

**INTRANASAL DEXMEDITOMIDINE AND INTRANASAL MIDAZOLAM AS
PREMEDICATION IN PEDIATRIC SURGICAL PATIENTS****Dr. Kharat Mohammed Bhat¹, Dr. Samiksha Khanooja^{2*} and Dr. Irshad Yousuf**¹MBBS, MD, Professor, Head of Department of Anaesthesiology, HIMSR, Jamia Hamdard.^{2*}MBBS, MD, Assistant Professor, Department of Anaesthesiology, HIMSR, Jamia Hamdard.³MBBS, DNB, Assistant Professor, Department of Anaesthesiology, HIMSR, Jamia Hamdard.***Corresponding Author: Dr. Samiksha Khanooja**

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ABSTRACT

Background: Many routes and drugs have been studied for premedication in pediatric surgical patients. Intranasal being one of them. Ease of administration makes it one of the preferred routes. **Objectives:** To evaluate the safety and efficacy of midazolam, and dexmedetomidine as intranasal premedication in paediatric surgical patients -to study their hemodynamics and respiratory consequences and post anaesthesia recovery in paediatric patients. **Method:** It was a prospective, randomized double blind study. 50 children aged 1 to 8 years were studied in each group (midazolam and dexmedetomidine). **Results:** The intranasal midazolam 0.2 mg/kg and dexmedetomidine 1.5 µg/kg produced effective and significant sedation which was seen at 30 min in dexmedetomidine group and at 15 min in midazolam groups and this change was maintained in all groups at 45 min and at the time of induction of anesthesia. **In conclusion Conclusion:** we found that midazolam, and dexmedetomidine produced adequate sedation with little side effects. We prefer to use midazolam due its efficacy and safety as well as availability and its low price in comparison to dexmedetomidine. Overall recovery profile was better in the patients who received dexmedetomidine.

KEYWORDS: Intranasal, dexmedetomidine, midazolam, premedication, pediatric.**INTRODUCTION**

Premedication includes the drugs administered before general anaesthesia to decrease the anxiety and to obtain smoother induction, maintenance and emergence from anesthesia. The term "premedication" was first used by McMahan in 1920.

The preoperative period is a stressful event for the majority of individuals undergoing surgery, especially in the pediatric patient.^[1]

Adequate premedication not only calms the child preoperatively but also prevents the postoperative pain, provides prophylaxis against PONV, decreases gastric secretions prevents reflux in response to surgical stimuli and decreases the anesthetic requirement for the surgical procedure.^[2] However the primary aim of premedication in pediatric patients is anxiolysis.^[3] It has been reported that there are correlations between heart rate, blood pressure and behavioral ratings of anxiety.^[4]

Many agents like benzodiazapines, ketamine, opioids, alpha 2 agonists etc. are used as premedicants. The ideal agent should have rapid onset, predictable duration and rapid recovery.

In our study we studied 2 drugs in pediatric patients via intranasal route. Midazolam and dexmedetomidine.

Midazolam

The advantages of midazolam include rapid onset, effective sedation, anterograde amnesia, anxiolysis and a reduction in postoperative vomiting.^[5,6] It has been used for preoperative sedation by intramuscular, rectal, oral, sublingual routes and intranasal routes, but each has its own advantages and disadvantages. Owing to high mucosal vascularity, intranasal route offers rapid and virtually complete absorption within 1-2 hours into systemic circulation.^[7] One relative disadvantage of the nasal administration is its dependence on the nasal mucous membrane for drug absorption, thereby permitting the common cold to be a contraindication for its use.

Dexmedetomidine

Its an alpha 2 agonist. It has become increasingly popular for premedication in children because it does not cause respiratory depression and can be administered via different routes including intranasal. However, high doses of Dexmedetomidine have been reported to result in bradycardia and hemodynamic fluctuation in pediatric patients.^[8]

Aim This study was planned -to evaluate the safety and efficacy of midazolam, and dexmedetomidine as intranasal premedication in paediatric surgical patients - to study their hemodynamics and respiratory consequences and post anaesthesia recovery in paediatric patients.

MATERIALS AND METHODS

This study is a prospective, randomized double blind study, was performed in department of Anesthesiology and Critical Care at Hamdard Institute of Medical Science, Delhi. Children aged 1-8 years, ASA1,2, scheduled for elective surgery were enrolled in the study. A written informed consent was obtained from the parents or legal guardians of all the patients. Children with chronic pain, central nervous system disorders,

known allergy to the study drugs were excluded from the study.

Children were randomly allocated to one of two groups;
1. Group M: children receiving intranasal midazolam (0.2mg/kg) (n=50), one hour prior to induction.
2. Group D: children receiving intranasal dexmedetomidine (2ug/kg) (n=50), one hour prior to induction.

In preoperative room, baseline NIBP, spO₂ and heart rate was recorded and then after 15 min interval of intranasal administration of study drugs until transfer to the operating theatre. Sedation scores was assessed every 15 mins for one hour (at 0, 15, 30 and 45 min) by a blinded observer using a four-point sedation scale (Table 1).

Sedation score

CRITERION	SCORE
Alert, awake	1
Drowsy, sleepy, lethargic	2
Asleep but responds to mild prodding or shaking	3
Asleep and does not respond to mild prodding or shaking	4

After connecting multichannel monitor, anaesthesia was induced with propofol 2mg/kg, sevoflurane and atracurium 0.5mg/kg. It was maintained with O₂: N₂O =1:1 with sevoflurane. At the end of surgery reversal was achieved by neostigmine 0.05mg/kg and glycopyrolate 10ugm/kg bwt. After extubation, patient was, shifted to recovery and assessed by post anaesthesia recovery score.

Stage 1 Awake; does not feel sleepy and initiates conversation.

Stage2 Awake; but feel sleepy.

Stage3 Asleep; responds to both verbal and painful stimuli.

Stage4 Asleep; responds to painful stimuli only.

Stage5 Asleep; does not respond to painful stimuli.

Postoperative analgesia

Pain was assessed at arrival and every 15 min in the recovery room using the observer pain scale as follows:

Criterion	Score
A. laughing; euphoria	1
B. happy, contented	2
C. calm or asleep	3
D. crying, grimacing, restless	4

Physiological parameters

BP, HR, RR and SpO₂ were recorded every 15 min during postoperative observation period. Occurance of hypotension and bradycardia also recorded.

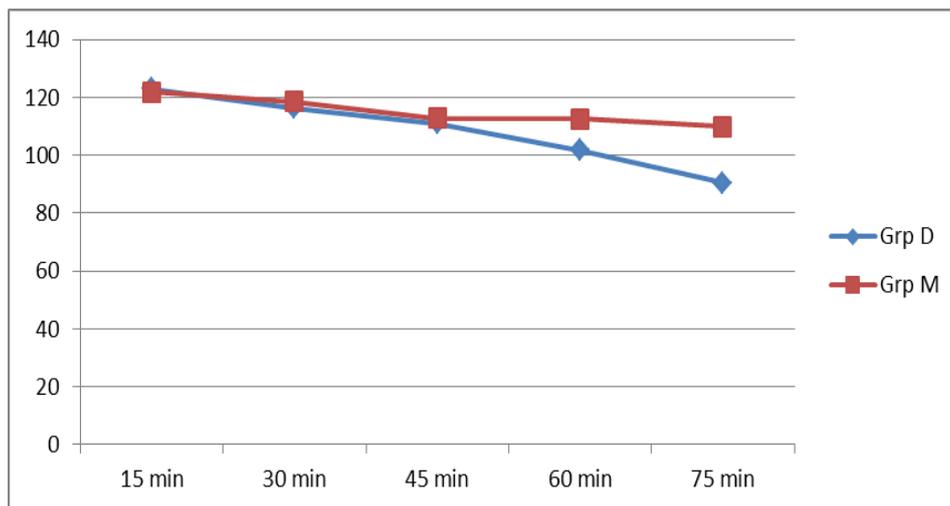
The patients were discharged from the recovery room when all of the following criteria met: fully awake, hemodynamic stability, absence of pain, bleeding, nausea and vomiting.

Statistical Analysis

The study patient were randomized into two groups using a computer generated table of random numbers. Data was analysed using the student t-test, Mann Whitney U-test and repeated measurement analysis to detect differences between two groups. A P-value of <0.05 was considered statically significant.

Age, gender, weight distribution among various groups was statistically insignificant(p value>0.05).

Heart rate at 45 and 60 min after giving study drugs was lower in dexmedetomidine group as compared to midazolam with a p value of 0.024 and < 0.001 which was found to statistically significant.



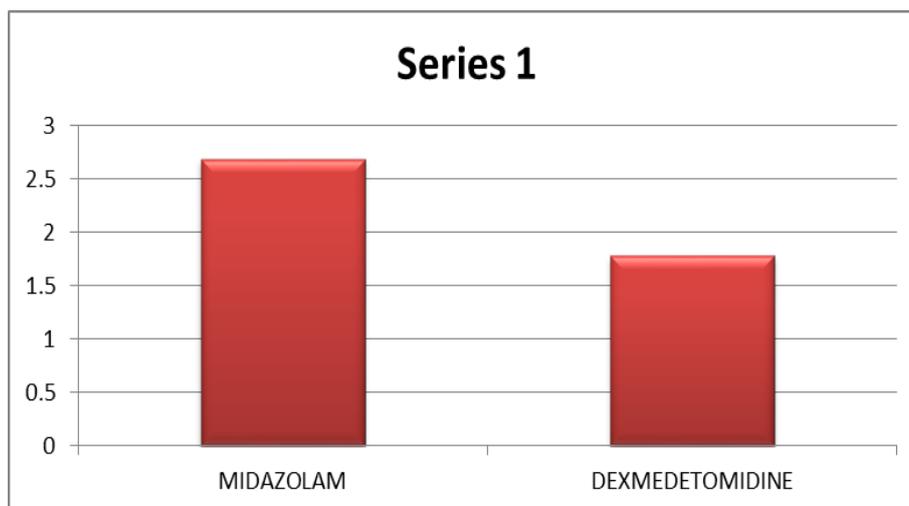
-Overall mean heart rate was lower in dexmedetomidine group as compared to midazolam group with p value of < 0.001 which was statistically significant.

-Overall mean arterial pressure was lower in dexmedetomidine group with p value<0.001 which was statistically significant.

Comparison of respiratory rate		
Time Interval	P-value	
	M vs D	
0 Min	0.975	
15 Min	0.559	
30 Min	0.013*	
45 Min	<0.001*	
60 Min	<0.001*	

Overall sedation score at 30min, 45min and 60min was better in dexmedetomidine group as compared to midazolam (p value < 0.001).

Comparison of postoperative SPO2 at 0 min, 15min, 30min, 45min and 60 min between two study drugs was statistically insignificant (p value < 0.05).



This bar diagram shows postoperative recovery profile between *midazolam* and *dexmedetomidine* groups.

Comparison of postoperative PONV was done. In midazolam group 4 children had PONV, in dexmedetomidine only 1 child experienced PONV, which was statistically significant with p value of 0.002 (p value < 0.05).

DISCUSSION

One of the challenges for anesthesiologists is to minimize distress for children in the operating room environment. All pediatric patients should be premedicated to decrease preoperative anxiety, allow smooth induction and prevent postoperative psychological and behavioral changes.^[9,10] Our study

evaluated the efficacy of intranasal midazolam and dexmedetomidine as premedicant in pediatric patient.

The intranasal midazolam 0.2 mg/kg and dexmedetomidine 1.5 µg/kg produced effective and significant sedation which was seen at 30 min in dexmedetomidine group and at 15 min in midazolam groups and this change was maintained in all groups at 45 min and at the time of induction of anesthesia and these results were comparable with the results of Naill *et al.*^[11] Malionovsky *et al.*^[12] found that intranasal midazolam 0.2 mg/kg produced more rapid sedation than when administered through other routes.

Over the past five years, dexmedetomidine has become a common option for providing IV sedation and analgesia in children. It is increasingly being studied as an alternative to standard agents for intranasal administration.

Our study showed that there was statistically significant change in heart rate, respiratory rate and systolic blood pressure in each group after 30 min and this may be due to increased level of sedation which is in agreement with Remadevi *et al.*^[13] Munro *et al.*^[14] reported that the reduction of blood pressure and heart rate were <20% of baseline in children who were sedated with initial dose of 1 µg/kg IV dexmedetomidine.

In conclusion we found that midazolam and dexmedetomidine produced adequate sedation with little side effects. We prefer to use midazolam due its efficacy and safety as well as availability and its low price in comparison to dexmedetomidine. Despite having a number of beneficial effects, midazolam is not an ideal premedicant as it has untoward side effects such as restlessness, paradoxical reactions, cognitive impairment, amnesia and respiratory depression.^[15,16] α₂-agonist like dexmedetomidine with both sedative and analgesic properties render it potentially useful for anesthesia premedication. Sedation produced by dexmedetomidine differs from other sedatives as patients may easily arouse and cooperative.

Overall recovery profile was better in the patients who received dexmedetomidine and the difference was found to be statistically significant between three study groups with p value of < 0.05.

Comparison of post operative pain score between midazolam and dexmedetomidine group was found statistically significant (p value<0.05). Our results are consistent with a study by Schmidt *et al.*^[17] (who compared transmucosal dexmedetomidine to oral midazolam and oral Clonidine as premedication in school children.

➤ Limitation

One major drawback for use of dexmedetomidine as a sedative premedicant is its slow onset of action.

Intranasal dexmedetomidine needs to be administered at least 45 min prior to the induction to achieve optimum sedation whereas satisfactory sedation be achieved 15min after ingestion of intranasal midazolam.

In this study, the premedication period was 60min and all children were transferred to OR at one hour as per study protocol, however if a long premedication period had been allowed, possibly more subjects could have attained satisfactory sedation at separation from parents and at induction of anesthesia. The sedation produced by dexmedetomidine differs from other sedatives as patients may easily arouse and cooperative.

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