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Original Research Article

Use of intranasal versus oral Midazolam as Preoperative Medication in Pediatric Patients

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Abstract

Background and Objectives: Administering premedication to pediatric patients undergoing surgery is crucial to alleviate separation anxiety, reduce apprehension, and facilitate cooperation. This study aims to compare the effectiveness and safety of intranasal and oral midazolam in terms of sedation onset.

Materials & Methods: The research cohort comprised 140 patients with ASA grade I and II, within the age range of 2-9 years, who were scheduled for elective surgeries at tertiary care medical hospital in India. The participants were randomly allocated into two groups, with each group consisting of 70 patients.

Results: The onset of sedation was significantly quicker when midazolam was administered intranasally compared to the oral route. Both intranasal and oral administration of midazolam were equally effective in achieving sedation, with no statistically significant differences observed between the two routes. Furthermore, the vital signs of the patients remained stable throughout the procedure in both groups, and no significant differences were noted.

Conclusion: Intranasal midazolam is faster acting, equally effective and safe as oral midazolam. It may be preferred over oral midazolam due to is faster onset of action, efficacy and safety profile.

Keywords: Premedication, Midazolam, Surgery, Sedation, Pediatric.

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Introduction

Children experience similar levels of anxiety as adults [1, 2]. Hospitalization, anesthesia, and surgery can be highly stressful for children, and excessive preoperative anxiety in children may result in delayed anesthesia induction and the onset of negative psychological effects after surgery, such as nightmares, eating disturbances, and enuresis [3,4].

The premedication aspect of pediatric anesthesia is often overlooked, despite its significance. In many busy pediatric

surgical theaters, it is common to encounter anxious and distressed children in the waiting area, expressing their distress through crying. Anesthetists frequently face challenges when attempting to start intravenous lines or induce anesthesia through inhalation due to the child's resistance. While we are cautious about inducing anesthesia in struggling adult patients to avoid a hypertensive response, we often neglect the proper premedication of pediatric patients before bringing them to the operating theater. Therefore, there is a need for an effective preanesthetic medication that can alleviate anxiety related to anesthesia and surgery, minimize the emotional distress associated with separation from parents, and facilitate the smooth induction of general anesthesia without prolonging the recovery period after anesthesia [5].

The topic of premedication in children remains a subject of debate and controversy, as there are various premedication options and delivery systems available, each utilizing different routes of administration.

The study aimed to achieve two main objectives: firstly, to compare the onset of drug action when administered orally and intranasally; and secondly, to evaluate the effectiveness and safety of the drug as a premedicant using these two routes of administration, focusing on sedation score and anxiety score. The study sought to determine whether there were differences in the time it took for the drug to take effect based on the route of administration, as well as assess the overall efficacy and safety of the drug in reducing anxiety and inducing sedation. By comparing these outcomes, the study aimed to provide valuable insights into the optimal route for premedication administration in children, thus contributing to the improvement of pediatric anesthesia practices.

MATERIAL & METHODS

The study took place at a prominent tertiary care teaching medical hospital in India providing specialized care, and extended over a period of two years. It involved patients who were admitted for elective surgeries in departments such as Paediatric surgery, General Surgery, Plastic Surgery, Otorhinolaryngology, Orthopaedics,

A total of 140 patients, ranging from 2 to 9 years of age and classified as ASA Grade I and II, were enrolled in this study. The inclusion criteria involved children scheduled for surgical procedures with durations ranging from 15 minutes to 2 hours. Random allocation placed the children into two groups of 70 each. Group 1 received intranasal midazolam at a dosage of 0.2 mg/kg, while Group 2 received oral midazolam syrup at a dosage of 0.5 mg/kg.

Preoperative anaesthetic checkup was conducted on all patients prior to their scheduled surgery to ensure their suitability for the procedure and anesthesia. During this assessment, the nature and purpose of the study were explained to the parents, aiming to alleviate any anxiety they may have had. Parents were also provided with instructions regarding fasting guidelines for their children. A comprehensive clinical examination, including a general physical examination and assessment of systemic health, was performed on each patient.

In accordance with the preoperative fasting guidelines for children, the following instructions were given: children were not allowed to consume any oral liquids within 2 hours prior to the scheduled procedure, and they were required to avoid consuming milk and solid foods for a period of 6 hours before the procedure. These fasting guidelines were implemented to ensure that the stomach was empty during the surgery, reducing the risk of complications such as aspiration [2].

The study employed specific criteria for inclusion and exclusion of participants.

Inclusion criteria encompassed patients who were scheduled for elective major or minor surgeries and fell within the age range of 2-8 years. Additionally, patients were required to have an American Society of Anesthesiologists (ASA) Grade 1 or 2 classification, indicating overall good health. On the other hand, exclusion criteria encompassed patients with ASA Grades 3 and 4, representing individuals with severe underlying medical conditions. Patients with a history of prematurity and chronic illnesses that could potentially affect the outcomes of the study were also excluded. Moreover, individuals with a history of developmental delay, which might impact the accurate assessment of premedication effects, were not included in the study. These criteria were carefully defined to ensure that the selected participants were within the desired age range, exhibited similar health statuses, and were appropriate candidates for receiving the premedication being investigated.

Baseline measurements of heart rate, respiratory rate, systolic blood pressure, and activity level of the children were recorded in the preoperative room. The study included a total of 140 cases, divided equally into two groups of 70 patients each. Group-1 received intranasal midazolam at a dose of 0.2 mg/kg, while Group-2 received oral midazolam syrup at a dose of 0.5 mg/kg. In Group-A, diluted midazolam 1mg/ml preservative-free was administered intranasally using a dropper, following the recommended dosage of 0.2 mg/kg, 45 minutes before the induction of anesthesia. The children in both groups were assessed for sedation adequacy using sedation score and anxiety score, as well as their response to a painful stimulus. In Group-A, this evaluation was conducted every 2 minutes, starting at 1, 3, 5, 7, minutes, and so on, specifically in response to a needle prick and their ability to undergo venipuncture. For Group-B, the evaluation was performed at 5-minute intervals, starting at 5, 10, 15, 20, 25, 30, 35, 40, and 45 minutes following the administration of oral midazolam syrup.

Both groups of children were closely monitored for any alterations in heart rate, respiratory rate, and systolic blood pressure. Additionally, their level of sedation, anxiety, and response to painful stimuli were assessed. Other factors such as the occurrence of vomiting, excessive salivation, abdominal movement, rigidity, and the ability to maintain the airway were also evaluated. The doses of midazolam administered in this study were approximately equipotent and fell within the effective range known to induce sedation.

The onset of sedation was determined as the minimum amount of time required for the child to exhibit drowsiness and fall asleep. Once the child reached a sedation score of 3, 4, or 5, indicating an appropriate level of sedation, they were transferred to the operating room. In cases where satisfactory sedation was not achieved within the maximum specified time interval, anesthesia induction was still carried out.

All children in the study were first secured with a 22G cannula. They were then premedicated with Inj. Glyco at a dosage of 0.01 mg/kg and provided with analgesia using Inj. Fentanyl at a dosage of 2 μg/kg. General anesthesia was induced using a combination of nitrous oxide (60%) and oxygen (40%) along with halothane (ranging from 0.5% to 3%). The child's acceptance of the anesthesia mask was recorded, and the time from mask application to the loss of the eyelash reflex, known as the induction time, was noted. Muscle relaxation was achieved using the depolarizing muscle relaxant succinylcholine at a dosage of 1-2 mg/kg intravenously. Laryngoscopy was performed using a rigid laryngoscope with a standard Macintosh blade, and endotracheal intubation was carried out using an appropriately sized high volume, low-pressure cuffed endotracheal tube. The

presence of secretions at the time of intubation was assessed and scored as either satisfactory or unsatisfactory [2].

Data Analysis: Descriptive statistics such as mean, standard deviation, and percentage were calculated for all groups in order to summarize the data. Continuous variables were analyzed using paired t-tests for paired samples and unpaired t-tests for independent samples. Categorical data were analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically significant, indicating a significant difference between groups or variables.

for categorical data. P-value of <0.05 was considered for significant difference.

RESULTS

In Group 1, there were 42 male and 28 female children, with ages ranging from 2 to 9 years (4.23 ± 1.75), and body weights ranging from 7 to 21 kg (12.99 ± 3.62). In Group 2, there were 43 male and 27 female children, with ages ranging from 2 to 9 years (4.19 ± 1.63), and body weights ranging from 7 to 21 kg (12.40 ± 2.78). The two groups were comparable in terms of age, gender, and weight distribution [Table 1].

Table 1: Thyroid cases as per The Bethesda System for Reporting Thyroid Cytology

	Group 1 (N=70)	Group 2 (N=70)	P value
Age in years (mean ± SD)	4.23 ± 1.75	4.19 ± 1.63	0.89
Weight in Kg (mean ± SD)	12.99 ± 3.62	12.40 ± 2.78	0.29
Gender			
Male, n (%)	42 (60)	43 (61.43)	0.86
Female, n (%)	28 (40)	27 (38.57)	

In both groups, there was a statistically significant increase in heart rate from baseline to pre-induction levels. However, this increase was not considered clinically significant [Table 2].

Table 2: Heart rate (beats/minute)

	Group 1 (N=70)	Group 2 (N=70)	P value
Pre-operative	103.5 ± 3.6	102.6 ± 2.6	0.09
Pre-induction	106.3 ± 4.6	105.7 ± 4.4	0.43
P value	<0.05	<0.05	

Sedation was evaluated using a 5-point sedation scale, where a score of 1 indicated agitation and crying, and scores ranging from 2 to 5 indicated varying degrees of sedation leading to sleep [Table 3] whereas Anxiety levels were assessed using a 4-point scoring system [Table 4]

Table 3: Sedation scores

	Sedation Scores [N (%)]			
	3	4	5	Total
Group 1	33 (47.13)	35 (50)	2 (28.57)	70 (100)
Group 2	32 (45.71)	36(51.42)	2 (28.57)	70 (100)

Table 4: Anxiety scores

	Anxiety scores [N (%)]		
	3	4	Total
Group 1	44 (62.86)	26 (37.14)	70 (100)
Group 2	42 (60)	28 (40)	70 (100)

Onset of sedation was significantly faster in intranasal administration of midazolam [Table 5]. During the intraoperative period, the observed changes in heart rate and respiratory rate were

below 15% in all the cases included in the study, indicating satisfactory stability in these parameters. Common postoperative complaints are compared in Table 6.

Table 5: Onset of Sedation in minutes

Onset of Sedation	Group 1 (N=70) In minutes	Group 2 (N=70) In minutes	P value
mean ± SD	8.21 ± 2.6	32.21 ± 4.3	<0.05

Table 6: Onset of Sedation in minutes

	Group 1 (N=70)	Group 2 (N=70)	P value
Vomiting			
Yes, n (%)	9 (12.86)	12 (17.14)	0.48
No, n (%)	61 (87.14)	58 (82.86)	
Restlessness			
Yes, n (%)	8 (11.43)	10 (14.29)	0.61
No, n (%)	62 (88.57)	60 (85.71)	

Discussion

The study aimed to evaluate the onset, effectiveness, and safety of midazolam as preanesthetic medication in pediatric patients. The intranasal and oral routes of administration were compared, considering parameters such as onset of action, effectiveness, and safety

Both groups exhibited a statistically significant increase in heart rate from baseline to the pre-induction level. However, the magnitude of the increase was similar in both groups and did not have clinical significance. These findings align with previous studies by [2] and [9].

The onset of sedation was notably faster in Group 1 compared to Group 2. Children who received intranasal midazolam in Group 1 achieved sedation within an average time range of 5-11 minutes. These findings are consistent with several previous studies [7, 10, 11, 12].

Children in Group B who received oral midazolam had an average onset time of sedation ranging from 27 to 37 minutes. These findings align with previous studies that utilized the same oral dose of midazolam at 0.5 mg/kg [3, 9, 13].

In a study evaluating the effect of midazolam syrup as premedication to alleviate discomfort during pediatric intravenous catheter insertion [14], both groups of children demonstrated cooperation for IV cannulation which was similar to our study. Therefore, our study findings indicate that premedication with intranasal midazolam at a dosage of 0.2 mg/kg or oral midazolam at a dosage of 0.5 mg/kg effectively achieved satisfactory sedation and anxiolysis. Furthermore, the intranasal route exhibited a significantly faster onset of sedation compared to the oral route.

Based on the comparison between intranasal and oral routes of midazolam administration as preanesthetic medication in pediatric patients, the following conclusions were drawn:

1. The onset of sedation was significantly faster with intranasal administration compared to oral administration.

2. Both intranasal and oral routes of midazolam administration were equally effective in terms of sedation score, anxiety score, emotional status score, acceptance of mask, and venipuncture score. There were no statistical differences observed between the two routes.

3. Throughout the procedure, all vital signs remained stable, and there were no significant differences between intranasal and oral administration, indicating the safety of drug administration through either route.

These findings highlight the advantages of intranasal administration in achieving faster onset of sedation, while also emphasizing the comparable effectiveness and safety of both routes of midazolam administration in pediatric patients.

Conclusion

Intranasal midazolam emerges as a favorable option compared to oral midazolam based on its faster onset of action, comparable effectiveness, and safety profile. With its ability to provide rapid sedation, intranasal administration may be preferred over the oral route in clinical practice. The findings suggest that intranasal midazolam can offer a suitable alternative for preanesthetic medication in pediatric patients, providing a balance between efficacy and safety.

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