful for the anaesthetists to make a right choice of volatile agent. The findings will also serve as baseline data for future reference and to undertake further research.

Materials and Methods:

The prospective randomized comparative study was carried out in the Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU

Hospital, Dhaka between the period of September 2009 to June 2011. Prior to the commencement of this study, the research protocol was submitted to the ethical review committee of BSMMU Hospital and approved. Study population was the patients of either sex, aged between18-50 years, ASA-I and II, patients undergoing elective surgery by general anaesthesia, lasting for 1 hour or more and remaining 24 hours after surgery. On the other hand, the patients with history of significant cardiac, pulmonary hepatic or renal diseases, history of chronic drug or alcohol abuse, morbid obesity, disabling neuro psychiatric disorder, pregnant & breast feeding women, patients who experienced hypo and hypertension, hypoxia and severe blood loss during surgery, patients who need narcotics as analgesic in first 3.5hours in the post-operative word were excluded from the study. A total number of 60 patients were divided into two groups. 30 patients were in Sevoflurane group (Group-S) and 30 in Halothane group (Group-H).

Study procedure:

Data were collected using a pre designed data collection sheet containing all the variables of interest. Randomization was done by lottery method. All patients were examined one day prior to surgery which was addressed as baseline value. Heart rate, SPO_2, systolic, diastolic, mean arterial pressure: before induction and every 15 minutes during surgery were recorded. Bangla adaptation mini-mental state examination (BAMSE) and paper pencil test-Trail making test part-A (TMT-A) were also assessed and recorded. We compared the post operative score with the baseline score that is the pre operative score.

Statistical analysis:

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) for windows, version17.0. The test statistics used to analyze the data were Student's

t-Test (for comparison of data presented on continuous scale), Chi-square (c^2) Test (for comparison of categorical data between groups) and Repeated Measure ANOVA statistics. The level of significance was set at 0.05 and $p < 0.05$ was considered significant.

Result:

I. Age distribution:

Table-I *Comparison of age between two groups*

Age* (years)	Group Savoflurane (n = 30)	Halothane (n = 30)	p-value
<30	12(40.0%)	13(43.3%)	
30 – 40	13(43.3%)	15(50.0%)	
e" 40	5(16.7%)	2(6.7%)	
Mean ± SD	31.6 ± 7.2	31.4 ± 5.9	0.938

* Unpaired student's't'-test was employed to analyze the data and data were expressed as mean ± SD.

II. Sex distribution:

Sex distribution between the groups was not identical. Females were significantly higher in the sevoflurane group than that in the halothane group (p = 0.020).

Fig 1 C*omparison of sex between groups*

Baseline characteristics:

Table II *Comparison of baseline characteristics between two groups*

Baseline characteristics Pre operative	Group Sevoflurane (n = 30)	Halothane (n = 30)	p-value
Weight*(kg)	56.4 ± 9.2	56.7 ± 8.7	0.886
ASA# Grade-I	24(80.0%)	25(83.3%)	
Grade-II	6(20.0%)	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

*Unpaired student's 't' test was employed to analyze the data and expressed as mean ± SD. #Chi-square (χ^2) test was employed to analyze the data and expressed as percentage.

Table III *Peroperative findings*
Comparison of per operative findings between two groups

Per operative findings	Group Sevoflurane (n = 30)	Halothane (n = 30)	p-value
Mean arterial pressure (mmHg)			0.074
At 15 min	86 ± 7	88 ± 5	0.203
At 30 min	83 ± 11	86 ± 12	0.223
At 45 min	86 ± 9	82 ± 13	0.783
At 60 min	83 ± 8	84 ± 11	0.003
At 75 min	90 ± 6	95 ± 7	
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 ± 1	9 ± 1	0.986
Emergence time	10.85+1.64	15.13±2.29	0.001

Data were analyzed using Unpaired student's 't'-test and presented as mean ± SD.

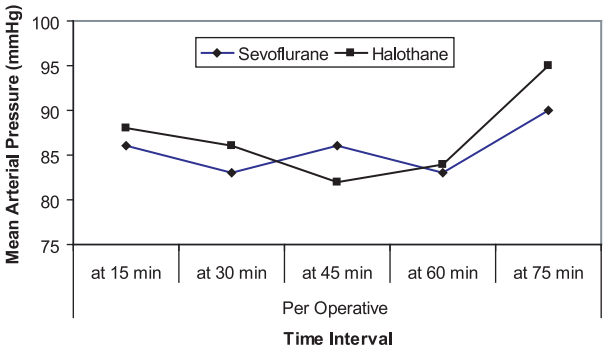

Fig 2 *Changes in mean arterial pressure in different time interval during operative period*

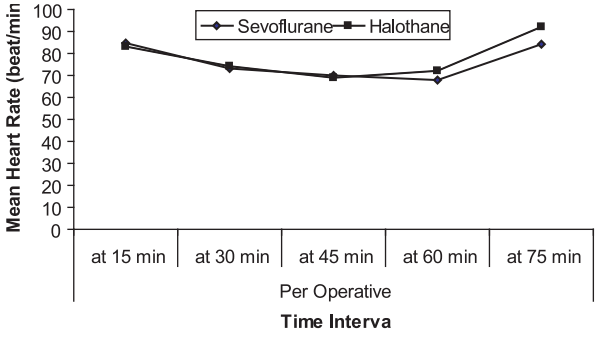

Fig 3 *Changes in heart rate in different time interval during operative period*

Table IV *BAMSE score after recovery:*
Comparison of BAMSE score at different time interval between two groups

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

Data were analyzed using repeated measures ANOVA and expressed as mean ±SD.

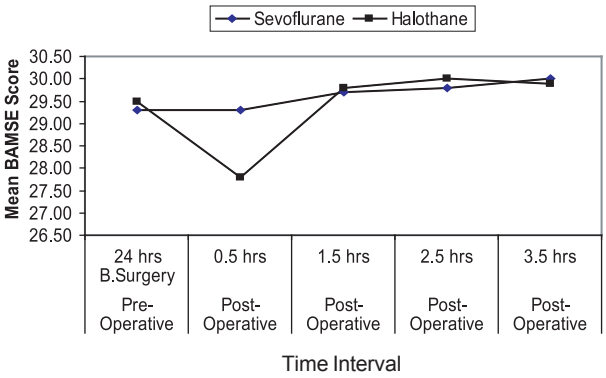

Fig 4 *BAMSE score at pre operatively and changes in post operatively at different time interval*

V *The mean time required to complete TMT-A*

Table VI *Comparison of time required to complete TMT-A at different time interval between groups*

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

Repeated measures ANOVA were used to analyzed the data and expressed as mean ±SD.

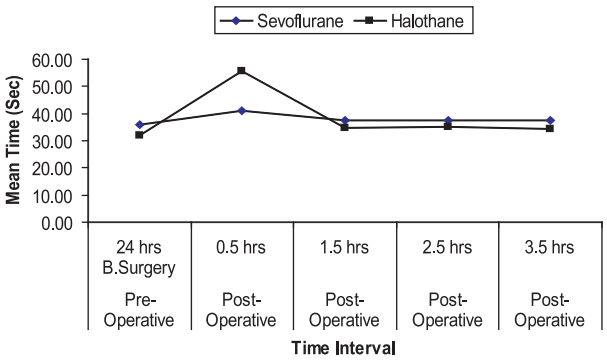

Fig 5 *Time required to complete (TMT-A) pre operatively and changes in post operatively at different time interval*

Discussion:

Sevoflurane is a desirable anaesthetic for induction and maintenance because of its low blood-gas solubility, rapid induction and emergence characteristics, nonirritating airway properties and stable patient haemodynamic characteristics. In spite of its beneficial effect, use of sevoflurane in our country is limited because of its high cost. In this study we demonstrated faster cognitive recovery of adult patient of prolong surgery with sevoflurane than commonly used agent halothane with a view to replace sevoflurane instead of halothane.The study was designed only to assess the cognitive recovery after anaesthesia but not the side effects of volatile agents.

In our study Bangla Adaptation Mini Mental State Examination, BAMSE and Trail Making Test Part-A, TMT-A was selected because it combined a high validity and reliability and ease of application for patients of low educational status of our country.

The present study demonstrates that the mean ages of both groups (sevoflurane and halothane) were almost identical (31.6 ± 7.2 vs. 31.4 ± 5.9 years, p = 0.938). However, a male predominance was observed in halothane group (p = 0.020), which was clinically non significant in relation to cognitive performance. The mean weight, mean arterial pressure, heart rate, SPO_2, BAMSE score and time required to complete TMT-A at baseline were almost similar between sevoflurane and halothane groups. ASA grading was also found similar (p<0.739) in sevoflurane and in halothane group. The mean arterial pressure and heart rates were observed to be almost homogeneous at 15, 30, 45 and 60 minutes interval following induction. At 75 minutes mean arterial pressure and heart rate were higher in halothane group compared to sevoflurane group. Epstein et al. (1995) conducted a study in which hemodynamic status like heart rate, oxygen saturation, end-tidal gas concentration and temperature were recorded to be similar in both sevoflurane and halothane groups, comparable to our study.

Aldrete recovery score (>9) was same in both groups (p = 0.986).Jerrold Lerman et al (1996) also found in their study, aldrete recovery score was same in both sevoflurane and halothane group.

In this study the mean BAMSE score of sevoflurane group patients at baseline was 29 and in post operative word at 0.5hrs, 1.5 hrs, 2.5hrs and 3.5hrs was 29, 29, 29, and 30 respectively. On the other hand BAMSE score at baseline in halothane group was 29 and 27, 29, 30, 29 at 0.5hrs, 1.5hrs, 2.5hrs, and 3.5 hrs respectively in the post operative word. So the study showed that sevoflurane group patient achieved their preoperative BAMSE score at 0.5hrs in post operative word after recovery and demonstrated no change throughout the period of observation where 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 by the patients of sevoflurane group at baseline was 36.1sec and in post operative word after recovery at 0.5hrs, 1.5hrs, 2.5hrs, 3.5hrs was 40.9sec, 37.6sec, 37.4sec, 37.5sec respectively. While patient of halothane group completed the TMT-A at baseline was 31.9sec and 55.8sec, 34.7sec, 35.1sec, 34.5sec at 0.5hrs, 1.5hrs, 2.5hrs, and 3.5hrs in post operative word respectively. So the time to complete TMT-A was identically distributed throughout the observation except at 0.5hrs after recovery, when sevoflurane group had much lower score (40.9sec) and more nearer to pre operative value (36.1sec) compared to their halothane counterpart (55.8sec). Apfelbaum et al (1996); Philip et al(1996) demonstrated in their study that cognitive function is more rapidly restored after sevoflurane anaesthesia administration compared with isoflurane or propofol plus nitrous oxide anaesthesia comparable to our study.

Postoperative cognitive impairement is a common problem in elderly.Xiaoguang et al, (2001) conducted a study to find out the cognitive function in elderly

with desflurane and sevoflurane and found desflurane was associated with a faster early recovery than sevoflurane. However, post operative recovery of cognitive function was similar with both volatile anaesthetics. Brita et al. (2000) found in their study, emergence and return of cognitive function was significantly faster after remifentanil-propofol based anaesthesia compared with desflurane and sevoflurane anaesthesia. Recently Schoen et al. (2011) demonstrated that sevoflurane based anaesthesia was associated with better short term post operative cognitive performance than propofol in their study. So it is clear that most of the studies have done to see the cognitive performance in elderly patients with newer volatile and intra venous agents in western countries. But no single study was done in our country to see the cognitive recovery after anaesthesia with volatile agents.

We found a single study comparing halothane and sevoflurane for their cognitive recovery characteristics in adult patients undergoing prolong(>1 hour) surgery.Besides most studies have done comparing these agents in paediatric and elderly patients undergoing ambulatory surgery.

We found in our study that emergence time from discontinuation of volatile agent up to attainment of aldrete recovery score >9 in sevoflurane group was 10.85 min and in halothane group was 15.13 min (P<0.001) demonstrating earlier emergence than halothane. Ravi et al. (2008) also found in their study that emergence time was 6.7 min in sevoflurane group and 9.07 min in halothane group. The difference between the values of the two study was Ravi and associates counted the emergence time from discontinuation of volatile agent up to extubation and we counted the time from discontinuation of volatile agents up to attainment of aldrete recovery score>9. Ravi et al, also concludes that sevoflurane provides a rapid recovery from anaesthesia due to its lower solubility. The clinical efficacy of sevoflurane lies in term of faster recovery, reduction in operating room time and postoperative care discharge time leading to reduced hospital stay of patients. We also observed a similar finding with sevoflurane being more effective than halothane in terms of faster cognitive recovery. The difference between the two studies is that the measuring tools for cognitive function in our study was Bangla Adaptation Mini Mental State Examination (BAMSE) and Trail Making Test Part-A, (TMT-A) while the tools used by Ravi and associates were P-deletion test for assessment of early recovery and digit symbol substitution test for assessing baseline recovery. So the findings derived from the present study could be considered comparable to those of Ravi and associates despite different scales being used to evaluate cognitive function.

Conclusion:

The findings of the present study suggest that sevoflurane group experience an early post operative cognitive recovery than halothane group. Though the sevoflurane vaporizer and sevoflurane itself is expensive, considering the benefits of patients in term of faster cognitive recovery, sevoflurane should be used instead of halothane.

Recommendation:

In the light of the findings of the present study the following recommendations are put forward.

1. Though sevoflurane is a costly drug, it should be considered instead of halothane, for faster cognitive recovery which may reduce the postoperative complications.
2. If further study is conducted to see the cognitive recovery in adult patient after abdominal surgery, a larger scale sample size is recommended.

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