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A COMPARATIVE STUDY BETWEEN HAEMODYNAMIC VARIABILITY AND AMOUNT OF SEVOFLURANE CONSUMPTION WITH COST ANALYSIS.

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ABSTRACT

Objective: The Objective of the study was to compare between haemodynamic variability and amount of sevoflurane consumption with cost analysis. **Method:** This double blinded randomized clinical trial was conducted among 120 patients aged 1-7 years undergoing routine elective paediatric day case surgery of under 60 minutes of duration at the Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Dhaka during the period of May 2018 to september 2018. **Results:** Majority patients were male (92.5%). Among group A patients, 90% were male and 10% were female. Whereas, among group B patients, 95% were male and 5% were females. Distribution of sex was similar across groups ($p>0.05$). Among all patients, majority belonged to ASA grade I (91.7%). Among group A patients, 93.3% were of ASA grade I and 6.7% were of grade II. Among group B patients 90% were of grade I and 10 % were of grade II. There were no statistically significant difference between groups ($p>0.05$). Peri-operative heart rate and blood pressure were significantly lower in group B patients in comparison to group A patients. Recovery profile was measured by modified Ramsay Sedation Score. Total volume percentage of anaesthetic gas required and mean volume percentage per min were significantly higher in Group A than group B ($p<.001$). Total volume of sevoflurane consumed, total cost of sevoflurane and per minute cost of sevoflurane were significantly lower in patients who were given midazolam as a premedication (group B) than those who were not given midazolam premedication (group A, $p<.001$ for each). The concentration of sevoflurane required during maintenance of anaesthesia was less. So total amount of sevoflurane was less required in experimental group. Adding the cost of oral midazolam tablet will contribute very insignificantly to the total cost. ***Conclusion:*** From our study we can say that premedication with midazolam provided better reduction in peri-operative anxiety, lesser consumption of sevoflurane in paediatric day case surgery with lower cost in these group compared to control.

KEYWORDS: Haemodynamic, anaesthesia, sevoflurane, midazolam.

INTRODUCTION

Sevoflurane is a relatively newer inhalational anaesthetic agent which is used for both induction and maintenance of general anaesthesia. Sevoflurane is particularly suitable for paediatric anaesthesia, because inhalation induction is the mainstay of paediatric anaesthesia as it offers needleless induction. Children are often afraid of needles and to obtain venous access in an awake and moving child is very difficult. So they are often induced by mask before venous access is possible.[1] Sevoflurane is not widely used in our country mainly because of it's high cost. Halothane has been used as a chief inhalational agent in paediatric anaesthesia specially in third world countries because of low cost and anaesthetic potency for long times. But children do not want to take breath and they fight when mask ventilation is attempted with halothane. On the other hand, favourable characteristics have made sevoflurane a suitable agent for paediatric anaesthesia.[2] Halothane may cause arrhythmia, respiratory depression, bradycardia. Another potent inhalational agent like Sevoflurane keeps patient haemodynamically stable. So, onset and recovery both occur smoothly and rapidly.[3] Different studies regarding inhalation anaesthesia reveal beneficial effects of

sevoflurane over other agents, i.e. desflurane, halothane or isoflurane.[4] In a developing country like Bangladesh, where per-capita income is very low, cost-effectiveness is the vital issue to decide which medication to use. At the same time, patient's safety is of greater concern.[5] Different methods have been tried to reduce the cost of sevoflurane including sequential induction and maintenance by sevoflurane and halothane, use of close circuit anaesthesia ventilator (Özelsel *et al.*, 2015), use of low flow anaesthesia (Tyagi *et al.*, 2014), use of Bispectral Index Monitoring to reduce the consumption of anaesthetic drugs (Nabaweya *et al.*, 2009).[6,7,8] One study involved the use of Fixed dosing versus Incremental dosing method of sevoflurane induction to reduce cost (Preet *et al.*, 2014), dexmedetomidine was also used to reduce the consumption of isoflurane (Reshma *et al.*, 2016).[9,10] But these methods are not used widely. Among sedative agents midazolam is a short acting benzodiazepine that is very lipophilic in physiological pH, which contributes to its rapid onset of action.[11] Midazolam given before induction of anesthesia is safe and effective.[12] Midazolam has been shown to induce satisfactory sedation and anxiolysis within 20 minute of administration.[13] So, the consumption of sevoflurane should be less which may reduce it's cost to some extent. Currently three major preoperative modalities for the reduction of anxiety in children: behavioral preparation programs of various kinds, parental presence during induction of anaesthesia (PPIA), and sedative premedication.[14] A randomized control trial (RCT) has shown that use of preoperative midazolam resulted in significant decrease in frequency of postoperative behavioral change like nightmares, eating disturbance, apathy and enuresis.[15] This study was designed to assess the effect of midazolam pre-medication on quality and cost of anaesthetic agent using sevoflurane in paediatric day case surgery in a tertiary care hospital of Bangladesh.

OBJECTIVES OF THE STUDY

General Objective

Compare between haemodynamic variability and amount of sevoflurane consumption with cost analysis.

Specific Objectives

- To measure amount of sevoflurane consumed in each groups.
- To compare parent separation characteristics, haemodynamic criterias like blood pressure, heart rate, and amount of sevoflurane consumption with cost analysis between the two groups.

METHODOLOGY

Study type

- This was an prospective double blinded randomized clinical trial.

Study place and period

- Department of Anaesthesia,Analgesia and Intensive Care Medicine, BSMMU from May 2018 to September 2018

Sampling method

- The sample was collected by random sampling.

Study population

- All patients aged 1-7 years attending at the department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU for routine day case paediatric surgery of less than one hour duration were enrolled.

Inclusion criteria

- Children of 1-7 years of age
- Children scheduled for routine day case surgery of less than one hour duration under general anaesthesia.
- Patient with ASA (American Society of Anesthesiologist) grade I & II

Exclusion criteria

- ASA grade III & IV
- Emergency surgery.
- Known allergic to midazolam.
- Diagnosed central nervous system disorders.
- Diagnosed neuromuscular disease.

Procedure of data collection:

All the data were collected in a preformed questionnaire. Following data collection, they were noted down in the questionnaire. After that, all were transcribed into the statistical software. This study was conducted following ethical approval of Institutional review board of BSMMU (Ref no – BSMMU/2018/4756, date - 05/05/2018). On the basis of inclusion and exclusion criteria 120 paediatric patients, aging 1 to 7 years, who underwent routine day case surgery were included. Types of surgeries included in this study were mostly herniotomy, circumcision, cystoscopy, incision and drainage of abscess etc. where muscle relaxation was not necessary and duration of surgery was limited to one hour only. Written informed consent were taken from the parents or legal guardians of eligible children.

Statistical analysis

Statistical analysis was carried out using the Statistical Package of Social Sciences version 21.0. Exploratory data analysis were carried out to describe the study population where categorical variables were summarized using frequency tables while continuous variables were summarized using measures of central tendency and dispersion such as mean, median and standard deviation. Age and sex difference across the groups were determined by student's *t*-test. Comparison of numerical variables were done using Student's t-test. Parent separation characteristics of patients and haemodynamic stability of patients between two groups were determined

by chi-square test. Moreover, anesthetic and post-anaesthetic recovery profile of patients and Sevoflurane consumption amount between two groups were determined by unpaired student's *t* test. P-value < 0.05 was considered statistically significant.

RESULT

Patients were randomly allocated into two groups: group A and group B. Group A patients were not given midazolam premedication before giving sevoflurane for inhalation anaesthesia. Group B patients were given midazolam premedication before inhalation of sevoflurane for anaesthesia. Majority of the children were aged 3 years. Among group A patients, majority were aged 3 years and among group B patients, majority were aged 5 years. There were no statistically significant difference in age distribution between two groups (p>0.05).

Table I: Age distribution of study population (n=120).

Age, years	Group A (n=60)	Group B (n=60)
Age (mean±SD)	4.06±1.32	3.76±1.21
Years	n(%)	n(%)
2	8 (13.3)	8 (13.3)
3	14 (23.3)	20 (33.3)
4	14 (23.3)	16 (26.7)
5	16 (26.7)	12 (20.0)
6	6 (10.0)	2 (3.3)
7	2 (3.3)	2 (3.3)

p value determined by respectively *unpaired Student's *t* test

Majority patients were male (92.5%). Among group A patients, 90% were male and 10% were female. Whereas, among group B patients, 95% were male and 5% were females. Distribution of sex was similar across groups (p>0.05)(Figure 1).

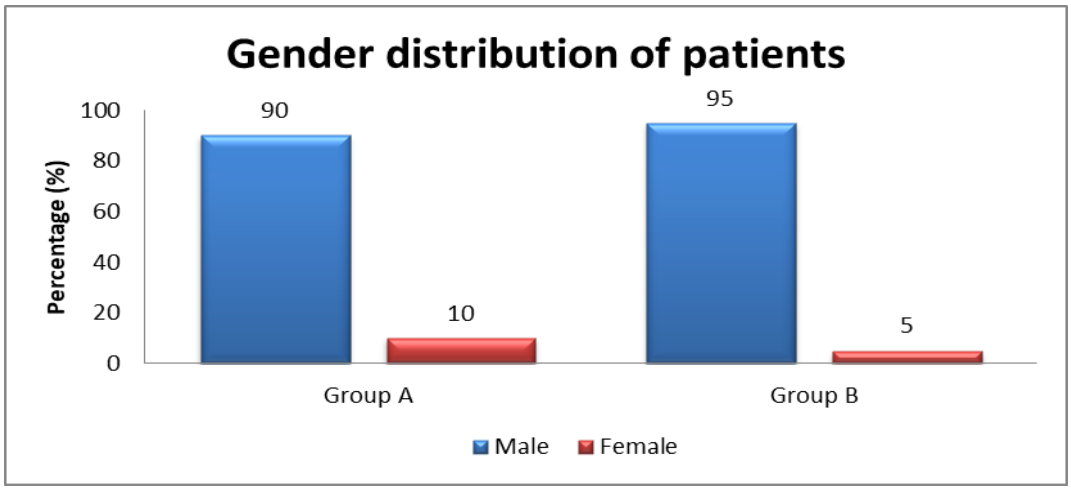

Figure 1: Gender distribution of patients (n=120).

Among all patients, majority belonged to ASA grade I (91.7%). Among group A patients, 93.3% were of ASA grade I and 6.7% were of grade II. Among group B patients 90% were of grade I and 10 % were of grade II. There were no statistically significant difference between groups (p>0.05) (Figure 2)

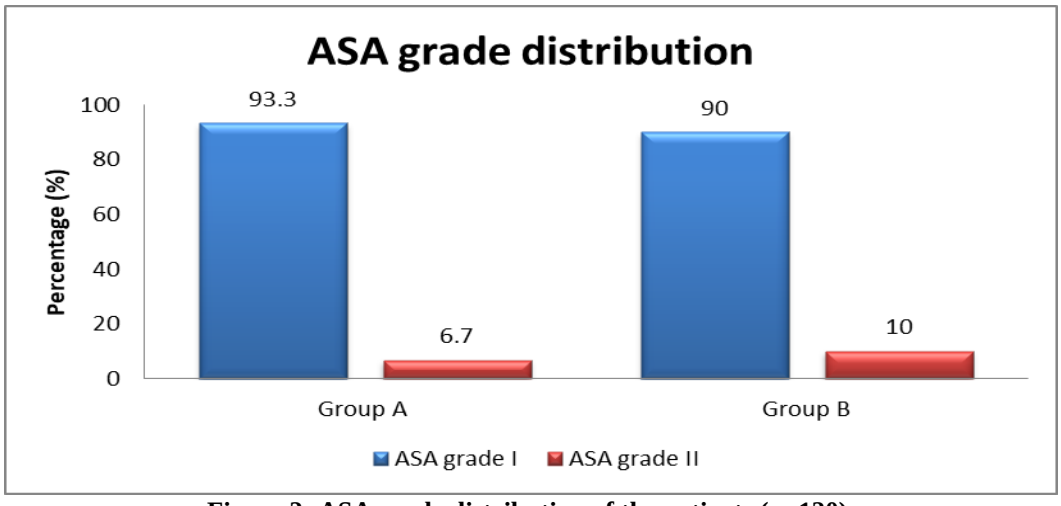

Figure 2: ASA grade distribution of the patients (n=120).

Table II shows that mean weight of all patients were 14.64±3.48 kg. Among group A and group B patients, majority had weight between 11 – 15 kg (respectively 48.3% and 53.3%). Distribution of weight were similar across groups.

Table II: Weight distribution of study population (n=120).

Weight, (in Kg)	Group A (n=60)	Group B (n=60)	Total (n=120)	p value
Weight (mean±SD)	14.75±3.60	14.53±3.39	14.64±3.48	.735*
Weight group (in Kg)	n(%)	n(%)	n(%)	
6 – 10	7 (11.7)	6 (10.0)	13 (10.8)	
11 – 15	29 (48.3)	32 (53.3)	61 (50.8)	.828**
16 – 20	20 (33.3)	20 (33.3)	40 (33.3)	
21 – 25	4 (6.7)	2 (3.3)	6 (5.0)	

p value determined by respectively *unpaired Student's *t* test and **Chi-squared test

Among group A patients 88.3% were uncomfortable and among group B patients 23.3% were uncomfortable. The difference between groups were statistically significant (p<.001). Group B patients comprised significantly more comfortable patients than group A (76.7 vs 11.7, p<.001).

Table III: Parent separation characteristics of patients between two groups (n=120)

Characteristics With scoring	Group A (n=60)	Group B (n=60)	p value
	n(%)	n(%)	
Uncomfortable	**53 (88.3)**	**14 (23.3)**	**<.001**
Inconsolable cry (0)	37 (61.7)	4 (6.7)	
Complaining (1)	16 (26.7)	10 (16.7)	
Comfortable	**7 (11.7)**	**46 (76.7)**	**<.001**
Quiet but awake (2)	5 (8.3)	12(20)	
Sleepy (3)	2 (3.3)	34(56.7)	

p value determined by Chi-Square test

Table VI denotes the quality of premeditations which depends mainly on induction characteristics. In this study, to assess the quality of premedication before induction of anaesthesia, focus was on parent separation characteristics before anaesthetic procedure, i.e., inconsolable cry, complaining, calm and quiet and sleepy. Point value for separation characteristics was given as follows, inconsolable cry=0, complaining=1, calm and quiet =2 and sleepy =3. Finally, patients having score ≥2 was considered to have excellent quality, having score 1 was considered to have good quality and patients having score = 0 was considered to have poor quality of premedication (Table IV).

Table IV: Quality of parent separation in both groups (n=120).

Characteristics (scoring)	Group A (n=60)	Group B (n=60)	p value
	n(%)	n(%)	
Poor quality (0)	37 (61.7)	4 (6.7)	
Good quality (1)	16 (26.7)	10 (16.7)	<.001
Excellent quality (2)	7 (11.7)	46 (76.7)	

p value determined by Chi-Square test

Total volume of sevoflurane consumed, total cost of sevoflurane and per minute cost of sevoflurane were significantly lower in patients who were given midazolam as a premedication (group B) than those who were not given midazolam premedication (group A, p<.001 for each). Midazolam premedication itself is sedative and central nervous system depressant, so the concentration of sevoflurane required during maintenance of anaesthesia was less. So total amount of sevoflurane was less required in experimental group. Adding the cost of oral midazolam tablet will contribute very insignificantly to the total cost, as it's per tablet cost is only 10 BDT.

Table V: Sevoflurane consumption rate and cost of the drugs used between two groups (n=120)

Variables	Group A (n=60)	Group B (n=60)	p value
	Mean±SD	Mean±SD	
Total FGF, L	149.66±1.10	145.88±7.05	.028
Mean FGF per min, L/min	4.60±0.17	4.53±0.30	.111
Total volume, %	81.80±6.49	55.80±4.61	<.001
Mean volume per min, %	2.51±0.08	1.72±0.11	<.001
Total volume of sevoflurane consumed, ml	20.40±1.36	13.57±1.02	<.001
Total cost of sevoflurane, BDT	1182.80±79.38	787.55±60.15	<.001
Mean cost of sevoflurane per min, BDT	36.49±2.23	24.59±3.07	<.001

p value determined by Unpaired student**'s** *t* test
Sevoflurane and Midazolam was purchased from Unimed and Unihealth Pharmaceuticals,Bangladesh.

DISCUSSION

Total 120 paediatric patients were studied by dividing them into randomly groups: group A and group B. Patients of both group were anaesthesized by sevoflurane. Alongside, group B was given premedication with midazolam and group A was not given any premedication. Patents aged 1 to 7 years were considered for inclusion. Majority patient belonged age 3 (28.3%) followed in second and third by age 4 (25%) and age 5(23.3%). Mean age of the total population was 3.91±1.27 years. Mean age of group A and group B patients are respectively 3.76±1.21 and 4.06±1.32 years. Both groups were age matched as distribution of patients were similar across groups. Köner *et al.* (2011) studied effects of hydroxyzine-midazolam premedication on sevoflurane-induced paediatric emergence agitation and included 84 children aging 1 to 7 years.[16] In their study mean age of groups were 2.5±1.6 years and 2.3±1.4 years, which is lower the findings of this study. In the study by Gómez B *et al.*, (2013) mean age of the population was 3.17±1.94 years, which was nearly similar to our study.[17] Cray *et al.*, (1996) found mean 4.5 years in midazolam group and 4 years in placebo group. Age distribution varied from study to study due to varying surgical procedure they are undergoing.[18]

In this study 92.5% patients were male and 7.5% patients were female. Similarly Köner *et al.* (2011) found approximately 95% male and 5% female in their study population.[19] Gómez B *et al.*, (2013) found slightly higher population male (68.5%) than female (31.5%) in their study.[20] This finding was expected as most of the surgeries were inguinal herniotomy, and ritual circumcision where male children were involved. In this study majority children had ASA grade I (91.7%) and rest had grade II (8.3%). Higher grades were purposefully excluded from the study, as only "day case surgeries" were included in this study and sick children would fail to fulfill the criteria of day surgery and discharge on the day of surgery. Distribution of grades were similar across groups- group A patients had 56 grade I and 4 grade II patients and Group B patients had 54 grade I and 6 grade II patients. This is concordant with the done by Sheta and AlSarheed (2009) majority children was ASA grade I, respectively 18 and 19 for medication and placebo groups and respectively 2 and 1 having grade II.

In this study parent separation characteristics of patients reveals that children who were not given premedication were more uncomfortable than who were given midazolam premedication (88.3% vs 23.3%) The difference was statistically highly significant (p<0.001). Sheta and AlSarheed (2009) found a similar pattern. They found that children who were given midazolam premedication had statistically significantly higher proportion of comfortable patients than controls.[21] They also found with incremental dosage of midazolam from 0.5mg/kg to 1mg/kg was associated increased number of comfortable childrens. On the other hand Cray *et al.*, (1996) did not find any effect of premedication with oral midazolam on pre-operative anxiety reduction.[22] Children are naturally afraid and anxious of unfamiliar environment, specially the operation room environment where sharp instruments and machineries are present. So they tend to resist when they are taken away from their parents. Anxiolytic medication reduce their anxiety and stress to some extent and make it easier to separate them from their parents.

In this study, pre-medication with midazolam was found to be significantly reducing the total volume of sevoflurane required in patients and thereby substantially reducing total cost of anesthesia (p<0.001). In term of BDT total cost of sevoflurane in placebo group was approximately 1183 taka and in midazolam group was approximately 788 taka. As midazolam premedication itself is sedative and central nervous system depressant, so concentration of sevoflurane required during maintenance of anaesthesia was less.

CONCLUSION

From our study we can say that premedication with midazolam provided better reduction in peri-operative anxiety, lesser consumption of sevoflurane in paediatric day case surgery with lower cost in these group compared to control.

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