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Intranasal midazolam versus intranasal dexmedetomidine as premedication in paediatric patients: A comparative study

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ABSTRACT

Background: Preanesthetic medication is important among the paediatric patients undergoing surgeries. A good preanesthetic medication reduces the anxiety and the post-operative pain among paediatric patients.

Materials and Methods: A randomised controlled trial was done to compare the two groups of Dexmedetomidine, and Midazolam given as preanesthetic medication intranasally.

Results: Both the groups had comparable baseline values before premedication but there was a significant difference in the vital parameters of heart rate and systolic blood pressure after medication. The mean Parental Separation Anxiety Scale was found to be 1.4 ± 0.85 and 2.5 ± 0.98 among Dexmedetomidine and Midazolam group respectively. This was found to be significant ($p < 0.001$).

Conclusion: Dexmedetomidine when given as preanesthetic medication intranasally significantly controls the vitals within the normal range and produces better parental separation anxiety scores and mask acceptance scores as compared to Midazolam.

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1. Introduction

The preoperative duration is very stressful for most of the individuals. The paediatric population is much more predisposed for the stress prior to the surgery.¹ Paediatric patients often present with fear, anxiety, uncooperative and resistance to most of the procedures. It is often more when separated from the parents. Hence a simple procedure of venipuncture or even anaesthetic mask becomes difficult among paediatric patients.² Preoperative anxiety can also lead to hemodynamic instability, metabolic side effects emergence of agitation and also increased post-operative pain.³ So the best way of reducing the child's anxiety and stress is by administration of sedatives to the child before entering a surgical room. This allows the children to

undergo smooth anaesthetic induction. The pre anaesthetic medication among children should ideally be nontraumatic, easily administrable, non-invasive and in acceptable route of administration. Intranasal route of drug administration is one of the easy, effective, acceptable and non-invasive methods with high bioavailability and rapid onset of action.

Dexmedetomidine is an alpha 2 adrenoreceptor agonist which has got excellent analgesic and sedative properties with minimal side effects. It also reduces hemodynamic stress response due to sympatholytic mechanism. Hence Dexmedetomidine is a preferred preanesthetic medication.⁴

Similarly midazolam is a benzodiazepine which is most commonly used as preanesthetic medication among children because of its benefits such as sedation, anxiolysis, rapid onset and short duration of action. But it has some side effects such as paradoxical aggressive reactions, respiratory depression and restlessness.⁵

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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 preanaesthetic medication in paediatric patients who undergo minor surgical procedures.

2. Materials and Methods

The aim of the study was to compare the effect of Dexmedetomidine and Midazolam given as intranasal pre anaesthetic medication among children posted for minor elective surgeries. The study also had the objective of comparing preoperative anxiety, heart rate, sedation and systolic blood pressure of the two groups.

After obtaining the necessary permission and approval from institutional scientific and review board and also from the institutional ethical committee the study was conducted. Based on the power analysis, a sample size of 30 patients in each group was required for detection of 30% difference in the outcome with beta error of 0.2 (80% power) and alpha error of 0.05 between Dexmedetomidine group and Midazolam group. So the sample size was rounded to 100, with 50 in each group.

2.1. Exclusion criteria

1. Children with ASA physical status of two or more
2. Runny nose or upper respiratory tract infection
3. History of allergies
4. Any central nervous system disorders
5. Refusal to consent

2.2. Inclusion criteria

1. All paediatric patients admitted for minor surgical procedure.
2. ASA status 1.
3. Those who give informed consent.

Initially a total of 118 paediatric patients were eligible as per inclusion and exclusion criteria but 18 paediatric patients withdrew from the study or the surgery was cancelled at the last minute. All the parents were explained in detail the benefits of intranasal pre anaesthetic medication and the possible side effects with outcomes. As the current study is a double blind randomised control trial, the paediatric patients were randomly divided into two groups ie Group D and Group M by computer generated table of random numbers. Both groups patients were fasted overnight and only clear fluids were allowed up to 4 hours prior to induction on the day of surgery the children were accompanied by one parent to the preoperative room and pre anaesthetic medication was given intranasally. Group D (n=50) received intranasal Dexmedetomidine at 1 μ g per kg and Group M (n= 50) received intranasal Midazolam at 0.2 mg per

kg. The intranasal Dexmedetomidine and Midazolam were prepared according to patients for the weight so that the calculated dose of the drug is diluted to the total volume of 2 ML. One hour before induction, in the presence of one parent in the preoperative area, equal amount of the drug was dipped into both nostrils using a 3 ml syringe with a child in the recumbent position. The drug was administered by anaesthetic technician who was not blinded to the group arrangement and in order to maintain the double blinding both anaesthesiologist and the parents were not informed which drug was administered.

The vital signs such as heart rate, blood pressure, oxygen saturation were recorded before administration of the nasal drug and again at the interval of 10 minutes for 30 minutes. The modified observer assessment scale of alertness/ sedation along with parental separation anxiety scale were used to assess at 30 minutes regularly. After pre medication the children were taken to the operating room and the acceptance of mask was checked by mask acceptance scale. Children were shifted to operation theatre and mask induction was carried out with 4 to 5% Sevoflurane in O₂.

2.3. Statistical analysis

The data was collected and analysed by using SPSS version 21. the quantitative data was analysed by using the measures of central tendency and deviation by calculating mean and standard deviation. Independent t test was done when the data was normally distributed. Qualitative data was presented and analysed by using chi square test.

3. Results

The current study was a randomised double controlled trial where we compared the Dexmedetomidine group with Midazolam group for intranasal preanaesthetic medication. 100 children were randomly divided into two groups of 50 each. The basic demography and anthropometric values were measured among the two groups and both were found comparable with p value being insignificant. The children who underwent minor procedures included such as inguinal hernia, tonsillectomy, K wire fixation, dental procedures etc. Both the groups were comparable in all the aspects prior to the procedures.

The study showed no significant difference in both the groups in the baseline vital parameters like heart rate, oxygen saturation and blood pressure before pre medication. After pre medication, the Dexmedetomidine group had significant lower values of heart rate as compared to Midazolam group. This was also found statistically significant. Similarly the blood pressure also had lower values 20th and 30th minute as compared to Midazolam group and was statistically significant. However the oxygen saturation before pre medication and after pre medication

and after compared with both the groups it was not found significant statistically. The modified observers assessment of alertness and sedation scale found statistically significant difference among both the groups at 20th and 30th minute.

The parental separation and mask acceptance scores when compared among both the groups were found to have statistically significant differences.

Most of the children had better pre anaesthetic medication acceptance in both the groups but Dexmedetomidine was better with respect to maintenance of vitals, parental separation and mask acceptance scores. All the children didn't have any side effects or complications with respect to the procedure or anaesthesia.

Table 1: Showing modified observer's assessment of alertness / sedation scale

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

Table 2: Showing response to induction (mask acceptance scale)

1	Combative, crying
2	Moderate fear of mask, not easily calmed
3	Cooperative with reassurance
4	Calm, cooperative

Table 3: Showing parental separation anxiety scale

Behaviour of the child during separation from parents	Criteria	Score
Excellent	Patient unafraid, cooperative, or asleep	1
Good	Slightly afraid/crying, quiet with reassurance	2
Fair	Moderately afraid and crying, not quiet with reassurance	3
Poor	Crying, need for restraint	4

4. Discussion

Anxiolytic pre medication prior to any surgical procedure is required among the paediatric patients. Even though mini pre anaesthetic medications are found acceptable among paediatric patients, Midazolam is most commonly used.

however Dexmedetomidine is a newer drug which is found to be better acceptable than midazolam.

A similar randomised control trial study was done by Deepak Singla et al⁶ among 60 children aged three to 10 years of age who were given intranasal Dexmedetomidine and Midazolam. The study found that intranasal Dexmedetomidine premedication resulted in statistically significant but clinically unimportant lower heart rate and blood pressure at 10th, 20th, and 30th minutes following administration of the drug as compared to intranasal midazolam group. children who had received Dexmedetomidine also achieved better separation from the parents and mask acceptance scores as compared to midazolam.

The current study results also found the similar values and is in concurrence with the study.

Similarly the study done by Mustafa et al⁷ which compared intranasal midazolam and ketamine with Dexmedetomidine found that Dexmedetomidine achieved easy and faster sedation and better child parent separations scores. Malinowasky et al⁸ did a study on faster rate of sedation and acceptance of midazolam as compared to other routes.

Jun et al⁹ found that the oral administration of 2µg/kg dexmedetomidine and 0.5mg/kg midazolam provides satisfactory mask acceptance and eases separation from parents 30 min before surgery. Yuen et al¹⁰ recommended 2.0 µg/kg dexmedetomidine nasal drops before the induction of paediatric anaesthesia in children aged 5-8 years; the nasal drops showed enhanced sedative effect without increasing the incidence of adverse reactions.

Telon et al¹¹ did a study with 2 µg /kg of Dexmedetomidine, which showed that time of onset of Dexmedetomidine was 15 min when administered with metered dose atomizer. A similar study done by Prabhu and Mehandale et al¹² on comparison of oral administration of Dexmedetomidine and Midazolam found that incidence of intranasal agitation with Dexmedetomidine is increased. However in our study we had no incidences of nasal agitation in both the groups. Similar results related to the faster rate of absorption of preanesthetic medication through intranasal route and better acceptance scores with Dexmedetomidine were seen in our study.

5. Conclusion

Pre anaesthetic medication plays a vital role among paediatric patients undergoing surgical procedures. It not only reduces anxiety among the patients but also increases the chances of better acceptance of anaesthesia. Both Dexmedetomidine and Midazolam are effective drugs which can be given as preanesthetic medication. However Dexmedetomidine produces better parental separation and mask acceptance scores as compared to Midazolam. Hence Dexmedetomidine should be used as preanesthetic

Table 4: Showing the demographic and anthropometric distribution among dexmedetomidine and midazolam groups

Variable	Group D (Dexmedetomidine) N =50	Group M (Midazolam) N = 50	P value
Age (in Years)	7.4 ± 0.7	7.6 ± 0.9	0.731
Sex (M:F)	24:26	25:25	0.649
Weight (in Kg)	20.4 ± 4.4	20.8 ± 5.6	0.681
Duration of Surgery (min)	25.1 ± 4.90	27.6 ± 3.68	0.791

Table 5: Showing the premedication and after medication vitals along with modified observer's assessment of alertness / sedation scale among Dexmedetomidine and Midazolam groups

Variable	Time interval (min)	Dexmedetomidine group (N - 50)	Midazolam group (N - 50)	p-value
Heart Rate	Before premedication	108.1 ± 8.19	109.7 ± 7.8	0.619
	After premedication	105.3 ± 7.31	107.4 ± 8.8	0.041
		103.6 ± 6.42	105.8 ± 6.9	0.034
Systolic BP	Before premedication	94.8 ± 5.81	100.7 ± 4.9	0.001
	After premedication	110.5 ± 9.3	110.8 ± 9.5	0.597
		108.9 ± 9.8	109.1 ± 8.8	0.318
Oxygen saturation	Before premedication	105.3 ± 9.5	107.7 ± 8.9	0.003
	After premedication	104.2 ± 9.1	106.3 ± 9.4	0.004
		98.3 ± 1.4	98.6 ± 1.5	0.812
Modified observer's assessment of alertness/ sedation scale	Before premedication	98.8 ± 1.6	98.3 ± 1.7	0.757
	After premedication	97.7 ± 1.2	97.9 ± 1.3	0.946
		97.4 ± 1.6	97.8 ± 1.7	0.619
	Before premedication	4.83 ± 1.04	4.80 ± 1.10	0.472
	After premedication	3.46 ± 1.08	3.8 ± 1.03	0.051
		2.83 ± 1.14	3.5 ± 0.98	0.006
		2.67 ± 0.91	3.2 ± 0.72	0.002

Table 6: Shows the comparison of parental separation anxiety score and mask acceptance score in Dexmedetomidine and Midazolam group

Variable	Dexmedetomidine Group (n= 50)	Midazolam Group (n= 50)	p- value
Parental Separation Anxiety Scale (PSAS)	1.4 ± 0.85	2.5 ± 0.98	0.001
Mask Acceptance Scale (MAS)	1.6 ± 0.78	2.41 ± 0.88	0.001

medication, which can be given through an easily acceptable and non-invasive route, preferably intranasally.

6. Source of Funding

The authors declare no conflict of interest.

7. Conflict of Interest

None.

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