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Comparison of intranasal dexmedetomidine and oral midazolam as premedication for cochlear implant surgery in children

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ABSTRACT

Background: Children undergoing surgical procedures can experience significant anxiety and distress during the perioperative period. The use of sedative premedication may help to reduce anxiety, minimize the emotional trauma, and facilitate a smooth induction of anesthesia. Midazolam is most commonly used as a premedication agent in children. Dexmedetomidine is a highly selective alpha-2 adrenoreceptor agonist that provides sedation, anxiolysis, and analgesic effects without causing respiratory depression. **Aims and Objectives:** The aim of the study was to compare intranasally administered dexmedetomidine and oral midazolam for premedication in pediatric patients undergoing cochlear implant surgeries. **Materials and Methods:** This prospective randomized controlled study included 60 ASA Grade I and II patients between 1 and 6 years of age who underwent cochlear implant surgeries under general anesthesia. Patients were divided into two groups. Group A received 1μg/kg intranasal dexmedetomidine and Group B patients received 0.5 mg/kg oral midazolam 45 min before induction. The pediatric separation anxiety was assessed using the pediatric separation anxiety scale (PSAS) while shifting the patient to operating room (OR) and mask acceptance was assessed by the attending anesthesiologist using mask acceptance scale (MAS) in OR who is blinded to the drug given. Heart rate (HR) and oxygen saturation were monitored till the end of procedure was noted on a pre-structured proforma. **Results:** The mean PSAS in intranasal dexmedetomidine group was 1.00 ± 0.00, while in the oral midazolam group was 2.10 ± 0.31 (P = 0.000). The mean MAS in intranasal dexmedetomidine group was 1.00 ± 0.00, while in the oral midazolam group was 2.13 ± 0.35 (P = 0.000). Mean HR (P > 0.05), systolic blood pressure (P > 0.05), and diastolic blood pressure (P > 0.05) were comparable between both the groups. There was a statistically significant association seen between sedation grade and the groups (P = 0.000), showing that groups are dependent on the sedation group. There was a statistically significant association seen between wake up behavior grade and the groups (P = 0.000), showing that groups are dependent on the wake up behavior grade. **Conclusion:** Intranasal dexmedetomidine is an effective and safe alternative for premedication in view of parental separation, mask acceptance, hemodynamic stability, and sedation for the children undergoing cochlear implant surgeries under general anesthesia.

Key words: Dexmedetomidine; Midazolam; Intranasal; Pre-operative anxiety; Atomiser

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INTRODUCTION

Children undergoing surgical procedures can experience significant anxiety and distress during the perioperative period.[1] The use of sedative premedication may help to reduce anxiety, minimize the emotional trauma, and facilitate a smooth induction of anesthesia. A cochlear implant is a surgically implanted neuroprosthetic device that provides a sense of sound to a person with moderate to profound sensorineural hearing loss.[2]

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Midazolam is most commonly used as a premedication agent in children. Dexmedetomidine is a highly selective alpha-2 adrenoreceptor agonist that provides sedation, anxiolysis, and analgesic effects without causing respiratory depression.[3,4] Hence, in this study, we made an effort to compare intranasally administered dexmedetomidine and oral midazolam for premedication in pediatric patients undergoing cochlear implant surgeries.

Aims and objectives

Hence, this study was conducted with the aim to compare the efficacy of intranasal dexemedtomidine (1 μg/kg) and oral midazolam (0.5 mg/kg) for premedication in pediatric age group undergoing cochlear implant surgery.

MATERIALS AND METHODS

This study was undertaken in the Department of Anaesthesiology and Critical Care, Sri Aurobindo Medical College and PG Institute, after valid approval of Ethics Committee of the institution on 60 pediatric patients of either sex scheduled to undergo cochlear implant surgery. The study was pre-approved by the Institutional Ethics Committee (IEC) for the final permission. After obtaining the permission of IEC, the study was conducted. Pediatric patients having age between 2 and 6 years of either sex belonging to ASA Grade I and II and patients posted for cochlear implant surgery under general anesthesia and those patients parents/guardians giving consent for getting included in the study were included in the present study. Patient belonging to ASA Grade III and IV and patient's parent refusal, patients with known history hypersensitivity or contra-indications to dexmedetomidine, patients of age <2 years and greater than 6 years, patients with history of nausea, vomiting, or retching 24 h before anesthesia and patients with active infection or history of motion sickness were excluded from the present study. Pre-anesthetic checkup was done for all patients before the procedure as routine. An informed consent was taken from the relatives/guardians explaining them the whole procedure and the aim behind conducting the study. Patients kept nil by mouth for 6 h before the procedure as per guidelines.

Sixty patients were randomly allocated into two groups of 30 patients each: Group A: Intransal dexmedetomidine 1 mcg/kg and Group B: Oral midazolam 0.5 mg/kg.

In Group A for dexmedetomidine: Intranasal drug was sprayed in both nostrils using 1 ml tuberculin syringe and atomizer with a child in recumbent position 60 min before shifting the patient to operating room (OR).

In Group B for midazolam: As oral midazolam is not commercially available in most of the countries. In this study, we mixed the calculated dose of injectable preparation (5 mg/ml) of midazolam in mango juice.

Patients were shifted to the OR and all mandatory monitors were attached like pulse-oximetry, blood pressure cuff, venturi mask for oxygen administration, and a large gauge i.v. line secured. Following parameters are been evaluated in this study: PSAS, mask acceptance scale (MAS), and hemodynamic variables: HR, BP, oxygen saturation (SPO_2), wake up behavior, and sedation score.

Pediatric separation anxiety score (PSAS): Parental separation anxiety was assessed using the parental separation anxiety scale (PSAS), which is a 4 point scale. (1) Easy separation, (2) Whimpers but easily reassurable, (3) cries and cannot be easily reassured but not clinging to parents, and (4) crying and clinging to parents. A PSAS score of 1 or 2 is classified as an acceptable separation, score of 3 or 4 is considered as difficult separation.

MAS: (1) Excellent (unafraid, cooperative, and accept mask readily). (2) Good (slight fear of mask and easily reassured). (3) Fair (moderate fear of mask and not calmed with reassurance). (4) Poor (terrified, crying, or combative). Subjects with score of 1 or 2 are considered as satisfactory acceptance of mask, scores of 3 or 4 are considered unsatisfactory.

Sedation Score: Does not respond to mild protruding or shaking. Responds only to mild protruding or shaking.

Wake Up Behavior: (1) Calm and cooperative. (2) Not calm but could be easily calmed. (3) Not easily calmed, moderately agitated or restless. (4) Combative, excited, and disoriented. Subject with score of 1 or 2 is considered as satisfactory for wake up behavior of a child, scores of 3 or 4 are considered satisfactory.

Statistical analysis

Data were collected and entered into the Excel sheet; the analysis was done using the 16.0 software. The mean of systolic BP, diastolic BP, heart rate (HR), and SPO_2, between different groups at same time interval was analyzed using Chi-square test. Unpaired t-test was used to compare the parent separation anxiety and mask acceptance in both the groups. Pearson Chi-square test was used compare the sedation and wake up behavior between both the groups. $P \leq 0.05$ was considered as statistically significant.

RESULTS

The mean PSAS in intranasal dexmedetomidine group was 1.00 ± 0.00, while in the oral midazolam group was 2.10 ± 0.31. The difference was found to be statistically

significant (P=0.000), showing a higher mean PSAS in oral midazolam group in comparison to the intranasal dexmedetomidine group (Graph 1).

The mean MAS in intranasal dexmedetomidine group was 1.00±0.00, while in the oral midazolam group was 2.13±0.35. The difference was found to be statistically significant (P=0.000), showing a higher mean MAS in oral midazolam group in comparison to the intranasal dexmedetomidine group (Graph 1).

The comparison of mean HR between the two groups showed that the mean HR was comparable between the two groups till 60 min (P>0.05). The mean HR in intranasal dexmedetomidine group from 75 min till end of 160 min was significantly lower than that in the oral midazolam group (P<0.05) (Graph 2).

The comparison of mean systolic blood pressure between the two groups was comparable till 105 min (P>0.05). The mean systolic blood pressure in intranasal dexmedetomidine group at 115 min till end of 160 min was significantly lower than oral midazolam group (P<0.05). The comparison of mean diastolic blood pressure between the two groups was comparable throughout the study period (P>0.05).

The mean diastolic blood pressure in intranasal dexmedetomidine group was lower than oral midazolam. The comparison of mean systolic blood pressure between the two groups was comparable till 105 min (P>0.05). The mean systolic blood pressure in intranasal dexmedetomidine group at 115 min till end of 160 min was significantly lower than oral midazolam group (P<0.05). The comparison of mean diastolic blood pressure between the two groups was comparable throughout the study period (P>0.05). The mean diastolic blood pressure in intranasal dexmedetomidine group was lower than oral midazolam.

In intranasal dexmedetomidine group, all the patients were having sedation Grade 1.

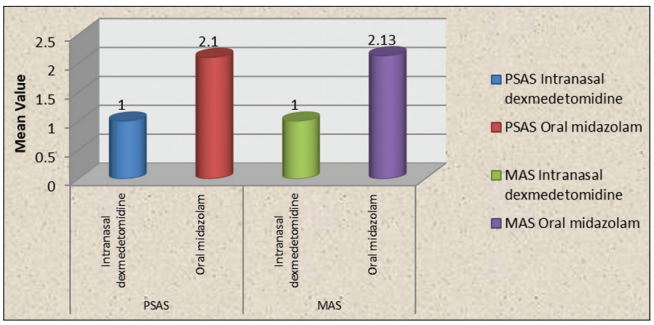
In oral midazolam group, all the patients were having sedation Grade 2.

There was a statistically significant association seen between sedation grade and the groups (P=0.000), showing that groups are dependent on the sedation group. In intranasal dexmedetomidine group, all the patients were having wake up behavior Grade 1 (Graph 3).

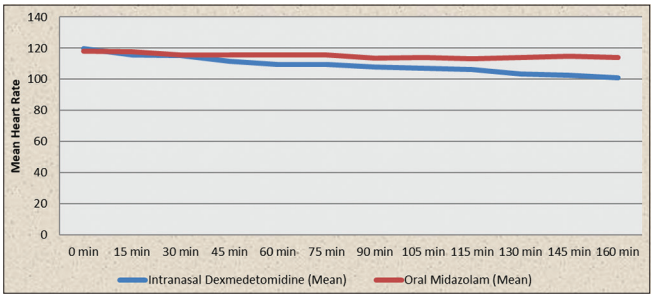
In oral midazolam group, all the patients were having wake up behavior Grade 2. There was a statistically significant association seen between wake up behavior grade and the groups (P=0.000), showing that groups are dependent on the wake up behavior grade (Graph 4).

DISCUSSION

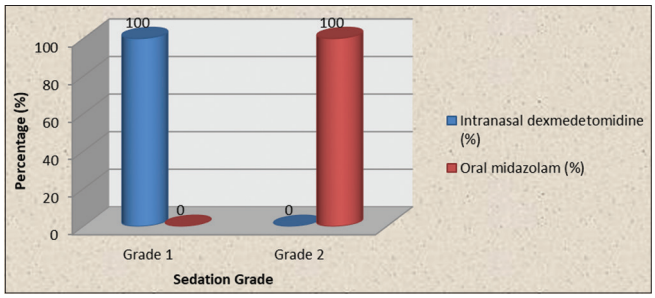
In our analysis, we found that intranasal dexmedetomidine is better and effective for parent separation anxiety and in comparison to midazolam. Mostafa and Morsy conducted



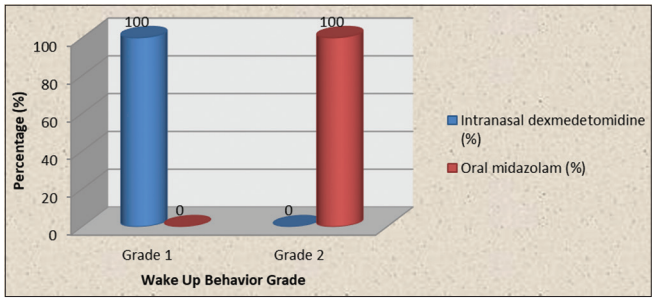
Graph 1: Comparison of mean PSAS and mask acceptance scale between the two groups



Graph 2: Comparison of mean heart rate between the two groups



Graph 3: Distribution of patients according to the sedation score



Graph 4: Distribution of patients according to the wake up behaviors grade

a randomized double blind controlled trial in 96 children aged 2–8 years scheduled for bone marrow biopsy and aspirate. Patients with child-parents separation score Grade 1 were significantly higher in dexmedetomidine group than midazolam.[5] In our analysis, we found intranasal dexmedetomidine is better and effective for mask acceptance and in comparison to midazolam. Single *et al.* conducted a prospective, randomized, and double-blind controlled trial on 60 children, 3–10 years of age with ASA physical Status I, scheduled for elective surgery. In this study, mask acceptance score (P=0.0472) was significantly lower in group dexmedetomidine as comparison to midazolam. Hence, intranasal dexmedetomidine is an effective and safe alternative and resulted in superior sedation.[6] In our analysis, in intranasal dexmedetomidine hemodynamic variables; HR and blood pressure values were lowered in comparison of midazolam. Sheta *et al.*, 72 two children of American Society of Anesthesiology classification (ASA) physical status (I and II), aged 3–6 years, were randomly assigned to one of two groups equally. Group M received intranasal midazolam (0.2 $mg \cdot kg^{-1}$), and Group D received intranasal dexmedetomidine (1 μg/kg). The patients hemodynamic parameters were recorded by an observer until anesthesia induction. There were no incidences of bradycardia, hypotension, in either of the groups during study observation.[7] In our analysis we found intranasal dexmedetomidine have better wake up behavior and sedation score in comparison to oral midazolam. Kawanda *et al.,* conducted a study in which 80 children (median age 3 years) were recruited and 140 surgical procedures were performed and found similarly that intranasal dexmedetomidine have better sedation and wake up behavior as comparison to oral midazolam.[8]

Limitations of the study

Only a small sample of population could be selected because of the resources and manpower constraints Due to the cross-sectional nature of the study, it is difficult to establish causal relationship between the dependent and predicting variables Due to small sample size, study findings cannot be generalized.

CONCLUSION

Intranasal dexmedetomidine 1 ug/kg is an effective and safe alternative for premedication in children undergoing cochlear implant surgery under general anesthesia. Intranasal dexmedetomidine decreases anxiety levels, allows better parent separation, and resulted in better mask acceptance at the time of induction when compared with oral midazolam 0.5 mg/kg. Intranasal dexmedetomidine works without causing much side effects or post-operative complications.

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Authors Contribution:
AnA- Concept and design of the study, aims and objectives, reviewed the literature, prepared first draft of manuscript, arranged all the references and this is his own dissertation work; **AS-** Contributed regarding conception or design of the study, developing the consent form, data collection, interpreted the results and manuscript preparation; **ArA-** Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript.

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