Original Article

Comparison of the Midazolam Transnasal Atomizer and Oral Midazolam for Sedative Premedication in Paediatric Cases

Paediatrics Section

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ABSTRACT

Background: The role of effective premedication in children is of utmost importance in the conduct of paediatric anaesthesia. Midazolam is a proven and safe sedative anxiolytic in the paediatric group.

Objective: To evaluate the safety and effectiveness of Midazolam by the transnasal and oral routes for paediatric sedation.

Materials and Methods: We evaluated 60 ASA grade I and II children who were randomized to receive either oral (0.5mg/kg) or transnasal (0.5mg/kg) midazolam. The demographic details, the sedation score and the separation score were noted by a blinded observer and were statistically analysed.

Results: Both the routes were equally effective in achieving the adequate sedation and the separation scores. The transnasal route showed a faster onset of the adequate sedation scores. The oral route was better accepted by children.

Key Words: Midazolam premedication, Oral, Transnasal, Atomizer

INTRODUCTION

Preanaesthetic medication in children should aim at relieving anxiety and the trauma which is associated with their separation from their parents and it should also facilitate the induction of anaesthesia without prolonging the recovery [1]. Numerous premedicants to facilitate the separation of children from their parents and to reduce the anxiety which is associated with unfamiliar persons and the strange operative room environment have been advocated. However, an ideal premedicant should provide good patient and parent acceptance, predictable results and nil/minimal side effects [2].

Midazolam has long been used as a premedicant due to its sedative and anxiolytic properties. It has been used through various routes, viz. oral, rectal, intramuscular and the intranasal and the intravenous routes [3], each route with its own merits and demerits.

The transmucosal route of administering midazolam has a rapid and reliable onset of action due to the rich blood supply of the airway mucosa and bypassing the first pass hepatic metabolism. Also, this route avoids the need for painful injections and trained personnel to administer the drug [4, 5, 6].

Intra nasal midazolam has been used for paediatric procedural and operative sedation for many years by conventional methods. However, with the recent availability of the Nasal-Mucosal Atomization Device (MAD, Atomizer) [7] and proprietary oral midazolam formulations (syrup), these routes of administration have been revisited.

Our study aimed to compare the safety, acceptability, degree of sedation and the ease of administration of midazolam by using oral and nasal sprays for paediatric sedation.

MATERIALS AND METHODS

After obtaining clearance from the institutional ethical committee and informed consent from the parents/guardian, sixty ASA–1 and ASA-2 children who were aged between 18 months to 84 months, who were scheduled for elective surgical procedures, were studied. Children with respiratory and cardiac diseases and those who had upper respiratory tract infections were excluded from the study. All patients were brought to the reception area of the OT complex along with their parents/guardian and were allocated to one of the two groups, based on a computer generated randomisation table. The oral group received midazolam 0.5 $mgkg^{-1}$ proprietary midazolam oral formulation (Mezolam syrup, Neon lab) and the transnasal group (Inmed atomizer Samarth pharmaceuticals) received midazolam 0.5 $mgkg^{-1}$, which was dispensed through a proprietary drug atomiser in the supine position during inspiration. To avoid interobserver variations, the same anaesthesiologist was involved in all the assessments, who was also kept blind to the route of administration which was used by the attending anaesthesiologist. The degree of sedation was assessed at 15 and 30 minutes by using a 5 point sedation scale [Table/Fig-1]. A sedation score of 3 and above was considered as satisfactory and scores 1 and 2 were considered as unsatisfactory. After administering the study drug, the child was monitored continuously for oxygen saturation, respiratory rate and bradycardia.

At 30 minutes, the child was separated from its parents and was taken to the operating room. The response to the child- parent separation was assessed and graded according to a 4 point scale at 30 minutes [Table/Fig-2].

Sedation level	Score
Agitated	1
Upset/wary	2
Relaxed	3
Drowsy	4
Asleep	5

[Table/Fig-1]

Separation score [8]		
Patient unafraid, cooperative, asleep	Excellent	1
Slight fear or crying, quite with reassurance	Good	2
Moderate fear, crying not quite with reassurance	Fair	3
Crying need for restraint	Poor	4

[Table/Fig-2]

	Oral	Transnasal
Age (months)	42.46 (21.03)	45.06 (24.02)
Weight (kg)	12.06 (5.34)	12.36 (3.44)

[Table/Fig 3]: Demographic profile, mean (S.D)

	Oral	Transnasal	p value
Sedation 15 min	2.13 (0.730)	3.90 (0.830)	0.001
Sedation 30 min	4.00 (0.871)	4.63 (0.669)	0.003
Separation 30 min	1.37 (0.556)	1.73 (0.740)	0.034

[Table/Fig 4]: Sedation and Separation scores, mean (SD)
Unpaired Student t test, $p < 0.05$ significant.

The subjects were also observed for any side effects like the watering of eyes and nose, transient irritation of the pharyngeal mucosa, hypoxia, bradycardia and hypertension.

A sedation score of 3 and above was considered as satisfactory, and scores of 1 and 2 were considered as unsatisfactory.

RESULTS AND OBSERVATION

In our study, we made an effort to compare the different routes of administration of a novel premedicant, Midazolam.

The study evaluated the onset, quality of sedation and separation when midazolam was administered through the oral and transnasal routes in paediatric age groups.

The age and sex profile of the study subjects were comparable in both the groups [Table/Fig-3]. After the administration of midazolam through the respective routes, the sedation scores were evaluated by using a 5 point sedation scale at 15 and 30 minutes (Table-4). We observed that the transnasal group achieved a faster sedation score of 3 or more at 15 min (p value of 0.001 was taken as significant)

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When the separation score was evaluated at 30 minutes in both the groups, it was noticed that the transnasal group achieved better separation scores. (p value of 0.034 was taken as borderline significant). Three children in the nasal group had sneezing and nasal irritation, and in 2 children of the oral group, we observed vomiting.

DISCUSSION

The success of the conduct of anaesthesia in the paediatric age group depends on adequate premedication. Premedication not only comforts the anxious child, but also comforts the parents or the accompanying guardians. An ideal premedicant should be easy to administer and fast and prompt in action, with minimal adverse effects. Many premedicants have been tried through many routes, with variable success eg, Midazolam, Fentanyl, Ketamine, Clonidine, etc.

At 15 min, the sedation scores were good in the transnasal group (p value of 0.001), which was in concordance with those in the study which was conducted by Karl et al. who noticed that 10 min post administration was the time of maximal sedation [5]. A faster onset of sedation in the transnasal group was due to a rapid and nearly complete absorption of the drug, owing to the rich blood supply of the nasal mucosa and the nose brain pathway through the olfactory mucosa into the CSF. The effective delivering of the drug through the atomiser in the form of droplets which measure 30 –100 micron in size [7], helps in a larger dispersion of the drug over the mucosa and hence results in better absorption. As midazolam has a high hepatic clearance, and as the transnasal route avoids first pass hepatic metabolism, a greater systemic bioavailability can be achieved, unlike the oral route [6], 9, 10]. The elimination half life of intranasal midazolam is similar to that when the drug is given intravenously [11].

At 30 minutes, the sedation score was again better in the transnasal route (p value of 0.003) unlike the inference which was drawn in a study which was conducted by Sunny Alex et al [12], where it was noted that the separation scores irrespective of the route, were similar. This apparent difference in the observations may be attributed to a higher dose (0.5mg/kg) and the use of an atomiser for delivering the drug in the present study, as compared to a dose of 0.2mg/kg and the use of a syringe for depositing the drug intranasally by Sunny Alex et al [12].

The separation scale at 30 min was comparable (weakly significant at a p value of 0.03) in both the study groups. Hence, the routes were equally effective in achieving the desired objectives (sedation and separation), apart from the fact that the transnasal route had a faster and prompt onset of action. The faster onset and prompt action was similar to that observed by Sunny Alex et al [12]. The acceptability with the oral route was better, which was similar to that which was noticed by Tolksdorf W and Fick C [13].

Sneezing and nasal irritation was found in 3 patients, which can be most likely be attributed to the acidic preparation of Midazolam (pH 3.34). Oral midazolam had a better acceptance, as was evaluated by the crying of the children on administration of the drug. Events like bradycardia, drop in the oxygen saturation and apnoea were not observed in any of the study subjects. The effect of midazolam on the intraoperative course and on the postoperative sedation was not studied, as it was likely to also be confounded by the drugs and the inhalational agents which were used in the intraoperative period. However, Peter J Davis et al [6] are of the opinion that nasal midazolam provides satisfactory anxiolysis without delaying the anaesthetic and hospital recovery times.

CONCLUSION

The authors conclude that both the routes are equally effective and provide adequate sedation and that they ease the separation of the child from the parents/guardian. With the availability of atomizers which allow the delivery of transnasal midazolam in a calculated dose (0.5mg/metered dose), it may be preferred over oral midazolam.

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