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Original Research Article

Safety and Efficacy of Intranasal Dexmedetomidine Compared to Midazolam in Pediatric Surgical Patients

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Abstract:

Introduction: Preoperative anxiety in pediatric patients undergoing surgery is a common issue that can lead to negative psychological and physiological outcomes. Effective premedication can reduce anxiety, facilitate smooth parental separation, and improve mask acceptance during anesthetic induction. This study aimed to compare the effectiveness of intranasal dexmedetomidine (1 µg/kg) and intranasal midazolam (0.2 mg/kg) in children aged 2-8 years undergoing elective surgeries under general anesthesia.

Materials & Methods: Ninety pediatric patients were randomly assigned to two groups: Group D (dexmedetomidine) and Group M (midazolam). The primary outcomes assessed were sedation scores, parental separation anxiety, and mask acceptance. Secondary outcomes included hemodynamic parameters and the incidence of adverse effects. Data were collected at baseline and various intervals after premedication. Statistical analyses were conducted using IBM SPSS 20.0 software, with a p-value of less than 0.05 considered significant.

Results: Group D had significantly higher sedation scores 30 minutes after premedication (2.85 ± 0.22) compared to Group M (1.10 ± 0.13). Parental separation anxiety scores decreased more in Group D (from 2.90 ± 0.26 to 1.85 ± 0.44) than in Group M (from 2.95 ± 0.30 to 2.15 ± 0.28). The mean mask acceptance score was higher in Group D (3.85 ± 0.21) compared to Group M (2.50 ± 0.47). Hemodynamic parameters such as heart rate and mean arterial pressure remained stable and comparable between the two groups at baseline and various intervals. Respiratory rate and SpO2 levels were similar in both groups with no significant differences. Importantly, no significant side effects were observed in either group, highlighting the safety profile of both medications.

Conclusion: Intranasal dexmedetomidine is more effective than intranasal midazolam for premedication in children undergoing elective surgeries. It provides better sedation, reduces parental separation anxiety, and improves mask acceptance without compromising hemodynamic stability or respiratory function. These findings suggest dexmedetomidine as a superior option for pediatric premedication.

Keywords: Intranasal Dexmedetomidine, Midazolam, Pediatric Surgery, PSAS, Premedication

Introduction

Preoperative anxiety in pediatric patients undergoing surgery is a common and significant concern associated with adverse psychological and physiological outcomes [1]. Effective premedication can help alleviate anxiety facilitate smooth parental separation and improve mask acceptance during anesthetic induction [2]. While various pharmacological agents have been used for premedication in children the search for an ideal agent continues [3]. Midazolam a benzodiazepine has been widely used for pediatric premedication due to its anxiolytic and sedative properties [4]. However it can cause paradoxical reactions and respiratory depression in some children [5]. Dexmedetomidine a highly selective α2-adrenergic agonist has emerged as a promising alternative

offering sedation anxiolysis and analgesia without significant respiratory depression [6]. The intranasal route of administration for premedication has gained popularity in pediatric anesthesia due to its ease of use non-invasive nature and rapid onset of action [7]. Both midazolam and dexmedetomidine can be effectively administered intranasally bypassing first-pass metabolism and achieving good bioavailability [8 9].

While several studies have compared the efficacy of intranasal midazolam and dexmedetomidine in pediatric premedication results have been variable and the optimal agent remains debatable [10 11]. This prospective randomized controlled study aimed to compare the efficacy of intranasal dexmedetomidine (1 µg/kg) with intranasal midazolam (0.2 mg/kg) as premedication in children aged 2-8 years undergoing elective surgeries under general anesthesia.

The primary outcomes assessed were sedation scores parental separation anxiety and mask acceptance. Secondary outcomes included hemodynamic parameters and the incidence of adverse effects. By evaluating these parameters this study sought to contribute to the growing body of evidence on optimal premedication strategies in pediatric anesthesia potentially improving perioperative outcomes and patient experiences [12].

Materials and Methods

This study was designed as a prospective randomized controlled trial and conducted in the Department of Anaesthesiology at M.G.M. Medical College and M.Y. Hospital, Indore, Madhya Pradesh over 12 months from July 1, 2021 to June 30, 2022. Approval was obtained from the Ethics and Scientific Review Committee before starting the study.

A total of ninety pediatric patients aged between 2 and 8 years, classified as ASA physical status I or II and scheduled for elective surgeries under general anesthesia, were included. Exclusion criteria included parental refusal, known allergies to the study medications, intranasal pathologies or congenital anomalies and any history of upper airway disease, CNS dysfunction or cardiovascular dysfunction. Informed consent was obtained from the parents of all participants. Patients were randomly assigned to two groups using simple randomisation with closed envelopes. Group D (n=45) received intranasal dexmedetomidine at a dose of 1 µg/kg while Group M (n=45) received intranasal midazolam at a dose of 0.2 mg/kg. The medications were administered 30 minutes before surgery using a needleless syringe with the total volume divided equally between both nostrils. Data collection included assessments of sedation status, parental separation anxiety, mask acceptance and hemodynamic parameters (HR, MAP, SpO2, RR) ,along with monitoring for any side effects. These assessments were conducted at baseline and at set intervals after premedication.

The primary outcome measures were sedation scores assessed using the University of Michigan Sedation Scale (UMSS) and parental separation anxiety scores assessed using the Parental Separation Anxiety Scale (PSAS) both evaluated at baseline and 30 minutes after premedication. Mask acceptance scores were recorded at the time of induction. Hemodynamic parameters including heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR) and oxygen saturation (SpO2) were monitored preoperatively at baseline and at 10, 20 and 30 minutes after premedication, as well as intraoperatively at 15-minute intervals. Statistical analyses were conducted, using IBM SPSS 20.0 software. The unpaired T-test was used to compare mean heart rates, systolic blood pressures & diastolic blood pressures between the two groups at different time points. The Chi-square test was used for categorical data analysis. A p-value of less than 0.05 was considered statistically significant. The results showed that Group D had significantly higher sedation scores, lower parental separation anxiety scores and better mask acceptance scores compared to Group M. Hemodynamic parameters remained stable and comparable between the groups and no significant side effects were observed.

Table 1: Comparison of Mean Sedation Score between Both Groups

Sedation Score	Group D (n=45)	Group M (n=45)	p-value (unpaired T test applied)
Before premedication	0	0	NA
30 Min. after premedication	2.85 ± 0.22	1.10 ± 0.13	<0.001, significant
Mean Difference	2.85	1.10	
p-value (paired T test applied)	0.000 significant	0.000 significant	

The mean sedation score, was higher in Group D (2.85 ± 0.22) than Group M (1.10 ± 0.13) 30 minutes after premedication, with a p-value of less than 0.001. The increase in sedation scores within each group was also significant. Group D showed a marked rise from baseline while Group M had a smaller increase.

Table 2: Comparison of Parental Separation Anxiety Score Between Both Groups

Parental Separation Anxiety Score	Group D (n=45)	Group M (n=45)	p-value (unpaired T test applied)
Before Pre-Medication	2.90 ± 0.26	2.95 ± 0.30	0.73
30 Min. After Pre-Medication	1.85 ± 0.44	2.15 ± 0.28	0.001, significant
Mean Difference	1.05	0.80	
p-value (paired T test applied)	0.000 significant	<0.001 significant	

Parental separation anxiety scores decreased significantly in both groups 30 minutes after premedication. Group D showed a greater reduction from 2.90 ± 0.26 to 1.85 ± 0.44 compared to Group M which decreased from 2.95 ± 0.30 to 2.15 ± 0.28. The p-value for the difference between the groups was 0.001 indicating a statistically significant reduction in anxiety scores for Group D.

Table 3: Comparison of Mask Acceptance Score between Both Groups

Group	N	Mean	SD	p-value (unpaired T test applied)
Group D	45	3.85	0.21	0.001, significant
Group M	45	2.50	0.47	0.001, significant

Group D had a higher mean mask acceptance score (3.85 ± 0.21) compared to Group M (2.50 ± 0.47), with a p-value of 0.001. This indicates that children in Group D were more cooperative and accepting of the mask during induction compared to those in Group M.

Table 4: Comparison of Heart Rate between Both Groups (Mean ± SD)

Time (min.)	Group D (n=45)	Group M (n=45)	p-value
Heart rate (preoperatively)			
Baseline	118.67 ± 8.90	117.0 ± 9.50	0.473
10	114.77 ± 8.45	116.6 ± 9.0	0.433
20	114.1 ± 9.05	115.8 ± 9.10	0.773
30	110.53 ± 9.30	115.03 ± 8.60	0.076
Heart rate (intraoperatively)			
Baseline	108.5 ± 9.05	110.57 ± 9.4	0.27
15	108.43 ± 9.60	111.57 ± 8.90	0.10
30	106.97 ± 9.40	109.53 ± 8.60	0.16
45	106.23 ± 10.25	109.03 ± 8.00	0.27
60	107.88 ± 10.70	108.10 ± 8.45	0.91
75	105.50 ± 10.20	108.50 ± 6.50	0.09
90	103.73 ± 9.55	106.11 ± 8.60	0.20

Heart rates were similar between the two groups at baseline and at various time points both preoperatively and intraoperatively. At baseline, the mean heart rate was 118.67 ± 8.90 in Group D and 117.0 ± 9.50 in Group M. At subsequent time intervals, heart rates remained close between the groups with no statistically significant differences ($p > 0.05$).

Table 5: Comparison of Pre-Operative RR (Respiratory Rate) Between Both Groups

Time (min)	Group D (n=45)	Group M (n=45)	p-value (unpaired T test applied)
0 min.	21 ± 2.5	20 ± 1.8	>0.05
10 min.	20 ± 1.8	19 ± 1.7	>0.06
20 min.	19 ± 1.7	19 ± 1.6	>0.07
30 min.	19 ± 1.7	18 ± 1.6	>0.08

The respiratory rates were comparable at baseline and at various preoperative intervals. Group D had a mean respiratory rate of 21 ± 2.5 per minute at baseline while Group M had 20 ± 1.8 per minute. The differences in respiratory rates between the groups were not statistically significant at any time point with p-values greater than 0.05.

Table 6: Comparison of MAP (Mean Arterial Pressure) Between Both Groups (Mean ± SD)

Time (min.)	Group D (n=45)	Group M (n=45)	p-value
MAP (preoperatively)			
Baseline	63 ± 2.8	62 ± 2.8	>0.05
10	62 ± 2.8	61 ± 2.8	>0.05
20	61 ± 2.8	61 ± 2.8	>0.05
30	61 ± 2.8	61 ± 2.8	>0.05
MAP (intraoperatively)			
Baseline	61 ± 2.8	61 ± 2.8	>0.05
15	61 ± 2.8	60 ± 2.8	>0.05
30	62 ± 2.8	61 ± 2.8	>0.05
45	62 ± 2.8	61 ± 2.8	>0.05
60	62 ± 2.8	62 ± 2.8	>0.05
75	62 ± 2.8	63 ± 2.8	>0.05
90	61 ± 1.0	64 ± 0.5	>0.05

Mean arterial pressures were similar between the two groups at baseline and at various intervals both preoperatively and intraoperatively. At baseline Group D had a MAP of 63 ± 2.8 mmHg while Group M had 62 ± 2.8 mmHg. Throughout the study period, MAP values for both groups stayed close to each other with no statistically significant differences ($p > 0.05$).

Table 7: Comparison of Spo2 between Both Groups (Mean ± SD)

Time (min.)	Group D (n=45)	Group M (n=45)	p-value
SpO2 (preoperatively)			
Baseline	100 ± 0.9	99 ± 0.9	>0.05
10	100 ± 0.9	99 ± 0.9	>0.06
20	99 ± 0.9	99 ± 0.9	>0.07
30	99 ± 0.9	99 ± 0.9	>0.08
SpO2 (intraoperatively)			
Baseline	100 ± 0.9	100 ± 0.9	>0.05
15	99 ± 0.9	99 ± 0.9	>0.05
30	99 ± 0.9	99 ± 0.9	>0.05
45	99 ± 0.9	100 ± 0.9	>0.05
60	99 ± 0.9	99 ± 0.9	>0.05
75	100 ± 0.5	100 ± 0.5	>0.05
90	100 ± 0.5	100 ± 0.5	>0.05

Oxygen saturation levels were stable & comparable between both groups at baseline and at various time points preoperatively and intraoperatively. Group D had a baseline SpO2 of 100 ± 0.9%, Group M had 99 ± 0.9%. The differences in SpO2 were not statistically significant at any time point with p-values exceeding 0.05.

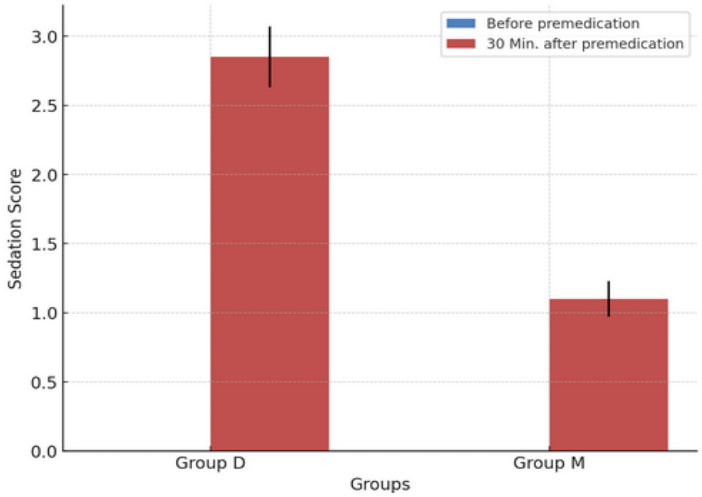

Figure 1: Comparison of Mean Sedation Score between Both Groups

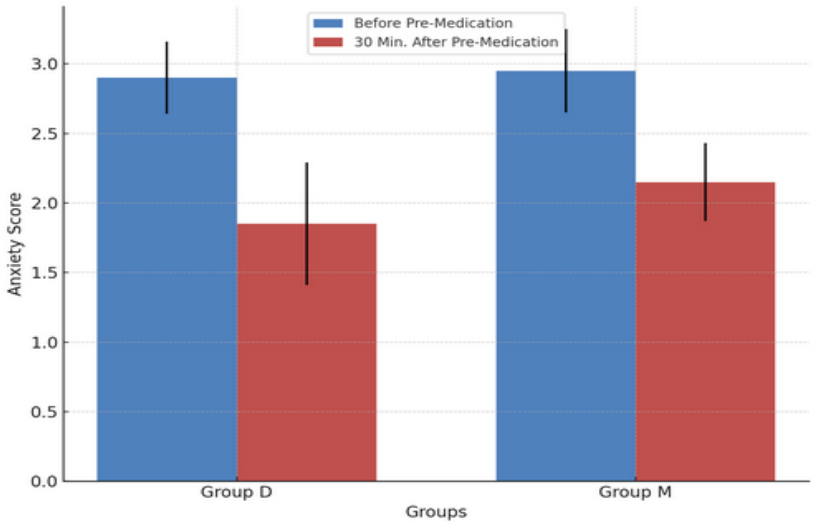

Figure 2: Comparison of Parental Separation Anxiety Score between Both Groups

Discussion

Preoperative anxiety in pediatric patients undergoing surgery is a common concern that can lead to adverse psychological and physiological outcomes [1]. Effective premedication is essential for reducing anxiety, facilitating smooth parental separation, and improving mask acceptance during anesthetic induction [2]. This study compared the effectiveness of intranasal dexmedetomidine (1 µg/kg) and intranasal midazolam (0.2 mg/kg) in children aged 2-8 years undergoing elective surgeries under general anesthesia. The results provide valuable insights into the best premedication strategy for these young patients.

The findings showed that dexmedetomidine provided higher sedation scores compared to midazolam 30 minutes after premedication. The mean sedation score was 2.85 ± 0.22 for Group D significantly higher than 1.10 ± 0.13 for Group M ($p < 0.001$). This aligns with previous studies showing dexmedetomidine's superior sedative effects in pediatric premedication [13,14]. For instance, Patil et al. reported a mean sedation score of 3.1 ± 0.3 with intranasal dexmedetomidine and 2.0 ± 0.2 with intranasal midazolam in their study of 60 children [14]. Parental separation anxiety scores also decreased significantly in both groups 30 minutes after premedication. The reduction was more pronounced in Group D which saw a decrease from 2.90 ± 0.26 to 1.85 ± 0.44 compared to Group M's decrease from 2.95 ± 0.30 to 2.15 ± 0.28. The p-value of 0.001 highlights the significant reduction in anxiety scores for Group D. These results align with studies indicating dexmedetomidine offers better anxiolytic effects compared to midazolam (15, 16). In Akin et al.'s study, parental separation anxiety scores were lower in the dexmedetomidine group (mean score 2.1) compared to the midazolam group (mean score 2.8) [15].

The mean mask acceptance score was higher in Group D (3.85 ± 0.21) compared to Group M (2.50 ± 0.47) with a p-value of 0.001. This suggests children premedicated with dexmedetomidine were more cooperative and accepting of the mask during induction. Prior research supports these findings showing better mask acceptance with dexmedetomidine [17,18]. For example, Davis et al. found that 80% of children in the dexmedetomidine group had excellent mask acceptance compared to 50% in the midazolam group [17]. Hemodynamic parameters including heart rate and mean arterial pressure remained stable and comparable between both groups at baseline and various intervals preoperatively and intraoperatively. Heart rates and MAP values did not show significant differences at any time point indicating both medications maintain stable hemodynamics [19,20]. Similarly, Yuen et al. observed no significant differences in heart rate and MAP between their dexmedetomidine and midazolam groups [20].

Respiratory rate and SpO2 levels were also comparable between the groups at baseline and at various intervals preoperatively and intraoperatively. Group D had a mean respiratory rate of 21 ± 2.5 per minute at baseline while Group M had 20 ± 1.8 per minute with no significant differences observed. SpO2 levels were stable and comparable with Group D showing 100 ± 0.9% at baseline and Group M showing 99 ± 0.9% [21,22]. Wu et al. also reported stable SpO2 levels in both groups supporting these findings [23]. Importantly no significant side effects were observed in either group highlighting the safety profile of both intranasal dexmedetomidine and midazolam. This aligns with other studies reporting minimal adverse effects with these premedication agents when used at appropriate doses [24,25].

Conclusion:

The results of this study suggest that intranasal dexmedetomidine is more effective than intranasal midazolam for premedication in pediatric patients undergoing elective surgeries. Dexmedetomidine provided better sedation, lower parental separation anxiety, and improved mask acceptance without compromising hemodynamic stability or respiratory function. These findings support the use of dexmedetomidine as a superior alternative to midazolam for pediatric premedication contributing to improved perioperative outcomes and patient experiences. Further research with larger sample sizes and diverse populations is recommended to confirm these findings and refine premedication protocols in pediatric anesthesia.

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