Section: Anaesthesiology

Original Research Article

EFFECT OF INTRANASAL MIDAZOLAM AS PREMEDICATION IN PAEDIATRIC ANAESTHESIA

I.Pravin Kumar[1], M.Prakash Kumar[1], R.Sathyaseelan[2]

[1]Assistant Professor, Department of Anaesthesiology, Government Medical College and Hospital, Karur, Tamilnadu, India
[2]Senior Resident, Department of Anaesthesiology, Government Kallakurichi Medical College, Tamilnadu, India

Received : 03/01/2026
Received in revised form : 04/02/2026
Accepted : 21/02/2026

Keywords:
Anesthesia, General; Anxiety; Child, Preschool; Conscious Sedation; Midazolam; Premedication, Anesthetic.

Corresponding Author:
Dr. R.Sathyaseelan,
Email: r.sathyaseelan@gmail.com

DOI: 10.47009/jamp.2026.8.1.198

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (1); 1036-1041

ABSTRACT

Background: Children undergoing surgery often develop perioperative anxiety, which affects sedation, parental separation, and procedural cooperation. Intranasal midazolam is widely used, but its behavioural and physiological effects in preschool children require evaluation. This study aimed to assess the effectiveness and safety of intranasal midazolam compared with intranasal normal saline on perioperative behaviour, haemodynamic parameters, recovery, and adverse effects in children aged three–six years. **Materials and Methods:** This prospective randomised study was conducted at Vinayaka Mission Kirupananda Variyar Medical College and Hospital between November 2013 and August 2015. Sixty children undergoing elective surgery were allocated to receive either intranasal midazolam (0.2 mg/kg) or intranasal normal saline (NS). Behavioural scores, vital parameters, recovery, and adverse effects were recorded. **Result:** Baseline age, sex, weight, and ASA status were comparable between the groups. Adequate sedation at 5 min was achieved in 25 children (83.3%) receiving midazolam versus 15 (50%) receiving saline ($p = 0.019$). Easy parental separation at 10 min occurred in 27 children (90%) in the midazolam group compared with four (13.3%) in the saline group ($p < 0.001$). A satisfactory response to venepuncture was observed in 21 (70%) and 7 (23.3%) children ($p < 0.001$). Mask placement was better tolerated, with no agitation in the midazolam group compared with 50% agitation in the saline group. Heart rate and respiratory rate were lower and more stable in the midazolam group, while systolic blood pressure remained comparable. The recovery scores at 10 min were similar in both groups. Mild nasal irritation or bad taste occurred in four children (13.3%) receiving midazolam, with no adverse effects in the saline group. **Conclusion:** Intranasal midazolam provides effective sedation, improves perioperative cooperation, and is safe without delaying recovery.

INTRODUCTION

Surgery and anaesthesia cause emotional stress in children.[1] This stress affects their behaviour during the perioperative period and may continue even after discharge from the hospital. Anxiety levels depend on age, parental anxiety, previous hospital experience, and the type of surgery.[2] Children between two and five years are more vulnerable because their understanding of medical procedures is limited. Preoperative anxiety activates sympathetic, parasympathetic, and endocrine responses, leading to increased heart rate, raised blood pressure, and increased cardiac excitability.[3]

In children who are not premedicated, anxiety is commonly seen as crying, clinging to parents, refusal to cooperate, and excessive movement.[4] These behaviours make venepuncture difficult, delay the induction of anaesthesia, and interfere with mask placement. After surgery, anxious children may develop sleep disturbances, feeding problems, enuresis, and fear of doctors and hospitals. These behaviours occur around induction and recovery and can be observed and assessed clinically.[3]

Methods to reduce anxiety include non-pharmacological and pharmacological approaches. Non-pharmacological methods include counselling, parental presence, and friendly interaction with the anaesthesiologist. These measures depend on the child's temperament and cooperation level. In preschool children, such methods alone often fail to achieve calm separation from parents and smooth induction, making drug premedication necessary.[5]

An ideal paediatric premedicament should be easy to administer, acceptable to the child, rapid in onset, and associated with minimal side effects. Many drugs

ISSN (O): 2687-5365; ISSN (P): 2753-6556

have been used for this purpose, including opioids, ketamine, barbiturates, alpha-2 agonists, and benzodiazepines.[6] Each of these agents has limitations, such as respiratory depression, agitation during induction, delayed recovery, or postoperative discomfort. Hence, no single drug fulfils all the requirements of an ideal premedicant.

Midazolam is an imidazobenzodiazepine with anxiolytic, sedative, amnestic, and anticonvulsant properties.[7] It is rapidly absorbed and has a short elimination half-life of approximately two hours. When administered at appropriate doses, it produces adequate sedation without significantly prolonging recovery. This making it suitable for short elective paediatric surgical procedures.

Different routes have been used to administer premedication in children. Intramuscular injections are painful and poorly accepted. The oral and rectal routes exhibit variable absorption and reduced bioavailability. Sublingual administration requires cooperation, which is difficult to achieve in young children. The intranasal route allows rapid absorption through the nasal mucosa and avoids needle use.[8] It also allows for predictable timing of sedation before separation, venepuncture, and induction.

Intranasal midazolam is commonly used, but there are limited structured data assessing its effects on multiple perioperative behaviours in preschool children. Many studies have assessed only sedation or included wide age groups.[8,9] There is a need to evaluate sedation, parental separation, venepuncture response, mask acceptance, recovery pattern, and side effects together. This study aimed to address this gap and evaluate the use of intranasal midazolam as a premedication in paediatric anaesthesia by measuring sedation level, ease of separation from parents, response to venepuncture, response to mask placement during induction, postoperative recovery characteristics, and adverse effects. We hypothesised that intranasal midazolam would provide superior sedation and perioperative cooperation without causing clinically significant haemodynamic instability or delayed recovery compared with normal saline.

MATERIALS AND METHODS

This prospective study was conducted among 60 paediatric patients undergoing elective surgical procedures at Vinayaka Mission Kirupananda Variyar Medical College and Hospital between November 2013 and August 2015. Institutional Ethics Committee approval was obtained prior to study initiation, and written informed consent was obtained from the parents or legal guardians of all participants.

Inclusion Criteria

Children aged 3–6 years of either sex with ASA physical status I or II scheduled for elective surgery were included.

Exclusion Criteria

Children with rhinopharyngitis, nasal pathology, drug allergy, sedative use, theophylline or H2 receptor antagonist therapy, prematurity, chronic illness, developmental delay, cardiopulmonary, hepatic, or renal disease, ASA grade III or higher, and those whose parents declined consent were excluded from the study.

Methods: The children were divided into two groups. Group S received intranasal normal saline at a dose of 0.04 ml/kg, and Group M received intranasal midazolam at a dose of 0.2 mg/kg using a preservative-free injectable preparation with a concentration of 5 mg/ml. The assigned drug was divided into two equal aliquots and administered into both nostrils using a 2 ml syringe without a needle, with the child seated on the parent's lap 15 min before the induction of anaesthesia.

Baseline heart rate, respiratory rate, oxygen saturation, and blood pressure were recorded before the drug administration. Sedation was assessed at 5 min using a five-point scale: agitated (1), alert (2), calm (3), drowsy (4), and asleep (5). At 10 min, the children were separated from their parents, and the response was graded as excellent (1), good (2), fair (3), or poor (4). The reaction to venepuncture was assessed as satisfactory (1) or unsatisfactory (2). At 15 min, general anaesthesia was induced, and the child's response to mask placement was recorded using a five-point induction score ranging from agitated (1) to asleep (5).

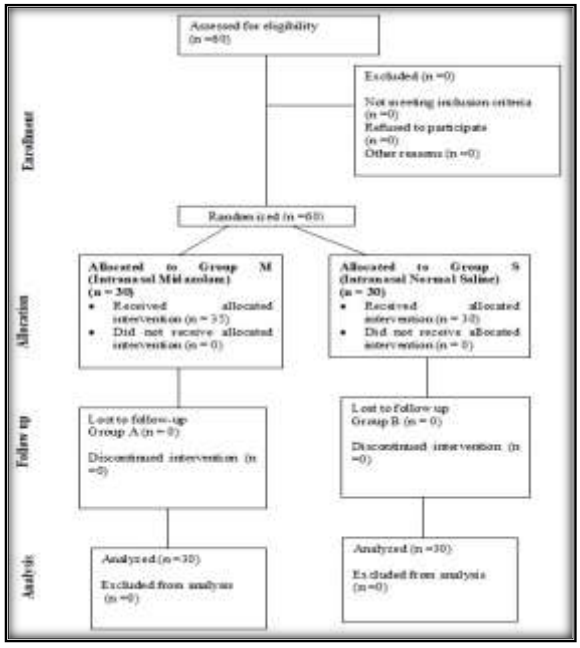

Figure 1: Consort diagram

Postoperative recovery was assessed at 10, 20, and 30 min using a structured recovery score based on colour, airway, respiration, level of consciousness, and movement, with each parameter scored from 0 to 2. Preoperative evaluation was performed on the day before surgery, including a general examination and routine investigations. On the day of surgery,

ISSN (O): 2687-5365; ISSN (P): 2753-6556

standard monitoring was applied, anaesthesia was induced and maintained according to surgical duration and body weight, and children were observed in the post-anaesthesia care unit until fully awake and met the discharge criteria. Adverse effects such as watering of the eyes, bad taste, nasal irritation, blurred vision, and nausea or vomiting were monitored for 24 h.

Statistical analysis: All data were entered and analysed using SPSS v29. Categorical variables were expressed as frequencies and percentages, and continuous variables were presented as means and standard deviations. Comparisons between groups for categorical variables were performed using Pearson's chi-square test. Continuous variables were compared using the independent samples t-test. Statistical significance was set at $p < 0.05$.

RESULTS

The mean age was 5.33 ± 0.96 years in the midazolam group and 4.93 ± 0.98 years in the normal saline group. Male children constituted 21 (70%) and 17 (56.7%) in the midazolam and normal saline groups, respectively. The mean body weight was 15.17 ± 3.72 kg in the midazolam group and 14.77 ± 4.02 kg in the normal saline group. Most children had ASA physical status I, accounting for 23 (76.7%) and 28 (93.3%) in the midazolam and normal saline groups, respectively [Table 1].

The midazolam group showed better perioperative behaviour than the normal saline group. Adequate sedation at 5 min was significantly higher in the midazolam group than in the saline group (83.3% vs. 50%, p = 0.019). Easy parental separation was achieved more with midazolam (90%) than with saline (13.3%, p < 0.001). A satisfactory venepuncture response was observed in 70% of children receiving midazolam compared with 23.3% receiving saline (p < 0.001) [Table 2].

Table 1: Baseline demographic and clinical characteristics

Variable		Midazolam group mean ± SD / N (%)	Normal saline group mean ± SD / N (%)	p value
Age (years)		5.33 ± 0.96 (3–6)	4.93 ± 0.98 (3–6)	0.116
Gender	Male	21 (70%)	17 (56.7%)	0.284
	Female	9 (30%)	13 (43.3%)	
Weight (kg) (range)		15.17 ± 3.72 (8–25)	14.77 ± 4.02 (7–20)	0.691
ASA physical status	ASA I	23 (76.7%)	28 (93.3%)	0.071
	ASA II	7 (23.3%)	2 (6.7%)	

Table 2: Perioperative behavioural outcomes between groups

Outcome	Category (Score)	Midazolam (n = 30) n (%)	Normal saline (n = 30) n (%)	p value
Sedation at 5 min	Agitated (1)	5 (16.7%)	15 (50%)	0.019
	Alert (2)	12 (40.0%)	12 (40%)	
	Calm (3)	10 (33.3%)	3 (10%)	
	Drowsy (4)	2 (6.7%)	0 (0%)	
	Asleep (5)	1 (3.3%)	0 (0%)	
Parental separation at 10 min	Excellent (1)	12 (40%)	0 (0%)	<0.001
	Good (2)	15 (50%)	4 (13.3%)	
	Fair (3)	2 (6.7%)	16 (53.3%)	
	Poor (4)	1 (3.3%)	10 (33.3%)	
Venepuncture response	Satisfactory (1)	21 (70%)	7 (23.3%)	<0.001
	Unsatisfactory (2)	9 (30%)	23 (76.7%)	

The midazolam group showed a more favourable response to mask placement, with no children exhibiting agitation, compared to 15 children (50%) in the normal saline group. Calm or drowsy behaviour was observed in 16 children (53.3%) in the midazolam group and 4 children (13.3%) in the normal saline group [Table 3].

Table 3: Response to mask placement at induction

Response to mask placement	Midazolam group (n = 30) n (%)	Normal saline group (n = 30) n (%)
Agitated	0	15 (50%)
Alert	11 (36.7%)	10 (33.3%)
Calm	13 (43.3%)	4 (13.3%)
Drowsy	3 (10%)	0
Asleep	3 (10%)	1 (3.3%)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

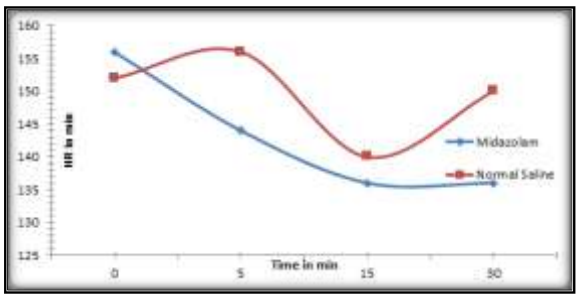

Figure 2: Changes in the heart rate after premedication

The heart rate decreased steadily in the midazolam group from 156 beats per minute at baseline to 136 beats per minute by 15 min and remained stable at 30 min, whereas in the normal saline group, the heart rate increased from 152 to 156 beats per minute at 5 min and remained higher at 30 min (150 beats per minute) [Figure 2].

Systolic blood pressure showed a gradual decrease in both groups, declining from 94 to 80 mmHg in the midazolam group vs. 100 to 84 mmHg in the normal saline group, with values remaining comparable between groups throughout the observation period [Figure 3].

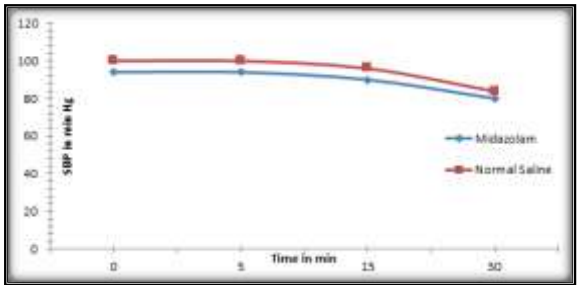

Figure 3: Changes in the SBP after premedication

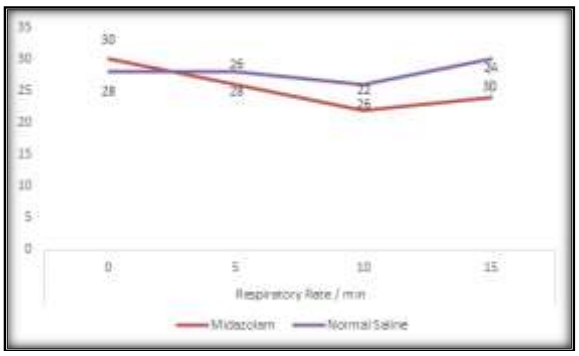

Figure 4: Changes in the respiratory rate after premedication

The respiratory rate decreased in the midazolam group from 30 to 22 breaths/min by 10 min, whereas in the normal saline group, it showed a smaller reduction from 28 to 26 breaths/min and increased to 30 breaths/min at 15 min [Figure 4].

At 10 min after anaesthesia, recovery scores were comparable between groups, with most children scoring 7 or 8 in both the midazolam (28 children, 93.3%) and normal saline (27 children, 90%) groups [Figure 5].

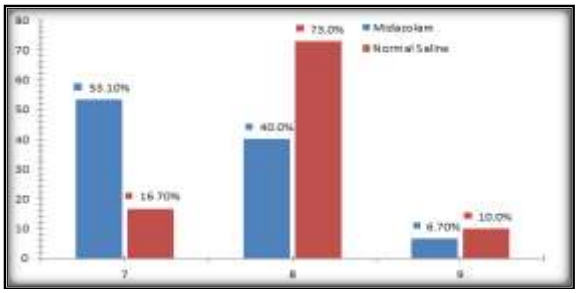

Figure 5: Post anaesthesia recovery score at 10 minutes

Adverse effects were minimal in the midazolam group, with nasopharyngeal irritation observed in two children (6.7%) and nasal congestion and bad taste noted in one child each (3.3%), while no adverse effects were reported in the normal saline group [Table 4].

Table 4: Adverse effects following intranasal premedication

Variable	Category	Midazolam group (n = 30)	Normal saline group (n = 30)
Adverse effects	Nasopharyngeal irritation (Yes/No)	2/28	0/30
	Nasal congestion (Yes/No)	1/29	0/30
	Bad taste (Yes/No)	1/29	0/30

DISCUSSION

This study showed that intranasal midazolam produced better preoperative sedation, easier separation from parents, improved cooperation during venepuncture and mask placement, stable heart rate and blood pressure, comparable recovery, and only mild and infrequent nasal side effects compared with normal saline. The rapid onset is attributed to direct systemic absorption through the highly vascular nasal mucosa, bypassing the first-pass metabolism.

The two groups were comparable at baseline with respect to age, sex distribution, body weight, and ASA physical status, with no significant differences observed. Similarly, Ramlan et al. found that the baseline characteristics were comparable between groups, with similar gender distribution (male 50.0% vs. 46.8%), overlapping age ranges (1–9 vs. 1–10 years), comparable body weight ranges (6–32 vs. 8–35 kg), and similar ASA I–II distribution.10 Because both groups had similar age, sex, weight, and ASA status, the groups were comparable at the start. This supports the notion that the differences observed later

ISSN (O): 2687-5365; ISSN (P): 2753-6556

were due to the drug effect and not because of baseline differences.

In our study, intranasal midazolam resulted in better preoperative sedation at 5 min, easier separation from parents at 10 min, and more satisfactory response to venepuncture, with fewer children showing distress or violent behaviour compared to the normal saline group. Musani et al. reported superior effects with intranasal midazolam, showing better sedation with total or minimal movement in 83.3% versus 70.0%, and easier parental separation with no crying in 76.7% compared to 36.7% in the saline group ($p = 0.0131$).[11] Mayel et al. reported that intranasal midazolam achieved better early sedation, with easy acceptance observed in 33 children (89.2%) compared to 14 children (36.9%) in the comparison group, and a significantly faster onset of sedation ($p \leq 0.001$).[12]

Chokshi et al. reported that children in the intranasal midazolam group showed better procedural cooperation, with eight of 25 children not requiring intravenous ketamine and others needing lower and less frequent supplementation compared to the placebo group. This indicated reduced distress during intravenous procedures.[13] These results showed consistent improvements in early sedation, parental separation, and procedural cooperation with intranasal midazolam and confirmed its reliable behavioural benefits across different paediatric settings.

In our study, mask placement during induction was better tolerated in the midazolam group, with no children showing agitation and a higher number indicating calm or drowsy behaviour. Rawat et al. reported that mask placement was better tolerated with intranasal midazolam, with no children showing agitation compared to 15 children (50%) in the normal saline group, and calm or drowsy behaviour observed in 16 children (53.3%) versus four children (13.3%).[14] These findings indicate the same pattern of improved mask acceptance and reduced agitation with intranasal administration of midazolam. This improvement was significant and confirmed better induction conditions with midazolam.

Our study showed that in the midazolam group, heart rate remained lower and stable, systolic blood pressure showed a comparable gradual decline in both groups, and respiratory rate decreased from 30 to 22 breaths per minute by 10 min, while the saline group showed greater respiratory variability. Similarly, Chokshi et al. reported greater haemodynamic stability with intranasal midazolam, with heart rate showing a significant reduction at 15 minutes compared with controls ($p < 0.05$), while systolic blood pressure remained stable and comparable between groups without clinically significant changes.[13] Rawat et al. reported that respiratory rate decreased more in the midazolam group, with values remaining within acceptable limits, while greater variability was observed in the normal saline group.[14] These findings show haemodynamic stability and controlled respiratory effects with intranasal midazolam, confirming its safety profile compared with normal saline during paediatric premedication. This stability likely indicates the anxiolytic and sympatholytic effects of midazolam, which attenuate stress responses.

In our study, adverse effects were minimal in the midazolam group, with only mild nasal irritation, congestion, or bad taste reported, and no adverse effects were observed in the normal saline group. Similarly, Mayel et al. reported that the adverse effects of intranasal midazolam were mild and infrequent, including restlessness in seven children (9.3%), delayed awakening in four (5.3%), nausea or hiccups in two (2.7%), and respiratory depression in one (1.3%), with no significant difference between groups ($p = 0.15$).[12] This supports our findings by showing that intranasal midazolam causes only mild, infrequent adverse effects without significant group differences, confirming its safety and tolerability in paediatric premedication. Intranasal administration provides a painless, simple, and well-accepted route that improves the perioperative workflow in children.

Limitations

The single-centre design and small sample size limit generalisability. Behavioural scores were observer-dependent. Blinding was not possible in this study. Long-term behavioural outcomes were not assessed. The dose-response relationships were not evaluated.

CONCLUSION

Intranasal midazolam produced effective sedation, improved perioperative cooperation, maintained haemodynamic stability, and did not delay recovery compared with normal saline. The adverse effects were mild, transient, and clinically insignificant. Intranasal midazolam is a safe and effective premedication option for paediatric anaesthesia. Future studies should include larger multicentre samples, assess optimal dosing, and evaluate long-term behavioural outcomes to strengthen clinical recommendations.

REFERENCES

1. Lethin M, Paluska MR, Petersen TR, Falcon R, Soneru C. Midazolam for anaesthetic premedication in children: Considerations and alternatives. Cureus 2023;15:e50309. https://doi.org/10.7759/cureus.50309.
2. Ahmed MI, Farrell MA, Parrish K, Karla A. Preoperative anxiety in children: risk factors and non-pharmacological management. Middle East J Anesthesiol 2011;21:153–64. https://pubmed.ncbi.nlm.nih.gov/22435267/.
3. Kain ZN, Mayes LC, Caldwell-Andrews AA, Karas DE, McClain BC. Preoperative anxiety, postoperative pain, and behavioral recovery in young children undergoing surgery. Pediatrics 2006;118:651–8. https://doi.org/10.1542/peds.2005-2920.
4. Fortier MA, Del Rosario AM, Martin SR, Kain ZN. Perioperative anxiety in children. Paediatr Anaesth 2010;20:318–22. https://doi.org/10.1111/j.1460-9592.2010.03263.x.
5. Kumar Kar S, Ganguly T. Preoperative anxiety in pediatric population: Anesthesiologist"s nightmare. Transl Biomed 2015;6. https://doi.org/10.21767/2172-0479.100030.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

6. Meredith JR, O'Keefe KP, Galwankar S. Pediatric procedural sedation and analgesia. J Emerg Trauma Shock 2008;1:88–96. https://doi.org/10.4103/0974-2700.43189.
7. Reddy SD, Reddy DS. Midazolam as an anticonvulsant antidote for organophosphate intoxication--A pharmacotherapeutic appraisal. Epilepsia 2015;56:813–21. https://doi.org/10.1111/epi.12989.
8. Bhakta P, Ghosh BR, Roy M, Mukherjee G. Evaluation of intranasal midazolam for preanaesthetic sedation in paediatric patients. Indian J Anaesth 2007;51(2):111–114. https://journals.lww.com/ijaweb/fulltext/2007/51020/evaluation_of_intranasal_midazolam_for.4.aspx?. (Accessed 27 January 2026)
9. Kalibatienė L, Kalibatas V, Macas A, Trepenaitis D. An evaluation of the effectiveness and safety of midazolam in children undergoing dental surgery. Medicina (Kaunas) 2015;51:180–6. https://doi.org/10.1016/j.medici.2015.04.001.
10. Ramlan AAW, Mahri I, Firdaus R, Sugiarto A. Comparison of efficacy of premedication between dexmedetomidine and midazolam intranasal for the prevention of emergence delirium in children undergoing ophthalmic surgery. Turk J Anaesthesiol Reanim 2021;49:439–44. https://doi.org/10.5152/TJAR.2021.1305.
11. Musani I, Bhure S, Choubey S, Musani SI, Surve S. Intranasal Midazolam Premedication for Anxiolysis in Children Reluctant to Receive Nitrous Oxide Sedation via Nasal Hood: An In Vivo Randomized Control Trial. Int J Clin Pediatr Dent 2021;14:S138–42. https://doi.org/10.5005/jp-journals-10005-2092.
12. Mayel M, Nejad MA, Khabaz MS, Bazrafshani MS, Mohajeri E. Intranasal midazolam sedation as an effective sedation route in pediatric patients for radiologic imaging in the emergency ward: A single-blind randomized trial. Turk J Emerg Med 2020;20:168–74. https://doi.org/10.4103/2452-2473.297461.
13. Chokshi AA, Patel VR, Chauhan PR, Patel DJ, Chadha IA, Ramani MN. Evaluation of intranasal Midazolam spray as a sedative in pediatric patients for radiological imaging procedures. Anesth Essays Res 2013;7:189–93. https://doi.org/10.4103/0259-1162.118954
14. Rawat HS, Saraf RS, Sunil Kumar V. Effects of intranasal midazolam as premedication in paediatric anaesthesia: A clinical study. Pediatr Anesth Crit Care J 2014;2(2):112–121. https://doi.org/10.14587/paccj.2014.23.

ISSN (O): 2687-5365; ISSN (P): 2753-6556