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Midazolam for Peadiatric Sedation: Assessing Efficacy of Intravenous vs Intransal Route

[1]Gaganpal Singh and [2]Gajendra Kumar

[1]*Department of Anesthesia, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India*

[2]*Department of Pediatric, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India*

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Corresponding Author
Gajendra Kumar,
Department of Pediatric, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India
ni2015rmay@gmail.com

Author Designation
[1]Associate Professor
[2]Assistant Professor

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ABSTRACT

Sedation is essential for facilitating the smooth execution of radiological procedures, especially in pediatric patients who may experience distress and apprehension during imaging. Among the available sedative agents, midazolam has been widely recognized for its effectiveness and favorable safety profile in pediatric practice. This research aimed to evaluate and compare the efficacy and safety of intravenous (IV) midazolam versus intranasal (IN) midazolam for sedation in pediatric patients undergoing radiological imaging. This prospective, randomized clinical study included children between 6 months and 8 years of age who required sedation for computed tomography (CT) imaging. A total of 112 participants were enrolled, with 56 children randomly assigned to each sedation method (IV midazolam or IN midazolam) using randomization. Sedation was administered according to the assigned group and imaging procedures were performed under sedation. The primary parameters assessed included sedation effectiveness and safety, focusing on sedation onset, depth of sedation, procedure completion rate, adverse effects and recovery duration. The time required to achieve sedation was shorter in the intravenous midazolam group compared to the intranasal group. No significant differences were observed in sedation onset and duration based on age or sex. The overall success rate of completing the radiological procedure was comparable between the two groups. However, the intranasal midazolam group demonstrated a faster recovery. Motion artifacts at the end of the procedure were more frequent in the intranasal group. Adverse effects, including severe complications such as respiratory distress and oxygen desaturation, were more commonly reported in patients receiving intravenous midazolam. Given its ease of administration, fewer side effects despite higher doses, and rapid recovery time, intranasal midazolam may serve as a practical sedation option for short, non-invasive imaging procedures such as CT scans.

INTRODUCTION

Sedation is essential for the successful execution of radiological procedures, especially in pediatric patients who may experience distress and unease during imaging. Among the various sedative agents available, midazolam, a benzodiazepine known for its sedative, anxiolytic and amnestic effects, is widely preferred due to its established safety and effectiveness in children. While the intravenous (IV) route has traditionally been the standard for midazolam administration, the intranasal (IN) approach has gained attention as a viable alternative, offering benefits such as easier delivery and eliminating the stress associated with needle use[1-4]. Several studies have explored the efficacy and safety of IV midazolam for pediatric sedation in radiological procedures. However, there is limited research directly comparing the IV and IN routes in this patient population. A thorough understanding of the safety and effectiveness of these two administration methods is crucial for refining sedation protocols and enhancing pediatric patient management during imaging[5]. The present study seeks to bridge this knowledge gap by conducting a randomized prospective clinical study comparing IV and IN midazolam for sedation in pediatric patients undergoing radiological imaging, particularly computed tomography (CT) scans[6]. By assessing variables such as time to sedation, sedation depth, procedural success rate, occurrence of adverse effects and recovery duration, this investigation aims to offer critical insights into the most suitable route for midazolam administration in pediatric radiological sedation.

MATERIALS AND METHODS

A prospective, randomized clinical study was carried out on children between 6 months and 8 years of age who required sedation for computed tomography (CT) imaging. A total of 112 participants were recruited, with equal distribution into two groups (IV midazolam and IN midazolam). Randomization was performed using an envelope-based method to ensure equal allocation. Sedation was administered according to the assigned group and imaging was conducted under sedation. The primary parameters evaluated included sedation efficacy and safety, with key outcomes such as sedation onset time, sedation depth, procedure completion rate, adverse effects and recovery duration. Children between 6 months and 8 years of age requiring sedation for CT imaging were eligible for inclusion. Additionally, patients with head injuries and a Glasgow Coma Scale (GCS) score of 13 or higher who required CT scans were also included. Patients with rhino-pharyngitis, nasal pathologies, a known allergy to midazolam, or those receiving sedative medications prior to the study were excluded. Children with cardio-respiratory disorders, hepatic or renal dysfunction and those with head injuries with a GCS score of 12 or lower were also not included. Children assigned to the intranasal midazolam group were either seated on their parents' laps or positioned on a trolley in the waiting area. The first dose (0.4 mg/kg) of midazolam was administered intranasally using an atomizer (midazolam 5 mg/5 mL, delivering 0.5 mg per spray). The total dosage was split into two portions and administered into each nostril using a metered-dose spray. Sedation was assessed at 15-minute intervals using the Ramsay Sedation Scale (RSS). If the sedation level was insufficient (RSS score below 4), additional doses (0.2-0.4 mg/kg) were administered as needed, with a maximum of three doses. A score of 4 was considered adequate for sedation. Children were positioned such that their heads faced forward as if reading a book. The atomizer nozzle was inserted into the nostril, directing the spray upward and posteriorly toward the eye and ear on the same side. This method minimized medication drainage into the throat and prevented irritation. Children were also instructed not to sniff or blow their noses immediately after administration. Patients with a pre-established intravenous catheter received an initial IV dose of midazolam (0.2 mg/kg). Sedation levels were assessed using the Ramsay Sedation Scale and if the desired sedation (RSS score $\geq$4) was not achieved, additional doses of 0.2 mg/kg were administered up to a maximum of three doses (total 0.6 mg/kg). For both groups, if adequate sedation was not achieved after the maximum permissible doses, an alternative sedative or anesthetic agent was administered to complete the procedure. These cases were classified as sedation failures. Data entry was conducted using Microsoft Excel 2013 and statistical analyses were performed using SPSS for Windows (version 23). Categorical variables were reported as percentages, while continuous variables were presented as mean±standard deviation (SD). The chi-square test or Fisher's exact test was employed to compare proportions. For continuous variables, Student's t-test was applied for parametric data, whereas the Wilcox on rank-sum test was used for non-parametric distributions. A $P<0.05$ was considered statistically significant.

RESULTS AND DISCUSSIONS

The baseline characteristics of the study groups, including age, weight and gender distribution, were comparable between the intravenous (IV) and intranasal (IN) Midazolam groups, with no statistically significant differences observed (Table 1).

Table 1: Baseline Variables of Study Groups

Variable	IV Midazolam	IN Midazolam	P-value
Age (months)	35.7±22.9	40.2±23.6	0.31
Weight (kg)	12.4±4.2	13.6±5.1	0.18
Gender			
Male (n)	38	36	0.68
Female (n)	18	20	
Imaging Study			
CT Head (n)	49	48	0.92
CT Thorax (n)	4	4	
CT Abdomen (n)	3	4	
GCS Score			
GCS 13 (n)	3	0	0.26
GCS 14 (n)	11	8	
GCS 15 (n)	42	48	

When comparing the variables between the two routes of administration, a significantly higher dose of Midazolam was required in the IN group compared to the IV group (Table 2). Despite this, the success rates of sedation were similar between the groups, with no significant difference in the number of successful or failed sedation cases. The sedation scores also did not differ significantly between the two groups. However, the time required to achieve maximum sedation was significantly longer in the IN group, while the duration for regaining orientation was significantly shorter compared to the IV group.

Table 2: Comparison of Variables Between Two Routes of Administration of Midazolam

Variable	IV Midazolam	IN Midazolam	P-value
Dose of Midazolam (mg/kg)	0.51±0.11	0.96±0.22	<0.05
Outcome			
Success., n	49	46	0.43
Failure., n	7	10	
Sedation Score			
≥4., n	50	47	0.41
< 4., n	6	9	
Mean duration (min) for achieving maximum sedation	26	33	<0.05
Mean duration (min) for regaining orientation	86.7	68.6	<0.05

Regarding side effects, IV Midazolam was associated with a significantly higher incidence of adverse effects compared to IN administration (Table 3). The total number of cases experiencing side effects was more than twice as high in the IV group, indicating a statistically significant difference between the two routes.

Table 3: Comparison of Side Effects Between Two Routes of Administration of Midazolam

Side effects	IV Midazolam	IN Midazolam	P-value
Total cases (n)	24	11	<0.01

Midazolam is a commonly used agent for procedural sedation in pediatric patients. Intravenous midazolam has long been the standard for sedation in these settings. However, the intranasal (IN) form of midazolam, introduced recently in India, is now gaining use for various procedural sedations, particularly in emergency departments. In our study, we employed the Ramsay Sedation Scale to assess the depth of sedation, with scores ranging from 1 (anxious/restless) to 6 (no response). A Ramsay score of 4 or higher was considered adequate sedation. Our results showed that >80% of patients in the INM group achieved the desired sedation level, compared to about 90% in the IV group, a difference that was not statistically significant. Notably, our study used higher doses of intranasal midazolam than previous studies, which used lower doses that resulted in less successful sedation outcomes. Fallah[7] conducted a similar study comparing the efficacy of oral chloral hydrate and INM in pediatric sedation during elective brain CT scans, achieving a desired Ramsay score in 40% of the INM group, compared to 93% in the chloral hydrate group. This lower efficacy was likely due to the smaller dose (0.2mg/kg) of INM used. Similarly, Malaviya[5] found that the desired sedation score (using a scale adapted from Wilton[8]) was achieved in 80% of patients in the INM group (0.2mg/kg) and 94% in the IV midazolam group, with a statistically significant difference. This disparity can likely be attributed to the lower dose of INM administered in the former group and the combination of two intravenous drugs in the latter. Regarding the maximum sedation score achieved, the IV group demonstrated a higher score compared to the INM group, with a statistically significant difference. While deeper sedation may facilitate easier procedures, it is also associated with risks such as respiratory depression and delayed recovery, which can extend hospitalization. Our study showed that, although INM led to a lower sedation depth than IVM, both groups were equally successful in completing the procedure and the INM group had faster recovery times. These findings are consistent with those of Acworth[9], who reported mean sedation scores of 2.5 in the IV midazolam group and 3.5 in the intranasal group ($p<0.01$). The time required to reach maximum sedation was longer in the INM group. This can be explained by the superior bioavailability of intravenous medications. These results align with Filho[10], who found that the time to achieve sedation via the intranasal route averaged 28.4 minutes when multiple doses were needed and 15.2 minutes for those requiring a single dose. Rose at al a and Roelofse[11,12] also reported that maximum sedation was reached at 20 minutes with INM. The variability observed in onset times across studies can be attributed to differences in doses, dosing intervals, sedation scales and patient populations. Regarding the presence of motion artifacts at the end of the CT scan, this difference did not reach statistical significance, which could be a concern if the radiological results are compromised. To our knowledge, no studies have specifically compared INM with other sedatives in terms of radiological artifacts. Filho[10] found that 93.3% of scans using INM showed no motion artifacts, suggesting that further research is needed to determine whether INM is linked

to a higher frequency of artifacts. Regarding the number of doses required to achieve sedation, no patients in either group achieved sedation with a single dose. This difference was statistically insignificant. Our use of higher doses of INM aligns with previous studies showing that lower doses of intranasal midazolam are less effective. Despite the higher dose used in our study, side effects in the INM group were fewer than in the IV group and the success rate was nearly comparable between the two groups. Fallah[7] compared INM with chloral hydrate for CT scan sedation and found that a single dose of chloral hydrate (0.2mg/kg) was more effective, concluding that low doses of INM resulted in suboptimal outcomes.

CONCLUSION

Despite requiring relatively higher dosages compared to the intravenous route, intranasal midazolam demonstrates a favorable safety profile, with a lower incidence of severe adverse effects such as respiratory depression and desaturation. Additionally, its faster recovery time enhances procedural efficiency by reducing post-sedation monitoring duration and minimizing hospital stay. These attributes make intranasal midazolam a viable, well-tolerated and easily administered sedative option for short, pain-free diagnostic procedures in pediatric patients.

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