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Comparative Evaluation of Sedation Score and Anxiolysis Level in Intranasal and Oral Midazolam as Premedication in Children

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Abstract

Introduction: Preoperative anxiety in children leading to postoperative negative changes and long-term behavioral problems needs better preanesthetic sedation. Across the world, midazolam is the most commonly used premedicant in pediatric patients. The fact that no single route has achieved universal acceptance for its administration suggests that each route has its own merits and demerits. *Aim of the Study:* This study compares oral midazolam syrup and intranasal midazolam spray as painless and needleless systems of drug administration for preanesthetic sedation in children. *Materials and Methods:* The study was in Government Stanley hospital Chennai. Period of the study was between 2012-2013. Seventy pediatric patients belonging to ASA physical status I & II scheduled for elective minor surgical procedures were included in the study. Children belonged to the age group of 2 to 8 years of both sexes. The children were randomly allocated into 2 groups with 35 patients in each group. (Group N & Group O). Demographic data including age, weight, and sex of the children were recorded. The children were given premedication 30 minutes before surgery orally or nasally. The reaction of the children to the premedication was noted. Group – N – received intranasal midazolam at a dose of 0.2 mg/kg using. Insideatomizer midazolam Nasal spray containing 100 microliters/ metered dose which delivers 0.5 mg/dose. *Results*: The median behavior score and sedation score were further analyzed with the children divided into different age groups age 2–5 and age 7–9yr. The median behavior scores at baseline, at separation from a parent, and at induction were not different among the children from groups N and 0 in all age groups. The median sedation scores of group D were significantly different from group M at separation from parent and at induction in children of age 2–5 yr. In age Group 2–5 yr, the median sedation scores at separation from the parent were 6 and 2 from group N and 0 respectively (p - 0.001). For the same age group, the median sedation scores at induction of anesthesia were 6 and 2 for group N and 0, respectively (p - 0.001). *Conclusion*: In conclusion, Intranasal midazolam when used as premedication in children, in a dose of 0.2 mg/kg hasa more rapid onset of action with satisfactory sedation and anxiolysis than oral midazolam. The rapid onset of action of nasal midazolam makes it an ideal route for premedication in children.

Keywords: Sedation Score, Anxiolysis Level, Intranasal Midazolam, Oral Midazolam

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Introduction

Surgery and anesthesia induce considerable emotional stress and psychological consequences in children. This stress may remain in the child's psyche long after the hospital experience has passed. Age, parental anxiety level, previous hospital experiences, and type of surgery are factors that can influence a child's anxiety level and psychological well- being [1]. Preoperative anxiety stimulates the sympathetic, parasympathetic and endocrine system leading to an increase in heart rate, blood pressure, and cardiac excitability. These reactions reflect the child 'sfear of separation from parents and home environment, fear of physical harm, fear of unfamiliar routines, fear of surgical instruments and procedures [2]. In pediatric anesthesia, premedication needs to be in an acceptable form, to have a rapid onset with minimal hangover effect and without side effects. Midazolam, a sedative with all the desirable properties of a benzodiazepine was introduced into clinical practice in the 1980s. Midazolam, a water-soluble benzodiazepine, may be administered by various routes [3]. Oral and rectal routes are used widely and provide effective sedation. However, there are concerns about the wide bioavailability when given by these routes, ranging from 18% to 44% with an appreciable first pass effect. Intramuscular administration is painful and the sublingual route has poor compliance [4]. The intranasal route for midazolam has been used since 1988 and has the advantage of rapid absorption directly into the systemic circulation with no first pass effect and bioavailability of 55-83%. Intranasal midazolam is absorbed from an area rich in blood supply and avoids the disadvantage of passing through the portal circulation, thus increasing the bio-availability of the drug [5]. Tolerance to midazolam is good, and the duration of action is shorter and more predictable than other benzodiazepines. Intranasal midazolam has all the advantages of intravenous administration without the disadvantages of pain and fear associated with intramuscular and intravenous injections [6]. Intranasal midazolam has been used for over a decade now for sedating children before anesthesia, due to its unique property of a good premedicant because of its sedative and anxiolytic properties [7]. Intranasal administration of midazolam results in bio-availability of 50% to 83% when compared to the IV administration [8]. The variation in bioavailability depends on the method of administration, with atomization demonstrating higher levels than dropper application [9].

Materials and Methods

Seventy pediatric patients belonging to ASA physical status I & II scheduled for elective minor surgical procedures were included in the study. Children belonged to the age group of 2 to 8 years of both sexes. The children were randomly allocated into 2 groups with 35 patients in each group. (Group N & Group O). It was a comparative study. The study was approved by the Institutional Ethical Committee and parents provided written informed consent before premedication of their children. *Inclusion Criteria:* ASAI and II physical status, Age group 2-8 yrs, weight < 20 kgs. *Exclusion Criteria:* ASA III & IV, Nasal Infection, Nasal Pathology, Nasal Allergy & URI, Children with a Seizure disorder, H/o adverse reactions to benzodiazepines, a patient taking other sedative drugs.

Preparation of the Patient

Written informed consent from the parent obtained. All patients fasted as per NPO guidelines. Demographic data including age, weight, and sex of the children were recorded. The children were given premedication 30 minutes before surgery orally or nasally. The reaction of the children to the premedication was noted. Group – N – received intranasal midazolam at a dose of 0.2 mg/kg using Insedeatomizer midazolam Nasal spray containing 100 microliters/ metered dose which delivers 0.5 mg/dose. The dose was calculated and divided equally into each nostril with the children in a sitting position on their mothers' lap. Half of the dose was placed in each nostril. Placing half the medication in each nostril reduced the volume while doubling the available area for absorption. Then the patient was kept in a slightly head-down position for 2 minutes for easy absorption.

Results

Time of Onset of Sedation, Sedation Score at various points of time (10 minutes intervals for 30 minutes), Anxiolytics scores at various points of time (10 minutes intervals for 30 minutes) The presence or absence of the following side effects and complications from the time of installation to 24 hours postoperatively, were noted. Nasal irritation Postoperative – nausea and vomiting, Respiratory depression, Laryngospasm/ Bronchospasm Other complications.

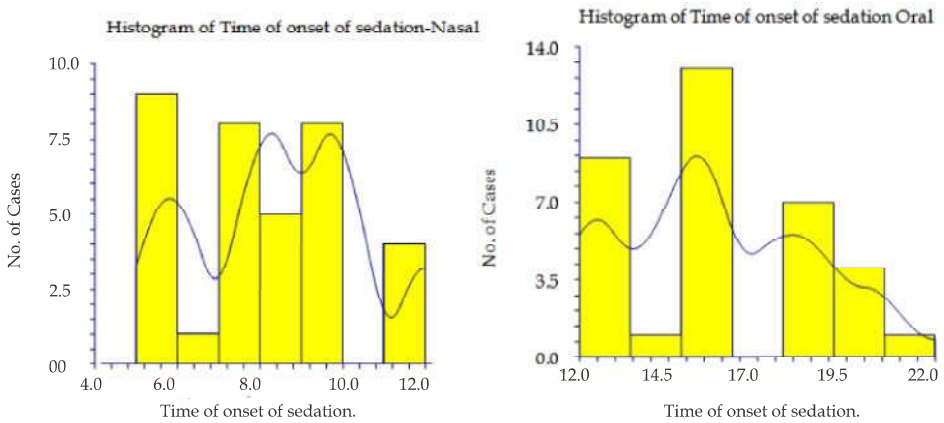
Chi-Square value is 54.348, Sedation score in 10 minutes is statistically significant with a P value of 0.065 statistically less significant (Table 1).

Chi-Square value is 27.055. Sedation score in 20 minutes is statistically significant with a P value of 0.089 statistically less significant (Table 2).

Chi-Square value is 11.926, p-value = 0.003. Sedation score in 30 minutes is statistically significant with a p value of 0.003<0.05 (Table 3).

Chi – Square value is 10.906, p value = 0.012 (Table 4).

Chi – Square value is 5.510, p value = 0.019 (Table 6).



Graph 1: Comparison of Time of Onset of Sedation

Table 1: Sedation Score at 10 Minutes in both Groups

Cross table					
			Group		
			Nasal	Oral	Total
Sedation Score 10 Minutes	1.00	Count	0	30	30
		% within Group	.0%	85.7%	42.9%
	2.00	Count	18	5	23
		% within Group	51.4%	14.3%	32.9%
	3.00	Count	16	0	16
		% within Group	45.7%	.0%	22.9%
	4.00	Count	1	0	1
		% within Group	2.9%	.0%	1.4%
	Total	Count	35	35	70
		% within Group	100.0%	100.0%	100.0%

Table 2: Sedation Score at 20 Minutes

Cross table					
			Group		
			Nasal	Oral	Total
Sedation Score 20 Minutes	1.00	Count	0	4	4
		% within Group	.0%	11.4%	5.7%
	2.00	Count	0	15	15
		% within Group	.0%	42.9%	21.4%
	3.00	Count	26	14	40
		% within Group	74.3%	40.0%	57.1%
	4.00	Count	9	2	11
		% within Group	25.7%	5.7%	15.7%
	Total	Count	35	35	70
		% within Group	100.0%	100.0%	100.0%

Table 3: Sedation Score at 30 Minutes

Cross table					
			Group		
			Nasal	Oral	Total
Sedation Score 30 Minutes	2.00	Count	0	1	1
		% within Group	.0%	2.9%	1.4%
	3.00	Count	7	20	27
		% within Group	20.0%	57.1%	38.6%
	4.00	Count	28	14	42
		% within Group	80.0%	40.0%	60.0%
	Total	Count	35	35	70
		% within Group	100.0%	100.0%	100.0%

Table 4: Anxiolysis at 10 Minutes

Cross table					
	Anxiolysis 10 Minutes Nasal		Group		
			Oral	Total	
	1.00	Count	0	6	6
		% within Group	.0%	17.1%	8.6%
	2.00	Count	13	17	30
		% within Group	37.1%	48.6%	42.9%
	3.00	Count	20	9	29
		% within Group	57.1%	25.7%	41.4%
	4.00	Count	2	3	5
		% within Group	5.7%	8.6%	7.1%
	Total	Count	35	35	70
		% within Group	100.0%	100.0%	100.0%

Table 5: Anxiolysis at 20 Minutes

Cross table					
	Anxiolysis 20 Minutes Nasal		Group		
			Oral	Total	
	2.00	Count	1	4	5
		% within Group	2.9%	11.4%	7.1%
	3.00	Count	23	18	41
		% within Group	65.7%	51.4%	58.6%
	4.00	Count	11	13	24
		% within Group	31.4%	37.1%	34.3%
	Total	Count	35	35	70
		% within Group	100.0%	100.0%	100.0%

Table 6: Anxiolysis at 30 Minutes

Cross table					
	Anxiolysis 30 minutes Nasal		Group		
			Oral	Total	
	3.00	Count	6	15	21
		% within Group	17.1%	42.9%	30.0%
	4.00	Count	29	20	49
		% wi11thin Group	82.9%	57.1%	70.0%
	Total	Count	35	35	70
		% within Group	100.0%	100.0%	100.0%

Discussion

Midazolam is used frequently for premedication in children, preferably by non-parenteral routes. Nasal administration of various drugs such as ketamine and midazolam has been recommended previously for premedication in children [10]. Midazolam has many desirable properties as a premedicant in children undergoing surgery [11]. Midazolam exerts a reliable dose-dependent anxiolytic effect without oversedation and provides minimal cardiovascular and respiratory effects [12]. Intranasal midazolam has generally been administered in the form of drops, which in the awake patient are difficult to keep in the nose and may be swallowed and subjected to first pass metabolism in the liver [13]. Twersky and colleagues used a Devilbiss 286 atomizer to deliver 0.2 mg/kg of midazolam. Kogan, Alexanderet alcompared two methods of administering midazolam intranasally in 44 day-care children and used midazolam 0.2 mg/kg as drops or midazolam 0.1 mg/kg from an intranasal spray device. Behavior was recorded on a four-pointscale andcoefficients were obtained representing the change in behavior score. There was no significant difference in the method of administration (coefficient 0.13, p=0.39) [14]. Each metered dose of 100 microliters of atomizer delivered 0.5 mg of midazolam. Oral midazolam used in this study was the preservative-freeinjectable preparation (5 mg/ ml) in an ampoule. The drug was mixed with the apple juice to mask the bitter taste and to increase the acceptability [15]. Lee-Kim, et studied 306 patients, using 3 different doses of oral midazolam syrup 0.25, 0.5, 1.0 mg/kg. Overall 97% of patients achieved satisfactory sedation (score>3) after treatment. The difference between the 0.25 and 0.1 mg/kg dosage was significant (p<0.01). There was no difference between the 0.5 and 1.0 mg/kg groups or between the 0.5 and 0.25 mg/kg groups. After study medication, 99% maintained satisfactory sedation scores and 97.5% achieved a satisfactory anxiolytic response (score>3). There was a positive association between dose and onset of anxiolysis (p=0.01); a larger proportion of children achieved satisfactory anxiolysis [16]. The proportion of subjects experiencing an adverse event was slightly larger in the 1.0 mg/kg.Hence it was decided to use oral midazolam in a dose of 0.5 mg/kg for all children in the oral group in this study and none of them experienced respiratory depression, nausea, vomiting or any adverse effect [17]. Malinovsky. J.M. et al. compared the effect of intranasal midazolam with intranasal ketamine and used intranasal midazolam in a dose of 0.2 mg/kg. In our study, mean time for onset of sedation, time for satisfactory sedation, level of sedation at 10 minutes, 20 minutes, and 30 minutes, level of anxiety at 10 minutes, 20 minutes, 30 minutes in both the groups were compared [18]. A four-point scale for sedation score, five-point scale for anxiolysis score and a four-point scale for co-operation score were used to compare the groups in this study. In our study, the mean time for onset of sedation in nasal midazolam group was found to be 8.42 minutes and in the oralgroup, it was 15.8 minutes [19]. Mittal Pankaj et al. Compared the effectiveness of intramuscular and intranasal midazolam as a premedication before intravenous conscious sedation. The patients ranged in age from 2-9 yrs (mean age 5.13 yrs) and received a dose of 0.2 mg/kg of midazolam via intramuscular or intranasal administration. They studied 23 patients and reported that patients who were given intramuscular midazolam were more deeply sedated than those receiving intranasal midazolam. Statistical analysis showed that sedation score at 10 minutes was better with the nasal group with a p value of <0.001 which is statistically highly significant. Sedation score at 20 minutes after premedication was better with nasal midazolam with a P value of < 0.001 which is again statistically significant [20]. Sedation score at 30 minutes was better in the nasal group with a p value of 0.003 which is statistically significant [21]. In our study, anxiolysis scores were better with the nasal group with the p-value of 0.012 at ten minutes and twenty minutes and a p value of 0.019 at thirty minutes which are statistically significant. This result can be correlated with the study of Parag Gharde et al., who had similar results. Co-operation scores at the time of venipuncture are found to be similar in both groups with a P value of 0.108 which is not statistically significant. This also correlates with the study of Sunny Alex et al., [25] who had the same results [22] The co-operation for mask application is comparable in both groups with a p value of > 0.05 which is not statistically significant. In both groups, no patient had coughing, gagging, vomiting, laryngospasm or respiratory depression [23].

Conclusion

In conclusion, intranasal midazolam when used as premedication in children, in a dose of 0.2 mg/kg hasa more rapid onset of action with satisfactory sedation and anxiolysis than oral midazolam. The rapid onset of action of nasal midazolam makes it

an ideal route for premedication in children.

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Conflict of Interest: None

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