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Original Research Article

Is Intranasal Midazolam Superior To Its Oral Administration For Preoperative Anaesthestic Sedation In Pediatric Patients?

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Abstract

Background and Objectives: The administration of premedication to pediatric patients undergoing surgery is essential to alleviate separation anxiety, reduce apprehension, and promote cooperation. The primary objective of this study is to compare the effectiveness and safety of intranasal and oral midazolam in terms of sedation onset. By assessing the sedation onset, the study aims to determine which route of midazolam administration is more efficient and well-tolerated in pediatric patients.

Materials & Methods: The research cohort consisted of 164 patients categorized as American Society of Anesthesiologists (ASA) grade I and II, ranging in age from 2 to 9 years. These patients were scheduled to undergo elective surgeries at a tertiary care medical hospital in India. The participants were randomly assigned to two groups, with each group comprising 82 patients.

Results: The study findings revealed that the onset of sedation was significantly faster when midazolam was administered intranasally compared to the oral route. However, 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 in this regard.

Conclusion: Based on the study findings, intranasal midazolam demonstrates faster onset of action, comparable effectiveness, and a similar safety profile to oral midazolam. Therefore, intranasal midazolam may be preferred over the oral route due to its quicker onset of action, as well as its efficacy and safety.

Keywords: Midazolam, Surgery, Premedication, Pediatric.

Introduction

Children, similar to adults, undergo experiences of anxiety [1, 2]. Hospitalization, anesthesia, and surgery can induce significant stress in children, and heightened preoperative anxiety may lead to delayed anesthesia induction and subsequent negative psychological effects post-surgery, including nightmares, eating disturbances, and enuresis [3, 4].

The significance of premedication in pediatric anesthesia is often underestimated, despite its importance. Within busy pediatric surgical theaters, it is common to encounter distressed and anxious children in the waiting area, expressing their distress through crying. Anesthetists frequently encounter challenges when attempting to establish intravenous lines or induce anesthesia through inhalation due to the child's resistance. While cautiousness is exercised when inducing anesthesia in struggling adult patients to prevent a hypertensive response, the proper premedication of pediatric patients before their arrival in the operating theater is often neglected. Consequently, there exists a demand for an effective preanesthetic medication that can alleviate anxiety associated with anesthesia and surgery, minimize emotional distress related to separation from parents, and facilitate the smooth induction of general anesthesia without extending the recovery period after anesthesia [5].

The topic of premedication in children is a subject of ongoing debate and controversy due to the availability of various options and delivery systems, each utilizing different routes of administration. The primary objectives of this study were twofold. Firstly, it aimed to compare the onset of drug action

when administered orally and intranasally. Secondly, it sought to evaluate the effectiveness and safety of the drug as a premedicant using these two routes of administration, with a focus on sedation score and anxiety score as outcome measures. The study aimed to investigate whether there were any differences in the time it took for the drug to take effect depending on the route of administration, as well as to 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, thereby contributing to the enhancement of pediatric anesthesia practices.

Material & Methods

The study was conducted at a prestigious tertiary care teaching medical hospital in India. The research spanned a duration of one and a half years and included patients who were admitted for elective surgeries in various departments such as Orthopedics, Pediatric Surgery, Otorhinolaryngology, General Surgery and, Plastic Surgery

The study included a total of 164 patients, aged between 2 and 9 years, who were classified as ASA Grade I and II. These patients were scheduled for surgical procedures with durations ranging from 15 minutes to 2 hours. The participants were randomly allocated to two groups, with each group consisting of 82 patients. Group N (N = Nasal) received intranasal midazolam at a dosage of 0.2 mg/kg, while Group O (O = Oral) received oral midazolam syrup at a dosage of 0.5 mg/kg.

Prior to the scheduled surgery and anesthesia, a preoperative anesthetic checkup was conducted on all patients to evaluate their suitability for the procedure. During this assessment, parents were informed about the nature and purpose of the study, aiming to alleviate any anxiety they may have had. Detailed instructions regarding fasting guidelines for their children were also provided to the parents. Each patient underwent a comprehensive clinical examination, which included a general physical examination and an assessment of their systemic health.

In adherence to the preoperative fasting guidelines for children, specific instructions were provided. Children were instructed not to consume any oral liquids within 2 hours prior to the scheduled procedure. Furthermore, they were required to abstain from consuming milk and solid foods for a duration of 6 hours before the procedure. These fasting guidelines were implemented to ensure that the stomach was empty during the surgery, thereby minimizing the risk of complications such as aspiration [2].

The study employed specific criteria for the inclusion and exclusion of participants. The inclusion criteria involved patients scheduled for elective major or minor surgeries within the age range of 2-8 years. Additionally, patients needed to have an American Society of Anesthesiologists (ASA) Grade 1 or 2 classification, indicating overall good health. Conversely, the 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 study outcomes 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 meticulously defined to ensure that the selected participants fell within the desired age range, exhibited similar health statuses, and were appropriate candidates for receiving the investigated premedication.

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 164 cases, equally divided into two groups of 82 patients each. Group N received intranasal midazolam at a dose of 0.2 mg/kg, while Group O received oral midazolam syrup at a dose of 0.5 mg/kg. In Group 1, 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, anxiety score, and their response to a painful stimulus. In Group N, 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 O, 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 changes 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 duration required for the child to display drowsiness and fall asleep. Once the child achieved a sedation score of 3, 4, or 5, indicating an

appropriate level of sedation, they were transferred to the operating room. In instances where satisfactory sedation was not achieved within the designated maximum time interval, anesthesia induction was still proceeded with.

All children participating in the study underwent the placement of a 22G cannula for intravenous access. They were then administered premedication 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%) in conjunction with halothane at concentrations ranging from 0.5% to 3%. The child's acceptance of the anesthesia mask was recorded, and the duration 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 administered intravenously. Laryngoscopy was performed using a rigid laryngoscope with a standard Macintosh blade, and endotracheal intubation was conducted using an appropriately sized high volume, low-pressure cuffed endotracheal tube. The presence of secretions at the time of intubation was evaluated and classified as either satisfactory or unsatisfactory [2].

RESULTS

In Group N, there were 47 male and 35 female children, with ages ranging from 2 to 9 years (mean age: 4.15 ± 1.65), and body weights ranging from 8 to 20 kg (mean weight: 12.67 ± 2.97). In Group O, there were 50 male and 32 female children, with ages ranging from 2 to 9 years (mean age: 4.27 ± 1.59), and body weights ranging from 7 to 20 kg (mean weight: 12.51 ± 2.69). The two groups demonstrated comparable distributions in terms of age, gender, and weight, as shown in Table 1.

Table 1: Demographic details of study population

Variable (mean ± SD)	Group N (82)	Group O (82)	P value
Age (in years)	4.37 ± 1.62	4.21 ± 1.57	0.78
Weight (in Kilograms)	12.76 ± 3.51	12.48 ± 2.85	0.33
Gender (n, %)			
Boys	47 (57.31)	50 (60.97)	0.79
Girls	35 (42.68)	32 (39.02)	

In both Group N and Group O, there was a statistically significant increase in heart rate from baseline to pre-induction levels, as indicated in Table 2. However, this increase was not deemed significant.

Table 2: Heart rate (beats/minute)

	Group N (82)	Group O (82)	P value
Pre-operative	104.2 ± 3.2	102.9 ± 2.9	0.13
Pre-induction	106.7 ± 4.8	105.5 ± 4.2	0.39
P value	<0.05	<0.05	

Sedation was assessed using a 5-point sedation scale, where a score of 1 indicated agitation and crying, and scores ranging from 2 to 5 indicated different levels of sedation leading to sleep (refer to Table 3). Anxiety levels were evaluated using a 4-point scoring system (refer to Table 4).

Table 3: Sedation scores

	Sedation Scoring [N (%)]			
	3	4	5	Total
Group N	34 (48.57)	34 (48.57)	2 (28.57)	70 (100)
Group O	33 (47.14)	37 (52.86)	3 (42.86)	73 (100)

Table 4: Anxiety scores

	Anxiety scoring [N (%)]		
	3	4	Total
Group N	44 (60.27)	29 (39.73)	73 (100)
Group O	41 (56.16)	32 (43.84)	73 (100)

The onset of sedation was significantly faster in the intranasal administration of midazolam, as shown in Table 5. Throughout the intraoperative period, the changes in heart rate and respiratory rate observed in all cases were below 15%, indicating satisfactory stability in these parameters. The common postoperative complaints are compared in Table 6.

Table 5: Onset of Sedation in study population

Onset of Sedation in minutes	Group N (82)	Group O (82)	P value
mean ± SD	7.85 ± 2.8	32.98 ± 4.1	<0.05

Table 6: Post-operative complaints in study population

	Group N (82)	Group O (82)	P value
Vomiting			
Yes, n (%)	11 (13.41)	9 (10.98)	0.51
No, n (%)	71 (86.59)	73 (89.02)	
Restlessness			
Yes, n (%)	7 (8.54)	15 (18.29)	0.58

Discussion

Group N demonstrated a significantly quicker onset of sedation when compared to Group 2. Specifically, pediatric patients administered intranasal midazolam in Group O achieved sedation within an average timeframe ranging from 6 to 12 minutes. These findings align with multiple prior investigations as referenced by studies [7, 10, 11, 12].

In Group O, children who were administered oral midazolam experienced an average onset time of sedation ranging from 26 to 36 minutes. These results are consistent with previous studies that employed a similar oral dosage of midazolam at 0.5 mg/kg, as documented in studies [3, 9, 13].

A study conducted by Mc Erlean et al. [14] aimed to evaluate the impact of midazolam syrup as premedication to alleviate discomfort during the insertion of intravenous catheters in pediatric patients. Both groups in the aforementioned study demonstrated similar levels of cooperation during IV cannulation, which aligns with the findings observed in our study. Therefore, the results of our study 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. Additionally, it is worth noting that the intranasal route exhibited a significantly faster onset of sedation compared to the oral route.

The present study conducted a comparison between the intranasal and oral routes of midazolam administration as preanesthetic medication in pediatric patients. The findings revealed that the onset of sedation was significantly faster when midazolam was administered intranasally compared to the oral route. Moreover, both routes of administration exhibited equal effectiveness in terms of sedation score, anxiety score, emotional status score, acceptance of mask, and venipuncture score, with no statistical differences observed between them. Importantly, throughout the procedure, vital signs remained stable, and there were no significant variations between intranasal and oral administration, indicating the safety of either route. These results underscore the advantages of intranasal administration in achieving a quicker onset of sedation, while also highlighting the comparable effectiveness and safety of both routes of midazolam administration in pediatric patients.

Conclusion

Intranasal midazolam stands out as a preferable choice when compared to oral midazolam, primarily due to its faster onset of action while maintaining comparable effectiveness and safety. The rapid sedation achieved through intranasal administration positions it as a favorable option in clinical settings. These findings support the notion that intranasal midazolam can serve as a viable alternative for preanesthetic medication in pediatric patients, striking a balance between efficacy and safety considerations.

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