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# A prospective randomised double blinded comparative study between nasal atomized dexmedetomidine and midazolam as premedicants in paediatric adenotonsillectomy

## Abstract

Adenotonsillectomy is one of the most common ambulatory surgeries in the pediatric population. Fear and anxiety at parental separation is one of the important challenges to the anesthesiologist in spite of improvements in the drug armamentarium, seen in 40-60% children. The gold standard of premedication is Midazolam, which is effective by all routes, intravenous, intramuscular, oral, submucosal and nasal.[1,2] Nasal Midazolam is commercially available, each puff delivering 0.5mg. Nasal route is now being popular because it is non-invasive, easy and has rich blood supply which ensures a faster absorption and faster onset of action. Besides, it bypasses the hepatic metabolism, so bioavailability is improved from 40-60% in oral route to about 82% in nasal route. The search for ideal premedicant continues[3] and Dexmedetomidine, alpha-2 agonist, is the new kid in town. It is effective by all routes including nasal.[3] But, so far only studies with nasal instillation of Dexmedetomidine, is available, especially in children. Syed et al. in 2019 has used atomized form of Dexmedetomidine in adults for minor orofacial procedures. Hence we decided to compare nasal atomized Dexmedetomidine and Midazolam using atomization devices like LMA MAD NASAL and INSED ATOMISER because atomization helps to break down particle to 30-100microns, hence absorption would be quicker with minimum or no side effects.

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**Aim:** To compare nasal atomized Dexmedetomidine and Midazolam regarding

**Primary**: 1. Sedation score at parental separation and mask induction 2. Behaviour score at parental separation and mask induction 3. Wakeup score at extubation

**Secondary:** 1. To compare the haemodynamic and respiratory parameters preop, intraop and postop, 2. To note the time taken to achieve recovery score of 9 3.To look for side effect, if any

**Study population**: This study was done in Lourdes Hospital, Cochin, Kerala, India over a period of 18months after Ethical and Scientific Committee clearance in 60 children, satisfying the inclusion criteria, after parental education about the study and their consent.

**Inclusion criteria**: 60 children, aged 3-8yrs, weighing 10-20kg, ASA 1&2, posted for elective adenotonsillectomy.

**Exclusion criteria**: 1. Children with organ dysfunction (ASA 3&4), 2. Children with anatomical defects of nose and upper airway which can pose difficulty in mask holding/intubation, 3. Children with known allergy to the study drugs or any drug used in the standard protocol for balanced anaesthesia in adenotonsillectomy, 4.Children on long term phenobarbitone therapy or any drug which is a hepatic enzyme inducer, 5.Children with ongoing respiratory infection or a blocked nose, 6.Children with H/O febrile seizures

## Materials and methodology

The materials used were DEXMEDETOMIDINE AMPOULE containing 100mcg/ml (XAMDEX by ABBOTT), LMA MAD NASAL, INSED ATOMISER (MIDAZOLAM) with each puff delivering 0.5mg Midazolam, BD Tuberculin syringe.

The sample size was calculated based on a previous study by Yuen et al. in where the sedation score at mask induction was 21.9% in Midazolam group and 75% in Dexmedetomidine group. The average % was noted, to get 95%confidence and 80%power,the sample size calculated was 13/group; to account for dropouts due to ongoing respiratory infection/parent refusal, we decided to take 30/group so total sample size population was 60.The sample size calculation is as follows:

$$n = \frac{[\{Z_{1-\alpha/2}\sqrt{2PQ} + Z_{1-\beta}\sqrt{P_1Q_1 + P_2Q_2}\}^2]}{(P_1 - P_2)^2}$$

Where, $P = \frac{p_1 + p_2}{2}, Q = 1 - P$

$\alpha$ = Level of significance (5%) $[Z_{1-\alpha/2} = 1.96]$

$1-\beta$ =Power (80%) $[Z_{1-\beta} = 0.84]$

$P_1$ = Proportion of sedation at parental separation in midazolam group (21.9%)

$$Q_1 = 1 - P_1(78.1\%)$$

$P_2$ = Proportion of sedation at parental separation in dexmedetomidine group (75.0%)

$$Q_2 = 1 - P_2(25.0\%)$$

## Method

The 60 children were subjected to randomization by computer-generated codes to receive either GroupA-0.2MG Midazolam by INSED ATOMISER or GroupB-1MCG/KG Dexmedetomidine by LMA MAD NASAL 45 mts before induction of anaesthesia in the premedication room in the semi recumbent position, while resting on the mother's lap. The drug was administered by an anaesthesiologist, not involved with the study, but trained to deliver it, according to opaque sealed envelopes allocating each group. The haemodynamic parameters, namely, heart rate, systolic blood pressure, respiratory rate and peripheral oxygen saturation were noted before delivery of the drug. Once the drug was given, the haemodynamic and respiratory parameters and the Sedation score and Behaviour score at parental separation were noted by the primary investigator at 15 mt intervals till 45 mts, when the child was transferred to the operation theatre. In the operation theatre, standard protocolised balanced anaesthesia was given after attaching the standard monitors namely, $SPO_2$, ECG, NIBP, $ETCO_2$. The child was preoxygenated with 100% Oxygen and Sedation score at mask induction and Behaviour score at mask induction were noted inhalational agent Sevoflurane was built up to 3% to allow intravenous access with 22G cannula and balanced salt solution was started at 4ml/kg/hr. Then sevoflurane was reduced and 1.5mg/kg propofol and 1.5mg/kg succinylcholine was given to facilitate placement of appropriate size flexometallic LMA for the wt of the child. Since we chose adenotonsillectomy and we wanted to ensure an atraumatic placement of LMA, we gave succinylcholine. After correct placement, as confirmed by 5point auscultation and $ETCO_2$, it was fixed and anaesthesia maintained with 50% $O_2$-$NO_2$-0.5MG/KG atracurium. Analgesia was achieved with 2mcg/kg fentanyl, rectal paracetamol 20mg/kg. The intraop haemodynamic and respiratory parameters were noted. On completion of surgery, child was reversed with 0.5mg/kg neostigmine and 0.02mg/kg atropine. Injection dexona 0.2mg/kg iv was given before reversal to tackle postoperative nausea and vomiting. Child was put in the left lateral position and LMA removed when child was fully awake. The Wake up score was noted score less than 3 was considered satisfactory. Then was shifted to the recovery room where recovery was scored using Modified Aldrete-Kroulik scoring and time taken to obtain a score of 9 was noted. The child was also monitored for side effects like nasal irritation, bradycardia, hypotension, nausea and vomiting, respiratory depression. Hypotension was taken as less than 20% of baseline, heart rate less than 60 was taken as bradycardia and treated with atropine; respiratory rate less than 10 was taken as respiratory depression requiring intervention like assisted ventilation. Once the child attained a recovery score of 9, he/she was shifted out. The scores and demographic data including the haemodynamic and respiratory parameters were analysed statistically using modified version SPSS20. The demographic variables were compared using Chi-square test; p value<0.05 was considered significant. The quantitative variables were analysed using independent student t test and repeated measures of Anova. p value <0.05 was considered statistically significant (Figure 1&2).

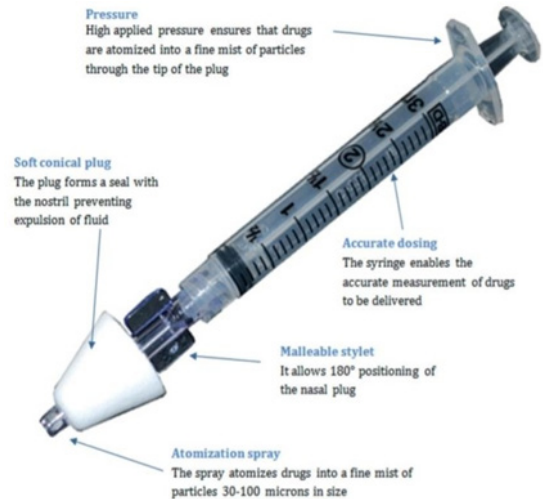



**Figure 1** LMA Mad Nasal.

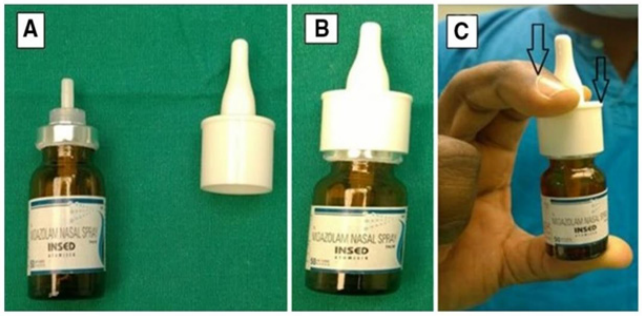
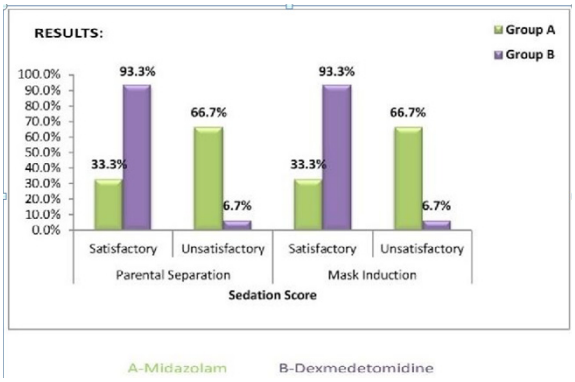



**Figure 2** A. Intranasal midazolam supplied with the nozzle for administration of the drug. B. Attach bottle and nozzle. C. Hold the bottle in the picture shown and press the nozzle in downward direction as shown by arrows in the picture (114).

## Results

1. The demographic variables like age, sex, weight and height were similar in both groups, no statistical significance (p>0.05).
2. Sedation score was less in Dexmedetomidine group compared to Midazolam (p<0.05) which was statistically significant both at parental separation and mask induction.93.3% children in Dexmedetomidine group had satisfactory sedation compared to 33.7% in Midazolam group both at parental separation and mask induction. The median Sedation score also was much less in Dexmedetomidine group compared to Midazolam at parental separation and on mask induction. This was also statistically significant (Chart 1).

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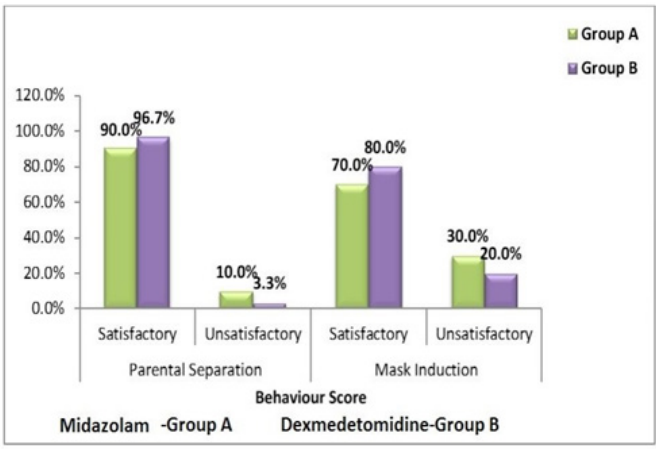
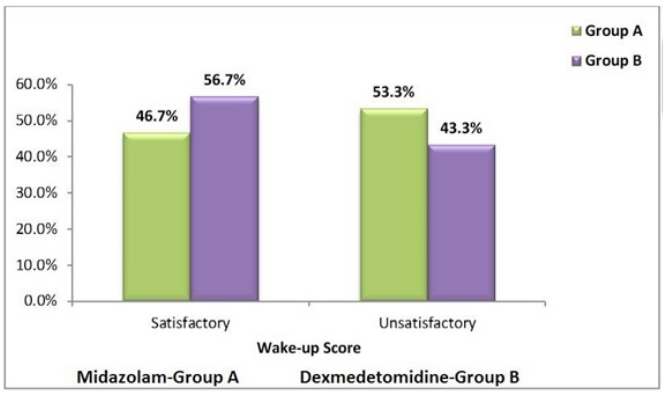
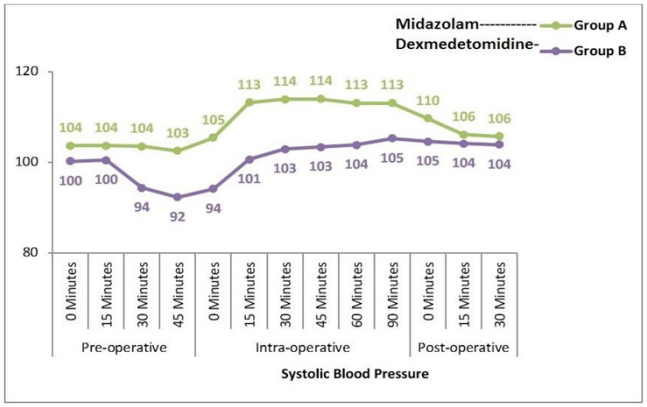
3. Behaviour score both at parental separation and mask induction were similar between both groups; so, statistically not significant (p>0.05) (Chart 2).

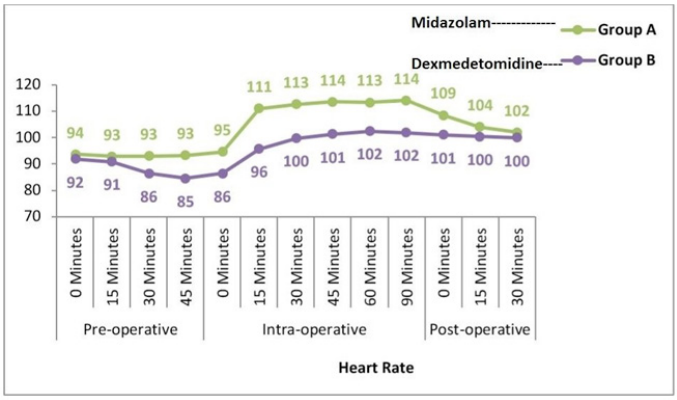



4. Wakeup score at extubation also was similar between both groups (p>0.05), not statistically significant (Chart 3).

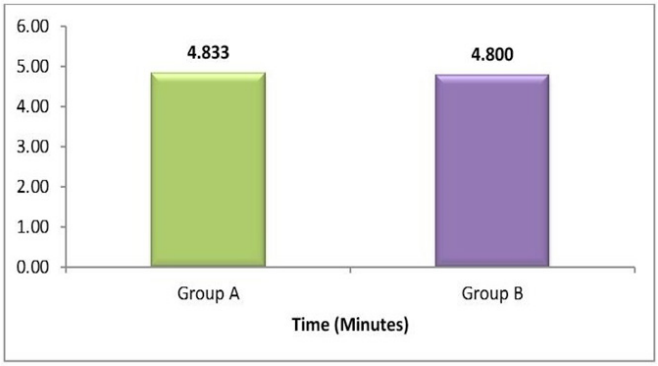



Haemodynamic and respiratory parameters were also statistically not significant. Though in Dexmedetomidine group, heart rate reduced compared to Midazolam, it was never less than 20%baseline.Blood pressure also showed decline in Dexmedetomidine group by 30mts pre induction and showed a rise but by 90mts towards end of surgery has stabilized. Yet there was no statistical significant difference between the two groups. Peripheral oxygen saturation never went below 95% in any group in the preop, intraop and postop periods (Chart 4).




5. Time taken to achieve Modified Aldrete Kroulik score was similar between both groups; 4.88mts in Midazolam (gp A) and 4.80mts in Dexmedetomidine groups (gpB) (Chart 5).




6. The adverse effects looked for were nasal irritation, bradycardia, hypotension, nausea, vomiting and respiratory depression**.** None of the patients in any group had any of these side effects in the doses prescribed (Table 1).

**Table 1** Comparison of Adverse Effects between Group A & B

| Adverse effects | Number of children in group A Midazolam | Number of children in group B Dexmedetomidine |
|---|---|---|
| Nasal irritation | 0 | 0 |
| Bradycardia | 0 | 0 |
| Hypotension | 0 | 0 |
| Respiratory depression | 0 | 0 |
| Nausea | 0 | 0 |
| Vomiting | 0 | 0 |

## Discussion

Midazolam has long been the ideal gold standard premedicant but the quest for the ideal one continues. Dexmedetomidine, alpha2 agonist, also has joined the race for the ideal premedicant. It is effective by all routes like Midazolam, but so far, no studies have tried to atomize the drug to compare it with Midazolam. Midazolam is commercially available as INSED ATOMISER, to deliver the atomized form of Midazolam. Dexmedetomidine is not commercially available in atomized form so, we used LMA MAD NASAL, the

atomization device, to break up the particles .This device breaks up particles to 30mcg-100mcg, which helps in faster absorption, more even distribution and hence faster onset with minimum or no side effects. That is why we have got a statistically significant difference in the Sedation score between the drugs both at parental separation and mask induction. Both drugs were acceptable to the children, no bitter taste in mouth, because there is no overflow into the oropharynx as it is atomized. Hence no nasal irritation, bradycardia, hypotension, respiratory depression, nausea, vomiting. Sedation score is as follows: 1.Does not respond to mild prodding or shaking, 2.Responds only to mild prodding or shaking, 3.Responds only after name is called loudly or repeatedly, 4.Lethargic response to name spoken in normal tone, 5.Appear asleep but responds readily to name spoken in normal tone, 6.Alert and awake and responds readily to name spoken in normal tone.

Sedation score less than 5 is considered as satisfactory. Behaviour score is done by 4point scale: 1.Calm and cooperative 2- Anxious but reassurable 3-Anxious and not reassurable, 4-Crying and resisting. Behaviour score less than 2 is acceptable. Wakeup score is done by the HOUPT scale (4point scale) 1-Calm and cooperative, 2. Not calm but can be calmed down, 3. Not calm slightly agitated, 4.Agitated or excited or disoriented .Wakeup score less than 3 is satisfactory.[4,5] L Kumar in 2017 has compared nasal instillation of Dexmedetomidine with oral Midazolam in various types of pediatric surgeries and has shown that both are effective premedicant in pediatric practice[6] Dexmedetomidine has been tried in various procedures for sedation like radiological procedures. But none have tried atomized form except Syed et al. who has used atomized Dexmedetomidine in adults for minor orofacial surgical procedures and has proved that it is effective.[7]

Cost effectiveness in the Indian scenario proves that both are cost effective. LMA MAD NASAL is an easily sterilisasble device by soap and water so 1 device could be used for 30 patients (Rs25 per patient). INSED ATOMISER if charged by the number of puffs also is cost effective.

## Conclusion

a) Dexmedetomidine is a much better sedative than Midazolam so it can be preferred as a premedicant in young children.

b) Dexmedetomidine is very well atomized by LMA MAD NASAL with no side effects at 1mcg/kg.

c) Use of atomization devices is advisable for nasal premedication which is also cost effective.

## Recommendations

1. Further studies on ASA3&4 children are to be done with larger multicentre sample size. 2. Role of Dexmedetomidine in mentally challenged children needs to be explored.

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## Acknowledgments

None.

## Conflicts of interest

Authors declare that there is no conflict of interest.

## References

1. Deutsch ES. Tonsillectomy and adenoidectomy: changing indications. *Pediatr Clin North Am.* 1996;43(6):1319–1338.

2. Creedon LR DM. Pharmacological management of patient behavior. 8th edition Macdonald RE, Avery DR, editors: Elsevier; 2004.

3. Rosenbaum A, Kain ZN, Larsson P, et al. The place of premedication in paediatric practice. *Paediatr Anaesth.* 2009;19(9):817–828.

4. Hosey MT, LMD Macpherson, P Adair, et al. Dental anxiety, distress at induction and postoperative morbidity in children undergoing tooth extraction using general anaesthesia. *British Dental Journal.* 2006;200:39–43.

5. Davidson A, McKenzie I. Distress at induction: prevention and consequences. *Curr Opin Anaesthesiol.* 2011;24(3):301–306.

6. Kumar L, Kumar A, Panikkaveetil R, et al. Efficacy of intranasal dexmedetomidine versus oral midazolam for paediatric premedication. *Indian J Anaesth.* 2017;61(2):125–130.

7. Syed S, Hakim T, Riyaz MR, et al. To evaluate efficiency of DEXMEDETOMIDINE in atomised intranasal form for sedation in minor oral surgical procedures. *Ann Maxillofac Surg.* 2019;9(1):89–95.