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Original Research Article

Comparing Intranasal Dexmedetomidine to Intranasal Midazolam: Effects on Paediatric Premedication

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Abstract:

Introduction: An effective pre-anaesthetic medication for use in children undergoing surgery is required to alleviate apprehension about anaesthesia and surgery, reduce trauma from separation from patents, and facilitate induction of general anaesthesia without lengthening the post-anesthesia recovery period.

Aim And Objectives: The objective of comparative study between intranasal dexmedetomidine and intranasal midazolam as premedication in paediatric age group is to evaluate and compare the following effects between two groups. (1) Time of onset of sedation, (2) Duration of sedation, (3) Level of sedation, (4) Anxiolytic effect, Ease of child parent separation, (5) Side effects.

Results: (1) The mean value of age with standard deviation are 6.43+1.43 Group D and 5.28+1.63 for Group M. There was no significant difference between two groups ($p<0.03$). (2) Study group D had 73.3% male and 26.7% female subjects whereas Group M had 58.3% male and 41.7% female subjects. No significant difference in sexwise distribution was observed between two study group. (3) Comparison of saturation of oxygen in the blood at an interval of 15,30,45 minutes respectively. Group D had mean SPO2 of 98.03+0.86 at 45 minutes interval. Whereas group 99.12+1.32 which is found to be statistically significant. (4) Mean sedation score at 15 minutes interval is 2.82+0.43 in Group D whereas in group M 4.83+0.39 ($p<0.000$) which is statistically highly significant. (5) Mean behavior score of 1.85+0.36 at 10 min. in group D whereas 2.87+0.34 in group M ($p<0.000$) which is statistically highly significant.

Conclusion: Compared to midazolam, intranasal dexmedetomidine resulted in reduced sedation, easier child-parent separation, and faster postoperative recovery with no side effects. Thus, intranasal dexmedetomidine may be administered effectively and safely as a pre-anaesthetic medication in children undergoing minor surgical procedures under general anaesthesia.

Keywords: Comparison, Intranasal Dexmedetomidine, Intranasal Midazolam, Paediatric Population.

Introduction

Children are more nervous and afraid because of their limited cognitive capacities, lack of comprehension of the health-care system, and lack of self-regulation.1 Hospital admission, anaesthesia, and surgery are all stressful events for children, therefore high preoperative anxiety in them may delay anaesthesia induction and contribute to the beginning of postoperative unfavourable psychological consequences such as nightmares, feeding disorders, and enuresis. [2,3] Premedication in children is still a study topic, since numerous medications and delivery methods have been created utilizing diverse routes of administration, such as oral, rectal, intranasal, intramuscular, intravascular, subcutaneous, and intraosseous, although none are optimal. [4]

Aim and Objectives:

The objective of comparative study between intranasal dexmedetomidine and intranasal midazolam as premedication in paediatric age group is to evaluate and compare the following effects between two groups.

- Time of onset of sedation
- Duration of sedation
- Level of sedation
- Anxiolytic effect
- Ease of child parent separation

- Side effects.

Materials and Methods

The present study was conducted on patients posted for elective minor surgeries like adenotonsillectomy, herniotomy etc. at MKCG Medical College and Hospital, Berhampur, Odisha during the period of June 2021 to September 2022.

In the computer-generated randomization technique, 120 patients of ASA Grade I and Grade 2 of either sex aged between 2-8 years posted for elective minor surgical procedures were included. The children were randomly allocated into Group D or Group M of 60 patients each supposed to receive intranasal dexmedetomidine I µg/kg and intranasal midazolam 0.2 mg/kg respectively after taking written informed consent from the parents/guardian.

Pre-operative fasting:

- pre-operative fasting guidelines for children were as follows:
- No oral liquids 2 hours prior to the procedure.
- Avoidance of milk and solids 6 hours prior to the procedure.

Inclusion criteria

- Patients of age between 2-8 years.
- Both sexes
- ASA grade I and 2
- Posted for minor surgeries (like herniotomy and adenotonsillectomy)

Exclusion criteria

- Previous history of allergy to anaesthetic medication.
- History of CNS disorder
- Cardiac arrhythmia or congenital heart disease.
- Mental retardation
- Children refusing intranasal administration of drug.
- ASA above 2

Result

Table 1: Age Distribution

Age in yrs.	Group D		Group M	
	Frequency	Percentage	Frequency	Percentage
2	1	1.7	0	0
3	1	1.7	6	10.0
4	3	5.0	8	13.3
5	9	15.0	12	20.0
6	17	28.3	12	20.0
7	10	16.7	9	15.0
8	19	31.7	13	21.7
Total	**60**	**100**	**60**	**100**

Table 2: Comparison of age

Group D		Group M		Unpaired t test	
Mean	Std. deviation	Mean	Std. deviation	t value	P value
6.43	1.43	5.82	1.63	2.2	P<0.03

The above table shows age distribution within the study groups and their comparison. The age range was 2-8 years for both the study groups. The mean value of age with standard deviation is 6.43±1.43 Group D and 5.28±1.63 for Group M. There was no significant difference between two groups (p<0.03).

Table 3: sex wise distribution

Age in yrs.	Group D		Group M	
	Frequency	Percentage	Frequency	Percentage
Male	44	73.3	35	58.3
Female	16	26.7	25	41.7
Total	**60**	**100**	**60**	**100**

Study group D had 73.3% male and 26.7% female subjects whereas Group M had 58.3% male and 41.7% female subjects. No significant difference in sex wise distribution was observed between two study groups.

Table 4: Diagnosis

Age in yrs.	Group D		Group M	
	Frequency	Percentage	Frequency	Percentage
Adenotonsillitis	27	45	31	51.7
Thyroglossa cyst	2	3.3	6	10.0
Foreign body	3	5	6	10.0
Tongue tie	2	3.3	8	13.3
Fracture and dislocation	23	38.3	4	6.7
Pre auricular sinus	3	5	1	1.7
Hernia	0	0	4	6.7
Total	**60**	**100**	**60**	**100**

Table 5: Surgery done

Surgery	Group D		Group M	
	Frequency	Percentage	Frequency	Percentage
Adenotonsillectomy	27	45	31	51.7
Thyroglossa cyst	2	3.3	6	10.0
Foreign body	3	5	6	10.0
Tongue tie	2	3.3	8	13.3
Fracture and dislocation	23	38.3	4	6.7
Excision	3	5	1	1.7
Herniotomy	0	0	4	6.7
Total	**60**	**100**	**60**	**100**

Table 6: ASA Grade

ASA grade	Group D		Group M	
	Frequency	Percentage	Frequency	Percentage
Grade – I	59	98.3	59	98.3
Grade – 2	1	1.7	1	1.7
Total	**60**	**100**	**60**	**100**

Above table shows in group D 59 out of 60 (98.3%) were ASA grade I, 1 out of 60 were ASA grade 2. In Group M 59 out of 60 were ASA grade I (98.3%), 2 out of 60 were ASA grade 2 (2%).

Table 7: Comparison of weight

Group D		Group M		Unpaired t test	
Mean	Std. deviation	Mean	Std. deviation	t value	P value
20.67	3.87	17.58	4.11	4.23	P<0.000

Table 8: Comparison of pre sedation vitals

Pre sedation vitals	Mean and standard deviation		Unpaired t test		
	Group – D	Group – M	t value	p value	Significance
HR	106.28±9.70	100.77±22.4	1.75	P<0.08	Not significant
SBP	100.23±7.98	95.3±6.74	3.58	P<0.000	Significant
DBP	67.17±5.24	64.83±6.76	2.11	P<0.03	Significant
SPO_2	99.33±0.84	99.2±1.44	0.61	P<0.53	Not Significant

Above table sows' comparison of pre sedation vitals heart rate, SBP, DBP, SPO_2 between group D and group M. Mean heart rate in group D 106.28±9.70 whereas in group M 100.77±22.4. In group D mean SBP 100.23±7.98, in group M 95.3±6.74, (p<0.000). In group D mean DBP 67.17±5.24, in group M 64.83±6.76, (p<0.03) and mean SPO_2 in group D 99.33±0.84, in group M 99.2±1.44 (p<0.53)

Table 9: Comparison of pre sedation vitals

Pre sedation vitals		Mean and standard deviation		Unpaired t test		
		Group – D	Group – M	t value	p value	Significance
HR	15 min	103.47±6.77	104.8±8.0	-0.99	P<.0.32	Not Significant
	30 min	98.7±5.17	102.17±7.76	-3.41	P<0.001	Significant
	45 min	94.7±3.86	100.1±7.72	-5.74	P<0.000	Significant

Above table shows comparison of heart rate between group D and group M at 15,30,45 minutes interval respectively. Mean heart rate at 45 min interval in group D found to be 94.7±3.86 and in group M 101.1±7.72, (p<0.000) which was statistically significant.

Table 10: Comparison of post sedation vitals

Pre sedation vitals		Mean and standard deviation		Unpaired t test		
		Group – D	Group – M	t value	p value	Significance
SBP	15 min	100.83±5.61	94.13±6.51	6.04	P<.0.000	Significant
	30 min	100.83±5.61	94.13±6.51	1.66	P<0.09	Not Significant
	45 min	100.67±5.48	94.13±6.51	6.04	P<0.000	Significant
DBP	15 min	67.17±4.54	65.33±7.24	1.66	P<.0.09	Not Significant
	30 min	67.17±4.54	65.33±7.24	5.94	P<0.000	Not Significant
	45 min	67.17±4.54	65.33±7.24	1.66	P<0.09	Significant

Above table shows comparison of SBP and DBP between Group D and Group M at an interval of 15,30,45 minutes respectively. In group D mean SBP at 45 minutes 100.67+5.48 in group M 94.13+6.51 (P<0.000) which is statistically significant. In group D mean DBP at 45 minutes is 67.17+4.54 in group M 65.33+7.24 (P<0.09) which was not statistically significant.

Table 11: Comparison of post sedation vitals

Pre sedation vitals		Mean and standard deviation		Unpaired t test		
		Group – D	Group – M	t value	p value	Significance
SPO_2	15 min	98.33±0.75	99.27±1.26	-4.92	P<.0.000	Significant
	30 min	98.17±0.67	99.10±1.35	-4.80	P<0.000	Not Significant
	45 min	98.03±0.86	99.12±1.32	-5.33	P<0.000	Significant

Above table shows comparison of saturation of oxygen in the blood at an interval of 15,30,45 minutes respectively. Group D had mean SPO_2 of 98.03+0.86 at 45 minutes interval. Whereas group 99.12+1.32 which is found to be statistically significant.

Table 12: Comparison of post sedation vitals

Pre sedation vitals		Mean and standard deviation		Unpaired t test		
		Group – D	Group – M	t value	p value	Significance
SE SCORE	5 min	4.03±0.36	5.88±0.32	-29.29	P<.0.000	Highly significant
	10 min	3.45±0.53	5.3±0.59	-17.98	P<0.000	Highly significant
	15 min	2.82±0.43	4.83±0.39	-26.63	P<0.000	Highly significant

Above table shows comparison sedation score between Group D and Group M at 5,10,15 minutes interval. Mean sedation score at 15 minutes interval is 2.82+0.43 in Group D whereas in group M 4.83+0.39 (p<0.000) which is statistically highly significant.

Table 13: Comparison of post sedation vitals

Pre sedation vitals		Mean and standard deviation		Unpaired t test		
		Group – D	Group – M	t value	p value	Significance
Behavour Score	5 min	1.98±0.12	3.01±0.13	-43.84	P<0.000	Highly significant
	10 min	1.85±0.36	2.87±0.34	-15.84	P<0.000	Highly significant
	15 min	1.03±0.25	2.53±0.50	-20.54	P<0.000	Highly significant

Above table shows comparison of behaviour score between Group D and Group M. Mean behaviour score of 1.85±0.36 at 10 min. in group D whereas 2.87+0.34 in group M (p<0.000) which is statistically highly significant.

Table 14: Comparison of post sedation vitals

Pre sedation vitals		Mean and standard deviation		Unpaired t test		
		Group – D	Group – M	t value	p value	Significance
SP SCORE	5 min	2.00±0.00	3.00±0.00	Cannot be calculated		
	10 min	1.78±0.41	2.85±0.36	-15.02	P<0.000	Highly significant
	15 min	1.00±0.00	2.1±0.32	-28.16	P<0.000	Highly significant

Above table shows that after 10 minutes of premedication with intranasal dexmeditomidine in group D 1.78+0.41 and group M mean separation score found to be 2.85+0.36 (p<0.000) which is statistically highly significant.

Table 15: PAWS score

PAWS score	Group D		Group M	
	Frequency	**Percent**	**Frequency**	**Percent**
1	55	91.7	3	5.0
2	5	8.33	56	93.33
3	0	0	1	1.67
4	0	0	0	0
Total	60	100	60	100

	Table 16: Mean and standard deviation		
t value	**Group D**	**Group M**	**t value**
4.92	1.08±0.28	1.96±0.32	

Above table shows that in group D 55 out of 60 (91.7%) study population had the score of 1, whereas in group M 3 out of 60 studies population (5%) had post anaesthesia wake up score of 1.

Discussion: Pre-anaesthetic medication in children should lessen anxiety and stress associated with separation from their parents, as well as enable anaesthesia induction without lengthening recovery time.

The primary method of administering pre-anaesthetic drugs is intranasal. Benefits of this method include simplicity of administration, painlessness, higher absorption, more bioavailability, and a faster beginning of effect. Midazolam has several beneficial features as a premedicant for children, particularly those having day care surgery. It causes drowsiness by activating GABA receptors in the cerebral cortex. Its elimination half-life is much less than that of diazepam or trimeprazine. It has a consistent dose-dependent anxiolytic effect without excessive drowsiness and has minimal cardiovascular and respiratory side effects. Also, the anterograde amnesia caused by midazolam should aid to lessen the physiological shock of anesthesia and surgery.

However, intranasal midazolam has been linked to an unpleasant burning sensation in the nasal cavity, respiratory depression, and postoperative shivering. As a result, nasal administration of midazolam is not recommended in clinical practice. Dexmedetomidine causes drowsiness by activating ά2 adrenergic receptors in the locus ceruleus. Activating ά2 adrenergic receptors at this region lowers central sympathetic output, resulting in increased firing of inhibitory neurons. Dexmedetomidine acts on the GABA receptor, resulting in drowsiness and analgesia without producing respiratory depression. It causes cooperative sedation, which means that even though the patient is drugged, they can communicate with healthcare providers. The current research was conducted to assess the timing of onset of sedation, duration of sedation, degree of sedation, anxiolytic effect, ease of child-parent separation, and side effects of dexmedetomidine and midazolam delivered intranasally in pediatric patients.

The results were compared in both groups using the relevant parameters. In the current research, children in the two study groups were between the ages of 2 and 8 years old, with a mean age of 6.43 + 3.87 in Group D and 17.58 + 4.11 in Group M, and a nearly equal male and female population. The two groups had no significant differences in age, gender, or weight. This contrasted with the research done by Darshana D. Patel et al [1] in the age range of 2 to 8 years. Darshana D. Patel et al [1] compared intranasal dexmedetomidine (1µg/kg) and intranasal midazolam (0.2 mg/kg) as a pre-anaesthetic medication in children. [4] The primary objective was to assess preoperative sedation and ease of child-parent separation, and the secondary objective was to assess analgesia in the post-operative period.

There were no significant differences among the demographic factors. In an intergroup comparison, Group D had a significantly lower pulse rate at 30 minutes compared to Group M, but there was no statistically significant difference in oxygen saturation in any of the groups. The mean sedation score in Group D at 45 minutes was 2.52 + 0.74, and in Group M it was 3.69 + 0.87, inferring Group D obtained better sedation after 45 minutes. At the time of patient transfer to the operating theatre, 54% of children in Group D had a child separation score of 1, compared to 40% in Group M.Group D's heart rate reduced from 106.28+ to 94.7+63.86, which was both statistically and clinically significant, but Group M's heart rate climbed from 100.77+22.4 to 101.1+7.72, which was clinically insignificant. These findings were similar to those of AL Meenakshi Sundaram et al, who found that after 45 and 60 minutes of intranasal dexmedetomidine treatment, heart rates decreased considerably from baseline. [5] After administering the relevant premedication, neither research group had a substantial variation from their baseline blood pressure. These findings were comparable to those of Saad A. Sheta et al. At 45 minutes, SPO2 in Group D went from 99.3+0.84 to 98.03+0.86,

while in Group M it moved from 99.2+1.44 to 99.12+1.32. [6]

The post-sedation differences among and between the two researches groups were clinically inconsequential, since the mean SPO2 never fell below 95%. These findings were comparable to those reported by Darshna D. Patel et al1.At 15 minutes after administering sedative premedication, the mean sedation score in Group D was 2.82+0.43, whereas in Group M it was 4.83+0.39 ($p<0.000$), indicating that children in Group D had better sedation than those in Group M. At 15 minutes, Group D had a mean behavior score of 1.03+0.25, whereas Group M had a mean score of 2.53+0.50 ($p<0.000$), indicating that Group D performed better in terms of anxiolysis. [4]

The findings were similar to those of A.L. Meenakshi Sundaram et al., who investigated the timing of in. At 15 minutes, the mean separation score in Group D was 1.00+0.00, whereas in Group M it was 2.10+0.32 ($p<0.000$), indicating that Group D had easier child-parent separation than Group M. The findings were analogous to those of Ashraf M. Ghali et al, who found that participants who got intranasal dexedetomidine had an easier time separating from their parents than those who received oral midazolam. [7] Post-anaesthesia recovery was measured using a wake-up score. In Group D, 100% of individuals had an acceptable post-anaesthesia wake-up score, whereas in Group M, it was 98.3%.

The findings were analogous to those of Saad A. Sheta et al, who found that postoperative agitation was considerably lower in Group D than in Group M (11.1% vs 30.6%, respectively).The only negative effect seen in the intranasal midazolam group was 40 out of 120 weeping children due to irritation and burning sensations on the nasal mucosa after medication administration. [8,9]

Conclusion

Compared to midazolam, intranasal dexmedetomidine resulted in lesser sedation, simpler child-parent separation, and improved postoperative recovery with no adverse consequences.

Thus, it is possible to infer that intranasal dexmedetomidine may be used efficiently and safely as a pre-anaesthetic drug in children having minor surgical operations under general anaesthesia.

Reference

1. Kogan A, Katz J, Efrat R, Eidelman LA. Premedication with midazolam in young children: a comparison of four routes of administration. Paediatr Anaesth 2002; 12:685-689.
2. Yuen VM, Hui TW., Irwin MJ et al A randomized comparison of two intranasal dexmedetomidine doses for premedication in children anaesthesia 2012; 67: 1210-1216.
3. Akin A, Bayram A, Esmaoglu A et al. Dexmedetomidine vs midazolam for premedication of paediatric patients undergoing anaesthesia. Pediatr Anesth 2012; 22:871-876
4. Darshna D. Patel, Lisha, Upadhyay MR. pre anaesthetic medication in children: A comparison of inranasal dexmedetomidine versus midazolam. JMR 2015; 1 (2):59-63.
5. Fazi L, Jantzen EC, Rose JB et al, A comparison of oral clonidine and oral midazolam as pre anaesthetic medication in the paediatric tonsillectomy patient. Anaesth Analg 2001; 92: 56-61.
6. Sheta SA, Ai-shareed MA, Abdelhalim AA. Intraanasal dexmedetomidine vs midazolam for premedication in children undergoing complete dental rehabilitation: a double blinded randomized controlled trial. Pediatr Anesth 2014; 24:181-189.
7. Ghali AM, Mahfouz AK, Al-Bahrani M. Preanaesthetic medication in children: A comparison of intanasal dexmedetomidine versusoral midazolam. Saudi J Anaesth 2011; 5:387-391.
8. N. Griffith, S. Howel and D.G. Mason. Intranasal midazolam for premedication of children undergoing day case anaesthesia: comparison of two delivery systems with assessment of intra-observer variability. British Journal of Anaesthesia 1998; 81:865-869.
9. P Bhakta B.R. Ghosh, M. R Roy, G. Mukherjee. Evaluation of intranasal midazolam for preanaesthetic sedation in paediatric patients. Indian J. Anaesth 2007; 51 (2): 111-116.