Open Access Journal

Indian Journal of Medical Research and Pharmaceutical Sciences

March 2016; 3(3) ISSN: ISSN: 2349-5340

DOI: 10.5281/zenodo.47203 Impact Factor (PIF): 2.672

A COMPARATIVE STUDY OF DIFFERENT DOSES OF ORAL MIDAZOLAM AS PREMEDICANT IN PAEDIATRIC PATIENTS BETWEEN THE AGE GROUP OF 1-6 YEARS

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Keywords:

midazolam, premedication, paediatric

Abstract

Aim: In paediatric anaesthesia premedication provides anxiolysis and ease of separation from parents. In context to this a randomized control trial using two different doses of oral midazolam as a premedicant was undertaken.

Methods: 50 children (25 each in group A & group B) between the age group of 1-6 years were included. Oral midazolam syrup with two different doses for each group (0.5mg/kg in group A and 0.75 mg/kg in group B) was given. The children were looked for the anxiolytic effect, sedation score, venepuncture score and acceptance of mask score. The data was analysed using SPSS software.

Results: In group A the sedation was satisfactory in 92% of the children. 88% were calm and accepted mask for induction. Venepuncture score was satisfactory in majority of patients. (Grade 2 in 36% and grade 3 in 56% of patients). In 8% of the patients it was difficult to start IV line (Grade 4). In group B the sedation was satisfactory in 92% of children. 84% of children remained calm and 92% accepted the mask easily. Venepuncture score was grade 2 in 44% and grade 3 in 44%. 4% was graded as 1 and could put intra venous line easily. 8% of the patients did not allow starting an intravenous line easily (Grade 4). This proved statistically not significant.Postoperatively none of the patients had any untoward side effects. Parents of 84% of children in both groups were happy with the premedication.

Conclusion:

Oral midazolam 0.5mg/kg provides safe and reliable sedation and anxiolysis compared with 0.75mg/kg.

Introduction

Paediatric patients hospitalized for surgery suffer anxiety. Preschoolers fear the operation room, surroundings and separation from family. While school age children develop a curiosity about the operating room, monitors, masks, etc. they continue to have a fear of surgery itself and potential pain afterward. Some children turn their anxiety into angry tantrums or defiant behaviour [1]. Such children will require some form of sedative premedication before surgery to allay their anxiety [2].

Any child old enough to understand conversation should be prepared for surgery with a basic, age-appropriate, truthful explanation of what is to happen before and at induction. A brief description of the operating room, monitors and mask can be nonthreatening. Infants less than 6 months of age require no anxiolysis. Children 6 months to 4 years of age have been reported to experience the greatest negative postoperative behaviour changes and benefit from premedication. Extreme preoperative anxiety in children may prolong the induction of anesthesia and lead to new onset postoperative negative psychologic effects such as nightmares, eating disturbances and enuresis

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[3]. Therefore an effective preanaesthetic medication in children undergoing surgery is required. Premedication leading to a calm patient also minimizes parental anxiety.

Premedication in children remains a controversial subject as various premedication and delivery systems have been developed using different routes of administration. Hence we studied the efficacy and safety of two different doses of oral midazolam (0.5mg/kg and 0.75mg/kg) for premedication in children between the age group of 1-6 years undergoing surgical procedures under caudal epidural. Midazolam, a benzodiazepine exerts a reliable dose dependant anxiolytic effect achieving a sedation, which is usually not sleep, but rather a compliant, happy state. It produces minimal cardiovascular and respiratory effects and brings about amnesia, which helps to reduce the psychological trauma of anesthesia and surgery. The syrup formulation of midazolam has become very popular as a premedicant in children posted for surgical, dental and endoscopic procedures, as it satisfies many of the characteristics of an ideal premedicant. The bitter taste of midazolam is masked using flavoured syrup, which is accepted by the children.

Materials and methods

This prospective randomized clinical trial study was conducted on children admitted for elective surgery after obtaining permission from ethical committee of the Institution. Informed consent was obtained from the parents. Fifty children of ASA grade I, of either sex aged between 1-6 years were included in this study. Children undergoing surgical procedure between 20 minutes to two hours duration were selected for the study. The children were divided in to two groups randomly. Children in Group A (Study group) received midazolam syrup 0.5 mg/kg and children in Group B (Control group) received 0.75mg/kg oral midazolam as premedication 20-30 minutes before induction in the premedication room. Also topical anaesthetic agent was applied on the dorsum of the hand. The condition of child was evaluated assigning a five point score for sedation, four point score for intravenous cannulation along with heart rate, respiratory rate in comparison with the baseline values. The sample size was calculated using the formula $N= 2\sigma^2 (z\alpha^2 + z\beta)^2 / \delta^2$

Inclusion Criteria:

Elective cases
Age between 1-6 years
ASA I

Exclusion criteria:

Weight more than 20 kg
Anticipated difficult airway
ASA II and above
History of chronic illness/developmental delay
Consuming medications that would interact with midazolam

All patients were visited and evaluated for fitness for the intended procedure and anaesthesia on the day prior to surgery. During this visit, the procedure of the study planned was explained to the parents. An attempt was made to alleviate the anxiety of the parents. Parents were given instruction on the nil per oral guidelines. General clinical examination of the patient was performed.

In the pre medication room baseline recordings of heart rate, respiratory rate and activity of the child were noted. Fifty patients were divided in to two groups of 25 each. Midazolam syrup (2mg/ml) 0.5mg/kg was given to Group A and 0.75mg/kg to Group B as premedication. The formulation contains sweet syrup to mask the bitter taste of the drug. The syrup is administered 20-30 minutes before the induction of anaesthesia in the premedication room. The children were evaluated for any changes in the heart rate and respiratory rate, adequacy of sedation and response to painful stimulus (venepuncture score). Side effects such as excessive salivation, abdominal movements or rigidity and ability to maintain airway were noted. Children were observed for any signs of upper airway obstruction, respiratory depression, apnoea and desaturation.

The effects of the drug were studied under various headings from the time of administration of midazolam syrup in the pre medication room. Intraoperative monitoring included ECG, Heart rate, oxygen saturation and blood pressure. Patients were taken into the operating theatre as soon as a stable level of sedation was obtained. General anesthesia was induced with oxygen 50%, nitrous oxide 50% with sevoflurane 5%. After induction venous access was established. Anaesthesia was maintained with oxygen, nitrous oxide and 2% sevoflurane (FiSevo). Inj. Fentanyl 1µg/kg was given. Meanwhile assessment of mask acceptance and response to venous cannulation were recorded.

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Apart from monitoring vital parameters such as heart rate, patients were observed for any intra-operative problems like increased secretions, desaturation and cardiovascular changes. Post-operative problems like respiratory depression, restlessness and increased salivation were noted. Parents were interviewed for the acceptance of sedation.

Statistical analysis was performed using the SPSS programme. The age, sex and body weight of the children, onset of sedation, acceptance of mask, venepuncture grade, emotional state score, heart rate, respiratory rate and duration of the surgical procedure were statistically analysed. In the postoperative period restlessness, oropharyngeal secretions and parental acceptance of the premedication were also assessed. Descriptive data that included mean, standard deviation and percentage were determined for all the age groups. Continuous data were analyzed by paired 't' test (for paired sample) and unpaired 't' test (for independent samples). Chi square test was used for categorical data. P value of <0.005 was considered for significant difference.

Results

The two groups were comparable in age, weight and sex distribution. In group A there were 20 male and 5 female children with mean 3.8 ± 1.5, body weight ranging from 11-18 kg with mean 14.2 ± 2.1.In group B there were 19 males and 6 female children with mean 3.6 ± 1.4,body weight ranging from 11-18 kg with mean 15.3±2.1.

There was minimal decrease in pre induction heart rate when compared with premedication room heart rate in both the groups, which was not statistically significant.

Table 1: Comparison of Group based on Heart Rate

		Mean	SD	N	t	P
Premedication Room	Group A	95.4	6.0	25	0.18	0.859
	Group B	95.7	8.1	25		
Pre Induction	Group A	90.8	7.7	25	0.09	0.925
	Group B	90.6	7.3	25		

There was minimal decrease in pre-induction respiratory rate compared to pre-medication respiratory rate in both groups after sedation. Though this was statistically significant clinically was insignificant.

Table 2: Comparison of group based on respiratory rate

		Mean	SD	N	t	P
Premedication Room	Group A	19.4	2.1	25	0.20	0.846
	Group B	19.3	2.3	25		
Pre Induction	Group A	16.6	2.0	25	0.28	0.781
	Group B	16.4	2.0	25		

Table 3: Comparison of group based on sedation score

Sedation was assessed on a 5 point sedation scale.
Sedation was graded as follows
Score 1 - Barely arousable
(Sleep, needs shaking or shouting to arouse)
Score 2 - Asleep
(Eyes closed, arousable with soft voice or light touch)
Score 3 – Sleepy
(Eyes open but less active and less responsive)
Score 4 – Awake
Score 5 – Agitated

None of the patient in both the groups had sedation score of 1. Three children in group A and one child in group B had score 5 and they were excluded from the study because they were not cooperative for the further interventions.

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Sedation score	Group A		Group **B**		X^2	P
	Count	Percent	Count	Percent		
Grade 1	-	-	-	-	-	-
Grade 2	6	24	9	36	0.89	0.641
Grade 3	17	68	14	56		
Grade 4	2	8	2	8		
Grade 5	-	-	-	-	-	-

Table 4: Comparison of group based on emotional state score

Emotional state score was graded as yes/No. Yes suggests calm (grade 1) and No suggests apprehension (grade 0).

Emotional state score	Group A		Group B		X^2	P
	Count	Percent	Count	Percent		
No	3	12	2	8	0.22	0.637
Yes	22	88	23	92		

Table 5: Comparison of group based on venepuncture score

Ability to perform venepuncture was graded as follows
Grade I – Asleep, no response to painful stimulus and IV cannulation
Grade II – Calm awake but not crying, no withdrawal to IV cannulation.
Grade III – Withdrawal for painful stimulus, but allows starting IV line, not crying
Grade IV – Crying and uncooperative, not able to start IV line

Venepuncture score	Group A		Group **B**		X^2	P
	Count	Percent	Count	Percent		
Grade I	0	0	1	4	1.56	0.668
Grade II	9	36	11	44		
Grade III	14	56	11	44		
Grade IV	2	8	2	8		

Table 6:Comparison of group based on acceptance of mask score

Acceptance of mask was graded as Yes/ No, Yes being the acceptable and No being non acceptable.

Mask acceptance score	Group A		Group B		X^2	P
	Count	Percent	Count	Percent		
No	3	12	2	8	0.22	0.637
Yes	22	88	23	92		

Patients in both the groups had minimal postoperative restlessness. But the difference between groups was not statistically significant.
Increased secretion in postoperative period was noted in 16% patients in group A compared to 12% patients in group B, which again is not statistically significant.
Post operatively parental acceptance for sedation was good in both groups (84%).

Discussion

Preanaesthetic medication in children should relieve anxiety, reduce the trauma associated with separation from their parents and facilitate induction of anesthesia without prolonging the recovery period. Although various combinations of drugs and routes of administration have been used in children for preanaesthetic sedation, the oral route remains the least threatening method of drug administration. Midazolam possesses many desirable properties

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of a premedicant for children undergoing day surgery. Its elimination half-life 1.5 – 2hrs is considerably shorter than those of diazepam and other agents [4,5,6]. It produces minimal cardiovascular and respiratory effects [7,8,9,10]. Oral midazolam has been found to be more effective in managing anxiety in children and parents [11]. It exerts a reliable dose dependant anxiolytic effect without over sedation with a minimal to no delay in recovery even for brief procedure in day care anaesthesia [12,13]. Hence midazolam is considered as the drug of choice for premedication in children.

In the present study, children in the two groups were of 1-6 years with a mean age of 3.48 years, mean weight of 14.42 kg with a male predominance of 80%. A satisfactory level of sedation was achieved by 20-30 minutes after the administration of the drug in the study group. This was comparable with the studies of McCluskey et al [2](mean 43 minutes) and Weldon B.C et al [8] (mean 36 minutes) with the same dose of midazolam 0.5mg/kg administered orally. The sedation score difference in both the group was not statistically significant. 92% of study population has achieved satisfactory sedation. Mask acceptance was satisfactory in both the groups. There was not any significant difference in the venepuncture scoring between the two groups. Oral midazolam premedication helped in starting an intravenous line with ease especially when it was used along with application of local anaesthetic on dorsum of hand. There was a statistically significant decrease in heart rate after 30 minutes interval of premedication. But this was not clinically important. Respiratory rate decreased minimally from the baseline rate, which again was not clinically significant. Overall there were no gross cardiovascular or respiratory side effects.

Postoperatively patients in both groups had minimal restlessness. Premedication offered to the children was accepted well by 84% of the parents in the study group. No untoward adverse effects were seen in any of the patients premedicated with the drug.

Conclusion

Our study demonstrates that premedication with oral midazolam in a dose of 0.5mg/kg when compared with 0.75mg/kg provides adequate sedation and anxiolysis. There can be a smooth induction of anaesthesia. Venous access is trouble free following sedation, with minimal or no cardiovascular or respiratory side effects. Other documented side effects such as loss of balance and head control, dysphoria and blurred vision did not occur at this dose.

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DOI: 10.5281/zenodo.47203 Impact Factor (PIF): 2.672

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