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# A comparative evaluation of intranasal dexmedetomidine with and without nalbuphineas premedication for pediatric dental patients

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ABSTRACT

**Introduction:** Management of children's fear and anxiety during treatment is a primary concern of paediatric dental practitioners. There are a number of children who are difficult to be managed by basic behaviour guidance techniques.
**Objective:** To evaluate the safety and efficacy of intranasal Dexmedetomidine with and without Nalbuphine procedural sedation in paediatric dental patients.
**Materials and Methods**: This study was conducted in Department of Pedodontics and Preventive Dentistry, Babu Banarasi Das College of Dental Sciences Lucknow in collaboration with Department of Pharmacology, King George Medical University Lucknow. Ninety six systemically healthy children (ASA type I) between 4-8 years of age for whom basic behaviour modification techniques were not successful in providing dental treatment were included in the study. Each parent/guardian was requested to fill a written informed consent form at the initial appointment. Data analysis was carried out using SPSS 16.0 version.
**Result:** Considering the efficacy parameter (duration, time of recovery) the intranasal dexmedetomidine (group 1, 2.5 $\mu$g/ kg) was found to be the better for procedural sedation. Intranasal administration with atomizer and nasal drop had no significant difference.
**Conclusion:** Intranasal dexmedetomidine alone and in combination with nalbuphine showed comparable sedative efficacy with no additional advantage of combination over dexmedetomidine alone. Use of a commercially available atomizer showed improved patient's acceptance of intranasal administered drugs but did not influence efficacy as compared to nasal drops.



## 1. Introduction

Dental care is necessary for the purpose of preventing and elimination orofacial diseases, infection and pain along, with, restoring the form and function of the dentition, correcting facial disfigurement or dysfunction in children. Safe and successful treatment of oral diseases requires a combination of mutual standing as well as behavior modification of child and parents. For the management of pain, anxiety and unwanted mobility in children, undergoing dental treatment, procedural sedation and analgesia has developed consequently during recent years and has substantially reduced the need of general anaesthesia. American College of Emergency Physician (ACEP) defines procedural sedation as "a technique of administering sedatives or dissociative agents with or without analgesic to induce a state that allows the patient to tolerate unpleasant procedure while maintaining cardio-respiratory function".[1] There is a long list of drugs that are used for procedural sedation by various routes these years but none of them have been proved ideal. Dexmedetomidine is approved by the Food and Drug Administration (FDA) in 1999 to be used in humans for short term sedation in intensive care unit. Initially, it has emerged as an native to premedication in pediatric anesthesia. Dexmedetomidine is one of the advanced drug that has gained popularity among the list of drugs used for procedural sedation but

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been sparingly used in our country.[2] In the search for opioid analgesics with less abuse potential a number of semi- synthetic opiates were developed. Nalbuphine is considered as a drug with a relatively low risk of inducing respiratory failure with specific mechanism of action providing potent analgesic effects, moderate sedation and rare side effects; and is readily used for pain management in children. Thus, the drug is reported to be safe and effective alternative for premedication in children.[3] Atomized intranasal administration is achieved by using a product known as Mucosal Atomizer Device (MAD). Use of MAD for administration, reduces the need for obtaining intravenous access which is often painful and depressing for the child with an additional risk of needle stick injury.[4] Delivery of Intranasal medication is relatively painless inexpensive, and easily rendered with a minimal training. Hence, this study is aimed to evaluate and compare the safety and efficacy of intranasal dexmedetomidine with and without nalbuphine procedural sedation in pediatric dental patients.

## 2. Materials and Methods

This study was conducted in Department of Pedodontics and preventive Dentistry, Babu Banarasi Das College of Dental Sciences (BBDCODS) Lucknow in collaboration with Department of Pharmacology, King George Medical University Lucknow. ASA type Ininety six systemically healthy children between four to eight years of age for whom basic behavior modification techniques were not successful in providing dental treatment were considered for the study after obtaining institutional ethical clearance. A thorough medical history followed by dental history was taken. Each parent/guardian was requested to fill a written informed consent form at the initial appointment. Risks and benefits of the sedation followed by the pre-sedation instructions were explained to the parent/guardian.

### *2.1. Inclusion criteria*

1. Scared and anxious children who were uncooperative towards dental treatment and difficult to be managed by non-pharmacological means of behavior management.
2. Children satisfying American Society of Anaesthesiologists (ASA I) physical status criteria.

### *2.2. Exclusion criteria*

1. Parents not willing to submit their consent in written.
2. Patients who were known allergic to the drugs to be used
3. Patients taking any other drug that causes sedation.
4. Patients with nasal infection & nasal pathology.

Patients were randomly divided into two groups (o n the basis of drug) and each group was subdivided (on the basis of mode to be used drug administration)

1. Group for administration of Dexmedetomidine (2.5mg/kg) with Nalbuphine (0.2mg/kg)
   1a) Nasal drop
   1b) Atomized spray
2. Group for administration of Dexmedetomidine (2.5mg/kg)
   2a) Nasal drop
   2b) Atomized spray

On day of dental treatment, to obtain assurance of the children's health they were re- evaluated by the anaesthesiologist. Critical signs and the peripheral oxygen saturation levels were observed and documented. Before the administration of drug, the body weight was measured and the drug was calibrated according to the weight and then was administered. Half volume of the total required amount of pus administered into each nostril with the child in semi recumbent position or in parent's lap using an insulin injection syringe without needle or atomizer device for intranasal administration. During each sedation session the children were evaluated for behavior response during the administration of drug while after the administration of drugs, they were evaluated to check onset, duration of sedation, side effects of drug and ease of completion of treatment. All the dental procedures were carried out by the first author himself in the presence of anaesthesiologist. After the onset of sedation the vital signs such as Pulse pressure, Blood Pressure, Oxygen saturation was recorded at regular interval of 10 minutes with the help of multi paramonitor.

**Table 1:** Ohio State behavioral Rating Scale as expressed by Lochary and co-workers.[5]

| Score | Temperament |
|---|---|
| 1 | Crying and struggling(CS) |
| 2 | Struggling(S) |
| 3 | Crying (C) |
| 4 | Quiet(Q) |

The patient was discharged subsequent to fulfilling the American Academy of Pediatric Dentistry discharge criteria.[7]

### *2.3. Statistical analysis*

Data entry and statistical analysis were performed using the Microsoft Excel and SPSS windows version 16.0 software. Outcomes are presented in frequencies, percentages and average and SD. Tests of significance like Chi- square test for categorical variables and unpaired t-test were used to compare continuous variables between the groups. Statistical significance was taken as p value $< 0.05$.

**Table 2:** Sedation rating scale and ease of treatment completion rating scale[6]

| **Sedation rating scale** | | |
|---|---|---|
| **Score** | **Sedation level** | **Response** |
| 1 | No Sedation | Typical response/cooperation for this patient |
| 2 | Minimal | Anxiolysis |
| 3 | Moderate | Purposeful response to verbal command |
| 4 | Deep | Purposeful Response after repeated verbal command or painful stimulation |
| 5 | General Anesthesia | Not Arousable |
| **Ease of treatment completion rating scale** | | |
| **Score** | **Classification** | **Behavioral sign** |
| 5 | Excellent | Quiet and cooperative, treatment completed without difficulty |
| 4 | Good | Mild objections or whimpering but treatment not interrupted. Treatment completed without difficulty |
| 3 | Fair | Crying with minimal disruption to treatment. Treatment completed with minimal difficulty |
| 2 | Poor | Struggling that interfered with operative procedures. Treatment completed with difficulty |
| 1 | Prohibitive | Active resistance and crying, treatment cannot be rendered |

## 3. Result

The present study comprised of 96 subjects in which various dental procedures were performed after achieving state of conscious sedation. These subjects were randomly divided in 2 groups of 48 each. Groups 1 and 2 were further subdivided into subgroups group la (Atomizer), group lb ( Nasal drop), group 2a (Atomizer) and group 2b (Nasal drop) on the basis of mode of administration of drugs

Table 3 shows mean value of onset of sedation for atomizer was 12.17±3.71 mins and nasal drop was 12.54=2.26 mins so atomizer has rapid onset of action. 29.2% in group 1a and 37.5% in group 1b poor ease of treatment. Depth of sedation, 4.2% in group 1a and 4.2% in group 1b showed no sedation. 33.3% in group 1a and 41.7 % in group 1b showed minimal sedation, 54.2% in group 1a and 37.5% in group 1b were moderately sedated 8.3% in group 1a , 16.7 % in group 1b were in deep sedation. There was no significant difference in the parameters between atomizer and nasal drop (Table 3)

Table 4 illustrates the mean value of onset of sedation for atomizer was 12.38±2.81 mins and nasal drop was 11.79±3.92 mins so atomizer has rapid onset of action. There was no significant ($p>0.05$) difference in the ease of treatment, acceptance of drug ($p=0.75$) and adequate depth of sedation (0.21) between me 2a and Group 2b. There was no significant difference in the parameters atomizer and nasal drop.(Table 4)

Table 5 shows that 16.7 % of subjects in group 1 and 29.2% in group 2 showed good ease of treatment, 50% in group 1 and 45.8% in group 2 showed fair ease of treatment and group 1 and 25.0% in group 2, showed poor ease of treatment. Depth of sedation was observed as, 4.2% in group 1 and 0% in I showed no sedation.37.5% in group 1 and 27.1 % in group 2 showed minimal sedation. Duration of action of group 1 was 78.38±19.03 mins and group 2 was 69.91 ±23.13 mins so combination has limited duration of action, recovery from sedation of group 1 was 116.60±20.90 mins and group 2 was 113.34±21.04 mins.

## 4. Discussion

The major cause behind the avoidance of dental treatment is fear, which is due to painful procedures that may precipitate fear and anxiety in patients. Another reason for ignorance towards the dental treatment may be cost concerns. Malamed (2003)[8] claims that fear, anxiety and pain have been associated with the practice of dentistry, although he explains that image of the dentist as an instrument of pain is not justified. O ne of the solutions to the treatment of unmanageable pediatric patients is the use of general anesthesia, but due to its high cost, questionable parental acceptability associated complications, it is thought to be the last choice as behavior management tool for providing dental treatment as stated by Fields et al (1984).[9] In a study by Jamses et al(2014),[10] it was observed that intranasal dexmedetomidine alone did not produce sufficient sedation and analgesia and the combination of dexmedetomidine with a potent opioid offers the potential for increased efficacy of sedation. Therefore, in the present study, combination of dexmedetomidine and an opioid-nalbuphine was used to attain more advantage and efficacious sedation. Henryal(1998)[11] compared intranasal administration of midazolam via nasal drop and atomizer in dogs and concluded that atomizer administration produces significantly higher CSF concentrations of midazolam compared to the nasal drop approach. Wolfe and Braude, (2010)[12]suggested that atomization of intranasal drugs by MAD device produces fine particles (30-100 um in diameter) and is thought to increase drug absorption and

**Table 3:** Comparison of parameters between atomizer and nasal drop in Group 1

| Parameters | Atomizer(1a) (n=24) | Nasal drop (1b) (n=24) | p-value |
|---|---|---|---|
| **Ease completion of Treatment** | | | |
| Good | 4(16.6) | 4(16.6) | |
| Fair | 13(54.2) | 11(45.8) | 0.81 Chi-square test |
| Poor | 7(29.2) | 9(37.8) | |
| **Acceptance of drug** | | | |
| Crying and struggling | 6(25.0) | 6(25.0) | |
| Struggling | 8(33.3) | 5(20.0) | 0.78 Chi-square test |
| Crying | 6(25.0) | 8(33.3) | |
| Quite | 4(16.7) | 5(20.8) | |
| **Adequate depth of sedation** | | | |
| No Sedation | 1(4.2) | 1(4.2) | |
| Minimal | 8(33.3) | 10(41.6) | 0.65 Chi-square test |
| Moderate | 13(54.2) | 9(37.5) | |
| Deep | 2(8.3) | 4(16.7) | |
| Onset of sedation (minutes) | 12.17 $\pm$ 3.71 | 12.54 $\pm$ 2.26 | 0.67 Unpaired ttest |
| Duration of action (minutes) | 78.79 $\pm$ 21.42 | 77.58 $\pm$ 20.88 | 0.88 Unpaired t test |
| Recovery time (minutes) | 117.58 $\pm$ 20.88 | 115.62 $\pm$ 21.33 | 0.74 Unpaired t test |

**Table 4:** Comparison of parameters between atomizer and nasal drop in Group 2

| Parameters | Atomizer (2a) (n=24) | Nasal drop (2b) (n=24) | p-value |
|---|---|---|---|
| **Ease completion of Treatment** | | | |
| Good | 6(25.06) | 8(33.3) | |
| Fair | 9(37.5) | 13(54.2) | 0.13 Chi-square test |
| Poor | 9(37.5) | 3(12.5) | |
| **Acceptance of drug** | | | |
| Crying and struggling | 3(12.5) | 5(20.8) | |
| Struggling | 9(37.5) | 6(25.0) | 0.75 Chi-square test |
| Crying | 7(29.2) | 7(29.2) | |
| Quite | 5(20.8) | 6(25.0) | |
| **Adequate depth of sedation** | | | |
| No Sedation | 0(0.0) | 0(0.0) | |
| Minimal | 9(37.5) | 10(41.6) | 0.21 Chi-square test |
| Moderate | 10(41.7) | 11(45.8) | |
| Deep | 5(20.8) | 9(37.5) | |
| Onset of sedation (minutes) | 12.38$\pm$2.81 | 11.79$\pm$3.92 | 0.55 Unpaired t test |
| Duration of action (minutes) | 65.92$\pm$16.46 | 67.93$\pm$31.89 | 0.78 Unpaired t test |
| Recovery time (minutes) | 112.42$\pm$17.58 | 99.38$\pm$27.94 | 0.06 Unpaired t test |

bioavailability. Thus in this study, dexmedetomidine with and without nalbuphine was compared through intranasal route via two different i.e. modes nasal drop and atomizer. In present study a dose of 2.5 $\mu$g/kg of dexmedetomidine was used, which was found to provide effective sedation. Similar, finding by Ibrahim(2014).[13] In the present study onset of sedation for group 1 with atomizer was 12.17$\pm$3.71 mins and with nasal drop 12.54$\pm$2.26 mins. On contrary to present study another study done by Talon (2009)[14] reported that onset of sedation of dexmedetomidine was 15 minutes when administered by a meter-dozed atomizer in a dose of 2$\mu$g /kg. In the present study, duration of action of group 1was 78.38$\pm$19.03 mins and in group 2 69.91$\pm$23.13 mins. Recovery time of group 1 was 116.60$\pm$20.90 mins and group 2 was 113.34$\pm$21.04 mins. This concludes that group 1and group 2 have comparable sedative efficacy. Similarly, in other study, done by Sury and Cole, (1988)[15] various doses of nalbuphine with midazolam administered intravenous, was compared for outpatient sedation. An interesting similar finding, by Shukry and Miller (2010) was also observed.[16] Therefore, we can say that Dexmedetomidine with and without nalbuphine administered by either an atomized device or nasal drop is safe and effective premedication for children. There was no significance difference in efficacy parameters between group 1 and group 2 which indicated that nalbuphine has no additional advantage over the effect of dexmedetomidine alone. In addition, dexmedetomidine offers an additional choice for the sedation of children receiving mechanical ventilation in the intensive care setting

**Table 5:** Comparison of time parameters between Group 1 and Group 2 irrespective of mode of administration

| Parameters | Group 1 (n=48) | Group 2 (n=48) | p-value |
|---|---|---|---|
| **Ease completion of Treatment** | | | |
| Good | 8(16.7) | 14(29.2) | |
| Fair | 24(50.0) | 22(45.8) | 0.31 Chi-square test |
| Poor | 16(33.3) | 12(25.0) | |
| **Acceptance of drug** | | | |
| Crying and struggling | 12(25.0) | 8(16.7) | |
| Struggling | 13(27.1) | 15(31.2) | 0.76 Chi-square test |
| Crying | 14(29.1) | 14(29.2) | |
| Quite | 9(18.8) | 11(22.9) | |
| **Adequate depth of sedation** | | | |
| No Sedation | 2(4.2) | 0(0.0) | |
| Minimal | 18(37.5) | 13(27.1) | 0.11 Chi-square test |
| Moderate | 22(45.8) | 21(43.8) | |
| Deep | 6(12.5) | 14(29.1) | |
| Onset of sedation (minutes) | 12.35±3.04 | 12.08±3.38 | 0.68 Unpaired t test |
| Duration of action (minutes) | 78.38±19.03 | 69.91±23.13 | 0.06 Unpaired t test |
| Recovery time (minutes) | 116.60±20.90 | 113.34±21.04 | 0.10 Unpaired t test |

or requiring procedural sedation. While dexmedetomidine is well tolerated when used at recommended doses, it has the potential to cause hypotension and bradycardia and requires close monitoring. [17]

## 5. Conclusion

In the given doses, dexmedetomidine alone as well as in combination with nalbuphine produced desirable sedative effects and comparable sedative efficacy with no additional advantage of combination over dexmedetomidinealone. The use of a commercially available atomizer showed improved patient's acceptance of intranasally administered drugs but did not influence efficacy as compared to drops.

## 6. Source of funding

None.

## 7. Conflict of interest

None.

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