



Evaluation of Intranasal Administration of Dexmedetomidine during Therapeutic Extraction

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Authors' contributions

This work was carried out in collaboration among all authors. Author SAX designed the study, carried out literature survey, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AW and MSK managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Aim: The purpose of this study was to evaluate the effectiveness of intranasal administration of dexmedetomidine during therapeutic extraction.

Materials and Methods: The study design is a split mouth double blinded randomized control trial. Patients who visited the department of oral and maxillofacial surgery for the therapeutic extraction of premolars were assessed for enrollment. Each subject participated in two surgical sessions, with the extraction of premolars of the upper and lower quadrant of the same side during a single session. A week later subjects were asked to report back for the extraction of the upper and lower premolar on the contralateral side. The patients were randomized by a computer generated number into two groups. Group A received intranasal dexmedetomidine (100 mcg/ml) and group B received intranasal saline at the first session. An alternate regimen was used during the second session during which group A received intranasal saline and in group B intranasal dexmedetomidine was administered. A mucosal atomization device was used to deliver the drug. Pain from local anesthesia infiltration was rated on the numerical rating scale from 0 (no pain) to 10 (worst pain imaginable). Sedation status was measured using the Observer's Assessment of Sedation. Blood pressure and heart rate of the patient were also monitored.

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Results: A total of 14 patients were involved in the study. Observer assessment scale indicated that significant sedation was obtained in group A when compared to group B. Compared to group B there was a significant reduction in heart rate and blood pressure in group A at the end of 10 minutes and 40 minutes. These parameters were normalized to the baseline at the end of 60 minutes. There was no significant difference in pain score noted during the local anesthesia infiltration. None of the patients had bradycardia, hypotension, and respiratory depression in this trial.

Conclusion: In this study, we conclude that the intranasal administration of dexmedetomidine controls the patient's fear and anxiety during the therapeutic extraction but not the pain during the administration of local anesthesia.

Keywords: Intranasal administration; dexmedetomidine; therapeutic extraction; observerssedation scale; local anesthesia.

1. INTRODUCTION

Prior to any surgical procedure, pain management is a vital protocol to be practiced. Effective pain management before a surgical procedure can significantly improve care and also can help in gaining the trust and the confidence of the patient. Cooperation of patients is of great importance in the field of surgery not just for the patients but for the surgeon also, anxiety for dental procedures and fear are common in children but it is also prevalent in adults. This is one of the prime factors which hinders patient cooperation.

Sedation is a common protocol practiced in dentistry in order to ease dental fear and anxiety [1]. Oral sedation is the most commonly followed protocol. Intravenous therapy is a gold standard for sedation. However intravenous sedative can be resource consuming for minor surgical procedures. Establishing an IV access can be painful and frightening for many patients [2]. The intranasal route is the most recent and noninvasive method in the administration of sedatives [3]. The advantages of intranasal administration include the patient's co-operation, better usage of the time, and resource. The nasal mucosa is highly vascularized and the olfactory tissue is in direct contact with the central nervous system. This allows the drugs to be rapidly transported into the bloodstream and the brain. Porous endothelial membrane, high total blood flow, surpassing of the first-pass metabolism, rapid onset and accessibility are factors that favor intranasal administration [4]. A study was done in our institute using the intranasal administration of dexmedetomidine during the therapeutic extraction of premolars.

The primary objective was to assess the efficacy of the drug in controlling the patients fear and

anxiety during the extraction of the premolars. With a rich case bank established over 3 decades we have been able to publish extensively in our domain [5-14]. Based on this inspiration we aim to evaluate intranasal administration of Dexmedetomidine during Therapeutic Extraction.

2. MATERIALS AND METHODS

After clearance from the institutional review board, a total of 14 patients who visited the outpatient Department of Oral and Maxillofacial Surgery, Saveetha dental college were screened and enrolled in this study. A written informed consent was obtained from all the patients. Patients were allocated into groups based on a computerized system. The inclusion criteria included all patients between the age group 18 - 30 years undergoing therapeutic extraction of all four premolars. Patients with ASA physical status 1 were only included in the study. Pregnant women, lactating mother, drug abusers and individuals with known allergy to dexmedetomidine, paracetamol and nonsteroidal anti-inflammatory drugs were excluded from the study. An intranasal atomization device was used to deliver drugs intranasally. A dosage of 100 mcg/ml of dexmedetomidine drug was administered intranasally. The primary outcome measured was the patient's response to sedation and the pain score during local anesthesia infiltration. A pulse oximeter was used to measure the heart rate and blood pressure.

2.1 Study Design

The patient and the operator were blinded. A split mouth study design was planned. Each subject participated in two surgical sessions, with the extraction of premolars of upper and lower quadrant of the same side during each session.

They were asked to report back one week later for the extraction of the upper and lower premolar on the contralateral side. The patients were divided into two groups by a computer generated number. Group A received intranasal dexmedetomidine and group B received intranasal saline at the first session. An alternate regimen was used during the second session during which those in Group A received intranasal saline and those in group B received intranasal dexmedetomidine.

The drug was administered intranasally half an hour before the procedure. The volume of the drug used was assessed. All the parameters were recorded only after thirty minutes of the administration of drugs. The pain score during the local anesthesia infiltration was recorded with the numerical rating scale. Observer's assessment of alertness/ sedation scale was used to assess the intranasal sedation status every 10 minutes of the procedure. Heart rate and blood pressure were recorded after every 10 minutes.

2.2 Statistical Analysis

Statistical analysis was performed with SPSS version 20,0. Numerical data were analyzed by an unpaired student t-test to detect the difference between both the groups.

3. RESULTS

A total of 14 patients were involved in this study out of which 7 were females and 7 males. Patients were observed for 90 minutes after the administration of intranasal dexmedetomidine. None of the subjects experienced anxiety at any point in the treatment. The observer assessment scale indicated that significant sedation was obtained in those administered with intranasal dexmedetomidine. Patients in Group A showed a significant difference in values at 10 minutes, 30 minutes and 40 minutes when compared to group B in the observer assessment scale of alertness/ sedation scale. There was also a significant reduction in heart rate and blood pressure in those receiving intranasal dexmedetomidine at 10 minutes and 40 minutes. These parameters were normalized to the baseline at the end of 60 minutes. There was no significant difference between both the study groups in relation to pain score during the local anesthesia infiltration. None of the patients in this trial had bradycardia, hypotension or respiratory depression.

4. DISCUSSION

In the dawn of the twentieth century, the FDA approved the usage of Dexmedetomidine as a short term medication for analgesia and sedation in the intensive care unit. It has a property to render analgesia and sedation during the whole perioperative period [15]. It is an alpha 2 - adrenoceptor agonist with dose-dependent alpha 2 adrenoceptor selectivity. It is a useful sedative agent that possesses analgesic properties, hemodynamic stability, and also has the ability to recover respiratory function in mechanically ventilated patients.

Literature suggests various uses of Dexmedetomidine which includes management of tetanus in ICU, as an antishivering agent. It can also be used as an adjunct in the repair of aortic aneurysms and in the treatment of withdrawal syndromes caused by alcohol, opioids, and recreational drugs.

Dexmedetomidine drugs can be given by the IV route however; this route of administration is considered to be invasive. Oral administration of Dexmedetomidine is associated with a poor bioavailability of 16% because of the extensive first-pass metabolism [16]. The double-blinded case controlled cohort studies have shown 1.0 microgram Kg⁻¹ is associated with a short duration of sedative effect [17]. In this study, we made use of 100 mg/ml of dexmedetomidine which was administered intranasally through a mucosal atomization device.

According to the study by Nooh and others [18], the among various extravascular routes of drug administration of dexmedetomidine, the intra nasal route has similar pharmacodynamics and sedative effect as I.V route. A mucosal atomization device was used to deliver the drug. A study has stated that intranasal administration of dexmedetomidine via an atomizer may produce sedation which directly affects the central nervous system. An animal study conducted revealed that a higher concentration of midazolam was present in the cerebrospinal fluid when administered in an atomized form intranasally than when applied by drops, this may be applied to dexmedetomidine [19].

This study did not indicate any significant difference between the two groups in the pain present during local anesthesia infiltration, as indicated by the numerical pain rating scale (Fig. 1). The patient responded similarly to LA

infiltration in both placebo and dexmedetomidine sessions. A study by Nooh [20] on third molar surgery also concluded with the same fact as in our study. Some studies revealed, this drug has an analgesic effect. The drug exerts its analgesic properties at the spinal cord and the supraspinal level. Analgesic effects of these alpha 2 agonists are mediated through alpha 2 receptors binding in the central and spinal cord alpha 2 receptors. The analgesic property of dexmedetomidine with a distinct focus on its effectiveness on peripheral analgesia is yet unclear and studies has to be done in near future to establish the exact mechanism. Based on the results obtained by randomized control trials opioid-dexmedetomidine combinations are considered safe and effective for post-operative, patient-controlled analgesia [21].

In this study, a sedation period of 50 minutes was observed in group A. The sedation effect commenced only after 10 minutes. All the patients easily aroused at the end of the sedation period. A sedation duration of 30 minutes was sufficient enough for the extraction of a premolar (Fig. 2). Literature states that the exact mechanism of the sedative effect of this drug is unknown. Unlike the existing sedative drugs such as propofol and benzodiazepines, dexmedetomidine doesn't act on the gamma-aminobutyric acid receptors instead they act on the alpha 2 receptors [22]. Dexmedetomidine acts on the locus coeruleus of the central nervous system, where it induces a state similar to natural sleep [23]. MekitarianFilho and others suggested that intranasal administration of

dexmedetomidine resulted in 1 - 2 hours of sedation with an onset time of 15- 45 minutes [24]. The lack of respiratory depression is the greatest advantage of this drug, enabling it to be frequently used as a sedative drug [25].

In our study, the vital status such as the heart rate and blood pressure were thoroughly monitored every 10 minutes (Figs. 3,4). The heart rate and blood pressure never decreased by 20% below the baseline. These parameters returned to their baseline by about 60 minutes of administration. The respiratory preserving property [26], analgesic sparing effect [27] and the lack of respiratory depression are factors that prevent the SpO₂ values from being significantly reduced compared to the baseline values.

Dexmedetomidine could result in cardiovascular depression which includes bradycardia and hypotension. In our study, these adverse effects were not noted in any of the participants. Aho et al stated that the incidence of postoperative bradycardia has been reported to be as high as 40% in patients who received a high dose of dexmedetomidine [28]. Several studies indicated that with the use of Dexmedetomidine clinically insignificant hemodynamic effects were observed [29]. Atrial fibrillation, hypoxia, nausea, hypertension were few other adverse effects noted with dexmedetomidine. Most of these side effects were reported during the intravenous administration, there were no such adverse effects observed with the intranasal use in the present study.

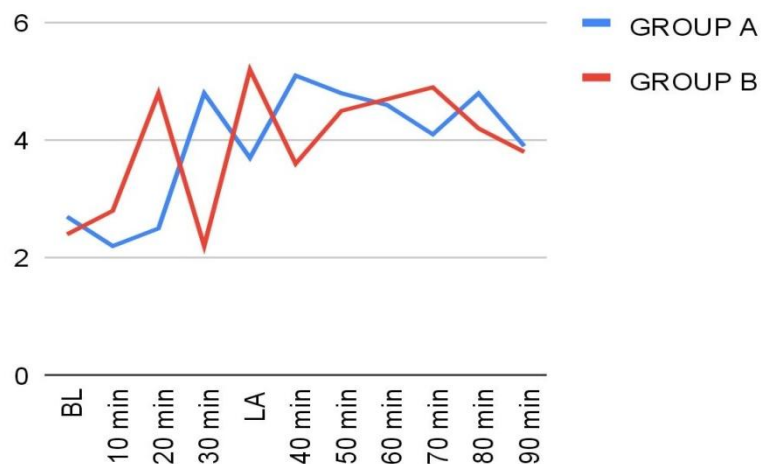


Fig. 1. This figure indicates the response to pain during local anesthesia infiltration. No significant difference was noted in pain during local anesthesia infiltration in both the groups(BL -Baseline , LA- Local Anesthesia)

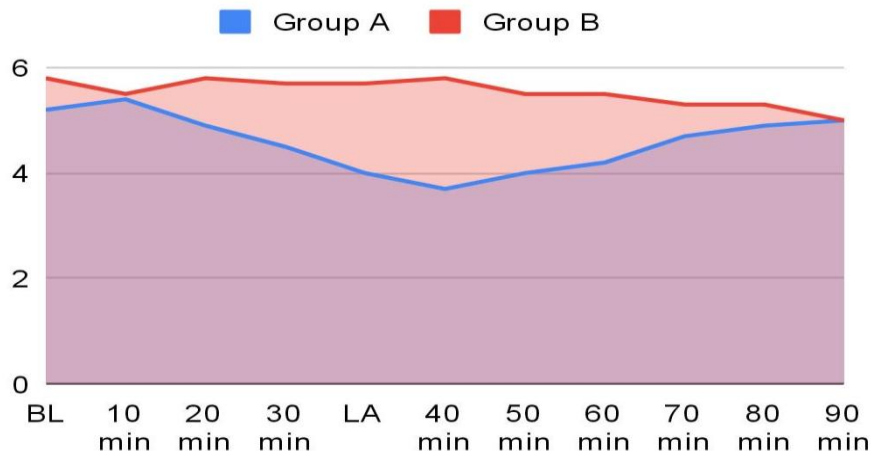


Fig. 2. Results of the Observer's Assessment of Sedation scale in a single session Group A (Intranasal administration of Dexmedetomidine) and Group B (Intra nasal saline) (BL- Baseline, LA- Local Anesthesia)

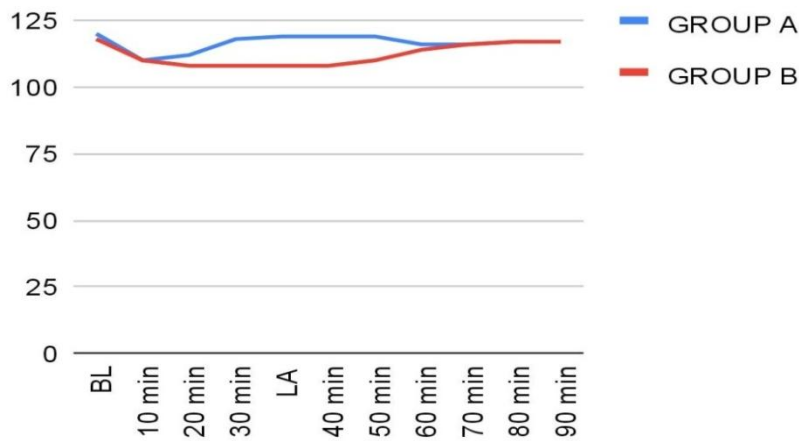


Fig. 3. Systolic blood pressure in Group A and Group B (BL-Baseline, LA- Local Anesthesia)

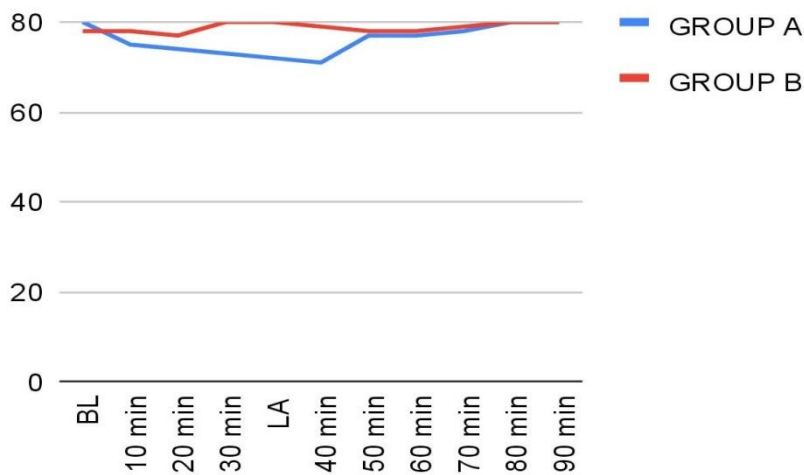


Fig. 4. Heart Rate in Group A and Group B (BL-Baseline, LA- Local Anesthesia)

Few Literatures states that dexmedetomidine is recommended as a sedative agent for dental procedures especially in patients with a high risk for respiratory depression and airway obstruction such as those obese patients and history of apnea patients [30]. Owing to its sedative, analgesic, safe respiratory profile along with its antisialagogue properties. Several prospective studies in dentistry is conducted using Dexmedetomidine [31]. The above findings are in consensus with the present study. It has been observed from various literatures, that the intranasal administration of dexmedetomidine (10-0 mg/ml) has helped in controlling the patient's fear and anxiety during the therapeutic extraction of premolars.

5. CONCLUSION

The results from this study highlighted on the fact that pain during the infiltration of local anesthesia were not significantly altered when dexmedetomidine was administered. The sedative effect of dexmedetomidine lasted for a duration of 50 minutes. The participants did not face any difficulty in arousal at the end of the sedation period. There were no significant changes noted in the heart rate and blood pressure of the patient. The major adverse effect of this drug is bradycardia and hypotension. Fortunately, these adverse effects were not observed in any of the participants. In this study, we conclude that the intranasal administration of dexmedetomidine has significant role in controlling the patient's fear and anxiety during the therapeutic extraction but not the pain during the administration of local anesthesia.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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