ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 12 | December - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF CLINICAL OUTCOME OF INTRANASAL DEXMEDETOMIDINE VERSUS INTRANASAL MIDAZOLAM AS PREMEDICATION IN CHILDREN UNDERGOING MRI: A RANDOMIZED DOUBLE BLIND STUDY

Anaesthesiology

Dr. Jaya Lalwani MD, FICA Professor Department Of Anaesthesiology And Pain Medicine, Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital, Raipur C.G., India

Dr. Pratibha Jain Shah MD, FICA, FIPM Professor And Head Of The Department Department Of Anaesthesiology And Pain Management, Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital, Raipur (C.G.), India

Dr. Manjulata Tandan MD Associate Professor Department Of Anaesthesiology And Pain Management Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital, Raipur (C.G.), India

Dr. Anamika Jain 3rd Year Postgraduate Resident Department Of Anaesthesiology And Pain Medicine Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital, Raipur (C.G.), India

ABSTRACT

Background: Providing anaesthesia to children undergoing MRI is challenging. Adequate premedication administered noninvasively, would make the process smoother. **Material And Methods:** Hundred paediatric patients between 3-8 years scheduled for MRI under sedation were divided into two groups of 50 each. Group I received Intranasal Midazolam (0.2 mg/kg) and Group II received Intranasal Dexmedetomidine (1 mcg/kg). Patients were observed for ease of parental separation (primary outcome), onset & level of sedation as well as hemodynamic parameters and occurrence of any side effects. **Results:** Intranasal midazolam had early onset than intranasal dexmedetomidine (15.72±11.45 mins vs 19.42±7.93 mins). The sedation score at induction in Group I was 4.06±1 and in group II it was 3.0 ±1.28 ($p<0.001$, significant). The mean difference in parental separation anxiety score was highly significant in group II as compared group I. None of the patients in either group had any significant adverse effects. **Conclusion:** Intranasal dexmedetomidine is a more effective option for paediatric premedication during MRI than intranasal midazolam because it provided successful parental separation, improved hemodynamic stability and higher sedation levels with minimal side effects.

KEYWORDS

MRI, Midazolam, Dexmedetomidine, Sedation, Parental separation anxiety.

INTRODUCTION:

Children undergoing MRI procedures frequently require sedation to allay preoperative anxiety and for ensuring a smooth and effective diagnostic experience.[1] Anxiety in children may be due to fear of separation from parents, unfamiliar hospital environments, and concerns about procedures like injections or being in the MRI machine itself. This anxiety not only impacts the child's emotional well-being but also presents challenges for medical staff during anesthesia induction and procedural completion.[2]

Nonpharmacological methods like pre-admission visits, showing informative videos, and establishing rapport with healthcare providers can help mitigate anxiety to some extent.[3] However, when these methods are insufficient, pharmacological intervention becomes necessary. The preanesthetic medication among children should ideally be rapid onset, effective anxiolysis with minimal sedation, be well-tolerated without significant side effects, ensure rapid recovery, and having acceptable and nontraumatic route of administration in order to reduce stress to the child.[4] Intranasal administration bypasses the discomfort of intravenous cannulation and provides rapid absorption into the bloodstream, making it an attractive route for paediatric sedation.[5]

Midazolam, a benzodiazepine, is commonly used for its anxiolytic properties, sedation and relatively fast onset and has a short duration of effect when administered intranasally.[6] On the other hand, dexmedetomidine, an α2-agonist, offers sedation and anxiolysis without respiratory depression, reduces emergence delirium and post op negative behaviour such as aggression. It is odourless and does not cause mucosal irritation making it suitable for intranasal use in children.[7]

Hence considering all the aspects of pre anaesthetic medication among paediatric patients, the present study was planned to compare the effectiveness of intranasal Dexmedetomidine with intranasal Midazolam as preanesthetic medication in children undergoing MRI in terms of ease of parental separation (primary outcome), onset & level of sedation as well as hemodynamic parameters and occurrence of any side effects.

MATERIAL & METHODS:

This prospective randomized double-blind study was conducted in Department of Anaesthesiology and Pain Medicine over a period of one year, after approval from Institutional Scientific Committee and Institutional Ethics Committee. This study was registered with Clinical Trials Registry of India (CTRI NO- CTRI/2024/05/066613). After obtaining informed and written consent from children's parents or guardian, a total of 100 patients of ASA I-II in between age group 3 to 8 years scheduled for MRI under sedation were included in the study. Patients with congenital heart disease, upper respiratory tract infection, patients on antipsychotics, anticonvulsants, any sedative drugs were excluded from the study.

The participants were divided by computer generated random sequence number into two groups of 50 each which was kept in sealed envelopes. Group I (received Intranasal Midazolam (0.2 mg/kg) and Group II (received Intranasal Dexmedetomidine (1 mcg/kg) 30 mins prior to scan. The attending anaesthesiologist was not present in the preoperative room at the time of drug administration, and the drug administrations were performed by a different anaesthesiologist.

All the parents were explained in detail about the benefits of intranasal premedication and the possible side effects. Preanesthetic assessment included a quick medical history, general and systemic examination; airway examination; and investigations such as complete hemogram and renal function tests. On the day of MRI, all the patients were kept nil by mouth for 4 hrs. Baseline saturation (SpO_2) and heart rate (HR) monitored using a pulse oximeter throughout the procedure.

Intranasal midazolam is available as preformed spray while intranasal dexmedetomidine was prepared according to the patient's weight and calculated dose of the drug was diluted to the total volume of 1ml.

The time of drug administration was noted, and the observer recorded baseline SpO_2 and HR. The monitoring of vital parameters and sedation level was done at 5-min intervals till the end of procedure. Anxiety at parental separation was assessed with a 4-point Parental Separation Anxiety Scale (PSAS). The sedation level was assessed using the Observer's Assessment of Alertness /Sedation (OAA/S) scale, a 6-point sedation scale.

Parent Separation Anxiety Score

1- Calm and Cooperative
2- Anxious but reassurable

3- Anxious and not reassurable
4- Crying, or resisting

Table 1: Observer's Assessment of Alertness /Sedation (OAA/S) scale

SCORE	RESPONSIVENESS
6	Agitated
5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Does not respond to mild prodding or shaking
0	Does not respond to deep stimulus

The onset of sedation was defined as an increase in the sedation level compared with the baseline minus 1 (change in OAA/S score from 6 to 5).

Within 15 min of cannulation the patients underwent MRI. At the time of induction the OAA/S score and PSAS was noted. OAA/S of 1 and 4 and PSAS score less than 2 was considered satisfactory.

At the end of the MRI, all the kids were shifted to the recovery room and their vitals were recorded at post operative room till complete recovery. Time for recovery was noted. Parents were advised to start oral feeds once the child was fully awake and active.

Statistical Analysis:
The sample size has been derived by taking reference from the study conducted by **Gupta A et al (2017)**[11]. Sample size was calculated by taking into considerations the mean difference of parental separation anxiety score in the two groups, which was the primary objective of our study.

The data was collected and analysed by using IBM SPSS (Statistical Package for Social Sciences) statistical version 21. Parametric data was analyzed using the unpaired t-test. Repeated measurements data was analyzed using the paired t-test, and binary data were analyzed using Chi-squared test. $P < 0.05$ was considered statistically significant.

RESULTS:
From a total of 110 patients screened, 100 patients were enrolled, randomized and allocated into two groups. (Figure 1) The demographic profile (age, sex, weight, height, ASA grade) and baseline parameters in both the groups were statistically comparable. (Table 2)

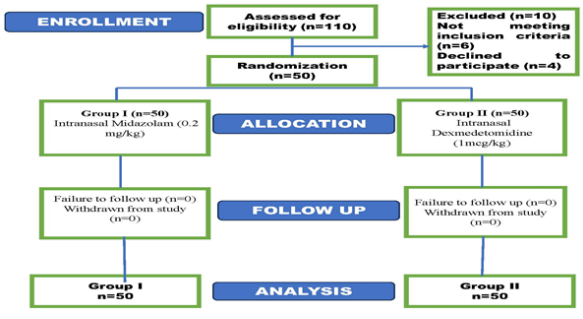

Figure 1: Consort Diagram

Table 2: Demographic profile

Variable	Group I	Group II	Statistical analysis
Mean age (years)	5.33±1.85	5.05±1.49	NS
Sex (M: F)	54:46	60:40	NS
ASA Grade (I/II)	100:0	100:0	NS
Mean weight (kg)	14.18±3.41	13.78±3.02	NS
Mean height (cm)	100.78±9.81	98.62±8.03	NS

Table 3: Onset of Sedation and Sedation Score at Induction

Variable	Group I	Group II
Onset of sedation (mins)	15.72±11.45	19.42±7.93
Sedation score at Induction	4.06±1	3±1.28

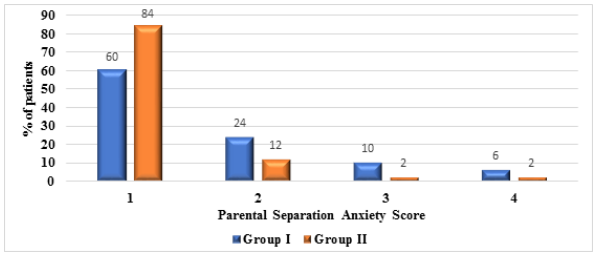

Figure 2: Parental Separation Anxiety Score

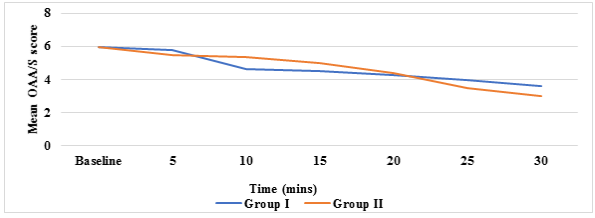

Figure -3: Sedation Score (OAA/S Score)

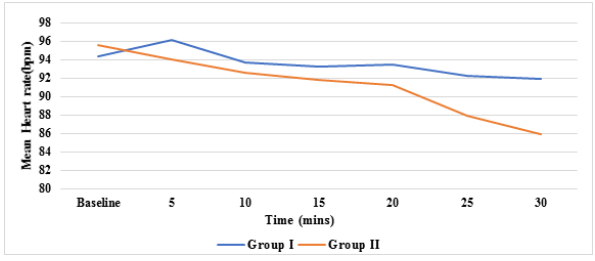

Figure -4: Mean Heart Rate (bpm)

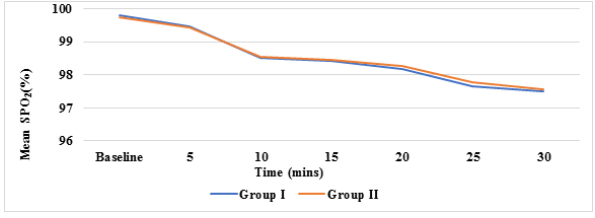

Figure -5: Mean Spo_2

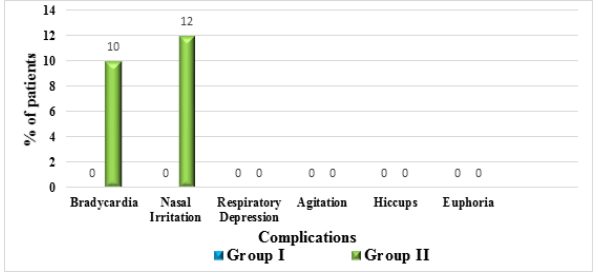

Figure 6: Complications

DISCUSSION:
Separation anxiety is most commonly experienced in children between 1 and 5 years of age and can be reduced effectively by pharmacological interventions. Various routes of premedication have been tried like, oral, intravenous (IV), intramuscular (IM), rectal, and transmucosal. Each drug and route of administration has its own disadvantages. The oral route has low bioavailability, IM and IV routes are invasive and painful, and the rectal route is not convenient.[2,5] Transmucosal routes like IN and sublingual have shown better compliance. They are more rapid and effective routes of drug administration because of their ability to bypass first-pass metabolism and rich mucosal vascularization. Intranasal administration of drugs can cause nasal irritation, sneezing, and coughing in some children, which can be prevented by using less volume of an undiluted solution of the drug.[8] Hence, we administered midazolam intranasally, dexmedetomidine is available only in an intravenous formulation; intravenous preparation has been used through oral, transmucosal, and intranasal routes. Dexmedetomidine has been extensively studied intranasally in both children and adults. Previous studies[9,10] have shown that intranasal

dexmedetomidine produces significant sedation in healthy adults and in children aged between 2 and 12 years When a large volume of drug is instilled into the nose, there is a high possibility of entering the drug into the pharynx producing coughing and sneezing. Keeping this in mind, we decided to administer 0.5 mL of study drug solution (total volume 1ml) to each nostril.

Midazolam acts on GABA- mimetic system and decreases the respiratory drive in a dose-dependent manner. The dose of midazolam administered in our study was not high enough to cause the decrease in respiratory drive.[2,7,11,12,13] The arterial oxygen saturation was well maintained throughout the perioperative observation period. (Figure 5)

Dexmedetomidine acts on central α2 receptors located at the presynaptic terminal where they mainly cause inhibition of release of noradrenaline. The site of action of dexmedetomidine is in locus coeruleus where it causes EEG activity similar to normal sleep. This results in anxiolytic effects, sedation and analgesia without excessive drowsiness.[4,6,7,13,14,15]

The intranasal dose of dexmedetomidine (1mcg/kg) was decided based on previous studies done Yuen VM et al[16], Talon MD et al[10] while standard intranasal dose of midazolam 0.2mg/kg was taken.

In this study, a statistically significant difference in the time of onset of sedation between the two groups was seen with early onset in midazolam. (Table 3) Previous studies[16,17] have shown that the dose of intranasal dexmedetomidine of 1 µg/kilogram has been shown to have a time of onset of sedation approximately 25 minutes and median duration of approximately 85 minutes.

Mean sedation score were lower in group II (3.0 ±1.28 Vs 4.06±1) which was statistically significant (P=0.003) which indicates that dexmedetomidine produces better sedation than midazolam. (Figure 3) **Sundaram et al[18]** have reported the peak effect of intranasal midazolam is 10-15 minutes and duration of action is 30-60 minutes. The bioavailability of intranasal dexmedetomidine was found to be higher compared to bioavailability after oral and buccal administration but lower than those after intramuscular and intravenous administration.[8,19,20] The median absolute bioavailability of intranasally administered dexmedetomidine was reported to be 83.8% (69.5%-98.1%) in children.[2] The intranasal delivery can be accomplished by either atomizer or drops and both techniques have been found to be equally effective leading to increasing its use as a paediatric premedication and procedural sedation. Previous studies[4,5,15] have reported that intranasal dexmedetomidine administration is easy, convenient and well tolerated whereas for nebulization cooperation is required especially in younger children as demonstrated by better medication acceptance score in patients receiving intranasal dexmedetomidine.

Dexmedetomidine decreases sympathetic outflow thereby decreasing the circulating catecholamine levels and increases cardiac vagal activity.[11,13,15,18] Our study showed that intranasal dexmedetomidine causes a significant reduction in the heart rate as compared to intranasal midazolam. However the decrease in heart rate was not clinically significant and bradycardia was noted and managed with inj Atropine 0.6 mg. (Figure 4)

Nasal irritation was observed in 12 % of patients in group II compared to group I and this difference is statistically significant. **Darshana D. Patel et al[5]** found that 28% of children in group M suffered nasal irritation at the time of intranasal administration. (Figure 6) No other side effects noted.

Acknowledgement of limitations addresses the gaps in literature to pave the way for future research.

Those children who were premedicated only were recruited and a control group was not included in our study. A relatively subjective sedation and parental separation scale was used because it was simple to use, although these scales are not validated and future studies, perhaps using the University of Michigan Sedation Score, could be undertaken. Age stratification is necessary as a relatively deeper sedation level are required in younger children to facilitate smooth anaesthetic induction however this may not be necessary in older children. Atomisers are available for midazolam only but it is not available for dexmedetomidine. It would have been easier to administer dexmedetomidine in Atomised/Spray form (if available) than the IV preparation. Sprayed or atomized intranasal medication delivery may lead to more bioavailability and higher satisfaction with the use of intranasal medications in children. It might have been possible to note greater sedative effects in the intranasal dexmedetomidine group if we had waited longer. But on waiting longer, the effect of midazolam would have been weaned off. We did not measure parents' and radiologist satisfaction scores.

CONCLUSION

Both intranasal dexmedetomidine and midazolam can be used safely for pediatric premedication during MRI. However, intranasal dexmedetomidine (1 µg/kg) is a more effective option than intranasal midazolam (0.2 mg/kg) because it provided successful parental separation, improved hemodynamic stability and higher sedation levels with minimal side effects.

REFERENCES

1. Pareek A, Gupta V, Mantan K, Sharma A. A Comparative Evaluation of Intranasal Dexmedetomidine and Intranasal Midazolam for Premedication in Children. Journal of Medical Science and Clinical Research. 2019;7(4): 938-946
2. Arun N, Choudhary A, Kumar M. Comparative Study of Intranasal Dexmedetomidine Versus Intranasal Ketamine as Premedicant in Children. Cureus. 2022;14(7)
3. Chatrath V, Kumar R, Sachdeva U, Thakur M. Intranasal Fentanyl, Midazolam and Dexmedetomidine as Premedication in Pediatric Patients. Anesth Essays Res. 2018;12(3):748-753.
4. Verma S; Bhatia PK; Sharma V; Mohammed S; Saran A. Comparison of intranasal and nebulized dexmedetomidine for premedication in pediatric patients: A non-inferiority randomized controlled trial. Journal of Anesthesiology Clinical Pharmacology 2022 38(4):617-623.
5. Darshna D. Patel L, M.R.Upadhyay. Pre anaesthetic medication in children A comparison of intranasal dexmedetomidine versus intranasal midazolam. The Journal of Medical Reseach. 2015;1(2):59-63
6. Davis J, Rijal T, Rai A. Intranasal dexmedetomidine vs intranasal midazolam for premedication in paediatric patients undergoing surgery under general anaesthesia. Indian J Clin Anaesth. 2018;5(3):315-320
7. Nagarajan G, Sekar P, Srinivasan NK, Kumar P, Kumar H. A comparative study of intranasal dexmedetomidine and intranasal midazolam for premedication - A prospective randomized double-blind study in children posted for tonsillectomy. Indian J Clin Anaesth 2022;9(1):66-70
8. Diwan G, Bharti AK, Rastogi K, Gupta PK. Comparison of Intranasal Dexmedetomidine and Midazolam as Premedication in Pediatric Surgical Patients: A Prospective, Randomized Double-Blind Study. Anesth Essays Res. 2020;14(3):384-389.
9. Lirola T, Vilo S, Manner T, et al. Bioavailability of dexmedetomidine after intranasal administration. European Journal of Clinical Pharmacology 2011;67(8):825-31.
10. Talon MD, Woodson LC, Sherwood ER, Aarsland A, Mcrae L, Benham T. Intranasal dexmedetomidine premedication is comparable with midazolam in burn children undergoing reconstructive surgery. J Burn Care Res. 2009;30(4):599–605
11. Gupta A, Dalvi NP, Tendolkar BA. Comparison between intranasal dexmedetomidine and intranasal midazolam as premedication for brain magnetic resonance imaging in pediatric patients: a prospective randomized double blind trial. J Anaesthesiol Clin Pharmacol 2017; 33: 236-240.
12. Gyanesh P, Haldar R, Srivastava D, Agrawal PM, Tiwari AK, Singh PK. Comparison between intranasal dexmedetomidine and intranasal ketamine as premedication for procedural sedation in children undergoing MRI: a double blind, randomized, placebo-controlled trial. J Anesth 2014; 28: 12-18
13. Ibrahim M. A prospective, randomized, double blinded comparison of intranasal dexmedetomodine vs intranasal ketamine in combination with intravenous midazolam for procedural sedation in school aged children undergoing MRI. Anesth Essays Res. 2014;8(2):179-86.
14. Kavya Kg, N P. Intranasal Dexmedetomidine with Intravenous Midazolam: A Safe and Effective Alternative in the Paediatric MRI Sedation. Cureus. 2023;15(10).
15. Khatavkar SS, Bakhshi RG. Comparison of nasal midazolam with ketamine versus nasal midazolam as a premedication in children. Saudi J Anaesth 2014; 8: 17-21.
16. Yuen VM, Hui TW, Irwin MG, et al. A randomised comparison of two intranasal dexmedetomidine doses for premedication in children. Anaesthesia. 2012 ;67:1210–6.
17. Singla D, Chaudhary G, Dureja J, Mangla M. Comparison of dexmedetomidine versus midazolam for intranasal premedication in children posted for elective surgery: a double-blind, randomised study. Southern African Journal of Anaesthesia and Analgesia. 2015;21(6):154-7.
18. Sundaram AL, Mathian VM. A comparative evaluation of intranasal dexmedetomidine and intranasal midazolam for premedication in children: A double blind RCT. JIDA 2011; 6:777-81.
19. Feld LH, Negus JB, White PF. Oral midazolam preanesthetic medication in pediatric outpatients. Anesthesiology 1990; 73: 831-34.
20. FitzSimons J, Bonanno LS, Pierce S, Badeaux J. Effectiveness of preoperative intranasal dexmedetomidine, compared with oral midazolam, for the prevention of emergence delirium in the pediatric patient undergoing general anesthesia: a systematic review. JBI Database System Rev Implement Rep 2017;15:1934-51.
21. Sivakumar G, Anitha K, Elango P, et al. Comparative study to evaluate the effects of intranasal dexmedetomidine versus midazolam as a premedication agent in children undergoing elective surgery. J. Evolution Med. Dent. Sci. 2017;6(35):2893-2897.