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ORIGINAL ARTICLE

A Comparative Study Evaluating the Efficacy of Lignocaine and Dexmedetomidine with Lignocaine and Adrenaline in Third Molar Surgery

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Abstract

Aim The aim of this study was to compare the anesthetic efficacy, duration of action, pain, and cardiovascular effects of dexmedetomidine when added to 2% lignocaine hydrochloride in bilateral symmetrical impacted third molars.

Materials and Methods This study comprised of 40 healthy patients who required extraction of identical bilateral impacted lower third molars. The left side of the patients was designated as test side where patients received local anesthesia with lignocaine plus dexmedetomidine (2% lignocaine + dexmedetomidine 1 μ/ml), and the right side of the patients was designated as control side where patients received local anesthesia with lignocaine plus adrenaline (2% lignocaine in 1:80,000 adrenaline). Both surgical interventions were performed at two different appointments with a minimum time interval of 2 weeks. The time to onset and duration of action were noted as primary outcome variables, while the secondary outcome variables included pain and hemodynamic changes associated with dexmedetomidine if any.

Results Onset of action of the local anesthesia was found to be faster in addition to having a relatively longer duration of action when the newer drug dexmedetomidine was added to lignocaine when compared with the conventional combination of lignocaine and adrenaline ($P < 0.05$). There were no significant changes in the systolic blood pressure, diastolic blood pressure, and heart rate from the baseline following the injection of dexmedetomidine.

Conclusion The study demonstrated that the combination of dexmedetomidine with lignocaine enhances the local anesthetic potency of lignocaine without significant systemic effects when locally injected into oral mucosa.

Keywords Dexmedetomidine · Lignocaine · Local anesthesia

Introduction

It is a well-known fact that the success of any minor oral surgical intervention relies predominantly on the efficiency of the local anesthetic agent and the anesthetic technique employed by the operator [1]. Ideally, a local anesthetic with an extended duration of action, good analgesia, and negligible systemic toxicity is the requisite [2]. Conventionally, 2% lignocaine hydrochloride with adrenaline (1:80,000) is used. The addition of adrenaline limits the use of this local anesthetic solution in patients with cardiovascular compromise. Hence, the quest for a local anesthetic with minimal cardiovascular risk to provide regional anesthesia for minor surgical interventions continued.

Dexmedetomidine is a highly selective alpha2 adrenoceptors (α2-AR) agonist recently introduced to anesthesia

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practice. It produces dose-dependent sedation, reduces anxiety, and causes analgesia without respiratory depression [3]. A recent study has revealed that dexmedetomidine has a weak amnestic action. It also stated that since the vasodilating effect of lidocaine is greater than the vasoconstrictor effect of dexmedetomidine, lidocaine with a vasoconstrictor should be used during oral surgical interventions when dexmedetomidine is employed [4]. Since an intravenously administered dexmedetomidine induces sedation in patients and occasionally influences the cardiovascular system and causes hypotension and bradycardia, the use of dexmedetomidine as an adjunct to local anesthetic may exert its effect with minimized systemic effects [5].

The hemodynamic changes associated with the drug do not exceed 20% of baseline, and they returned to normal base values after about 60 min [6]. A recent study used dexmedetomidine to perform an oral surgical intervention under local anesthesia with dexmedetomidine sedation in a morbidly obese patient with aortic dissection and advocated that dexmedetomidine enables to plan and safely perform oral surgical procedures associated with very high risk particularly those which might not have been possible without sedation [7]. The primary objective of this study was to evaluate the beneficial effects of dexmedetomidine when combined with lignocaine in third molar surgery. Hence, this study aimed to compare the anesthetic efficacy, duration of action, pain, and cardiovascular effects of dexmedetomidine when added to 2% lignocaine hydrochloride in bilateral symmetrical impacted third molars.

Materials and Methods

This was a comparative study comprising of 40 healthy patients belonging to the age group of 20 and 30 years who were diagnosed clinically and radiographically with bilateral symmetrical impacted lower third molars necessitating their surgical removal between the periods of January 2019–February 2020. The Institutional Ethical Committee approved was obtained (KIMS/KIIT/IEC/02/2019). A diagnostic criterion was an OPG. The left side of the patients was designated as test side where patients received local anesthesia with lignocaine plus dexmedetomidine (2% Lignocaine + dexmedetomidine 1 μ/ml), and the right side of the patients was designated as control side where patients received local anesthesia with lignocaine plus adrenaline (2% lignocaine in 1:80,000 adrenaline). Both surgical interventions were performed at two different appointments with a minimum time interval of 2 weeks. The study drug was prepared by addition of 30 μ of dexmedetomidine using appropriate dilution with insulin syringe to 30 ml vial of 2% lignocaine plain solution under the guidance of an anesthesiologist.

Patients with bilateral symmetrical impacted lower third molars with a similar difficulty index and were not associated with any acute infection or any other systemic problems were included in the study. Patients were excluded if they gave a history of an allergy or hypersensitivity to lignocaine or dexmedetomidine; if they had any coexisting cardiac or neurological diseases or were immunocompromised; if they were pregnant or lactating; or if they were taking central nervous system depressants or any other analgesics preoperatively.

Consent of the patients was obtained before beginning the procedure. The same surgeon operated on all the patients. All patients received intradermal dexmedetomidine as a test dose. The visual analogue score (VAS) was explained preoperatively, and patients were instructed to inform as soon as the lip and tongue became numb. A classic inferior alveolar and long buccal nerve block was given using a sterile luer lock disposable syringe (3 ml), and a standard surgical technique was used to remove the teeth. Postoperatively patients were given a treatment regimen of antibiotics (amoxicillin + clavulanic acid) and analgesics (diclofenac) for 5 days. They were instructed not to take any analgesics until the lip and tongue were no longer numb. All patients were admitted for 24 h for hourly observations to note any hemodynamic changes if present. The surgical interventions adhered to the ethical guidelines of Declaration of Helsinki.

The volume of the drug used, the need for reinforcement, the time to onset of action, and the duration of action were noted. Primary outcome variables in the form of intensity of pain and depth of anesthesia were assessed subjectively using a VAS that ranged from 0 = no pain to 10 = the worst pain imaginable. Secondary outcome variable included hemodynamic changes (blood pressure and heart rate) which were monitored throughout the procedure, and a calculated amount of saline was used during all procedures. The residual amount of blood collected after excluding the saliva content (roughly usually 30 ml, considering the fact that 1.5 L/day is secreted in healthy individuals) and saline, in the manual suction was counted as blood loss. Gauze or absorbent swabs were not used during the procedure. Any postoperative complications such as paresthesia and trismus were also recorded.

Statistical Methods: The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Data were expressed as Mean ± SD. Student's independent *t* test was employed to compare onset of action and duration of action between two groups. A P value of less than 0.05 was considered statistically significant.

Results

This study included 40 healthy patients aged between 20 and 30 years who required prophylactic (n = 18, 10 men and 08 women) and symptomatic (n = 22; 09 men and 13 women) removal of bilateral symmetrical impacted lower third molars. Bilateral symmetrical impacted lower third molars that demonstrated a moderate difficulty index were included in this study. All 40 patients were given equal amounts of drug on either side (2 ml for the inferior alveolar and lingual nerve block, and 0.5 ml for the long buccal nerve block). The duration of the procedure ranged from 30 to 45 min. Onset of action was found to be shortened significantly for dexmedetomidine group with prolonged duration of action ($P < 0.05$). It was observed that the pain threshold was noticeably increased following the injection of lignocaine plus dexmedetomidine solution when compared with lignocaine plus adrenaline. There were no significant changes in the systolic blood pressure, diastolic blood pressure, and heart rate from the baseline following the injection of dexmedetomidine. None of the patients included in this study encountered postoperative trismus or postoperative paresthesia of inferior alveolar nerve or lingual nerve following surgical removal of third molars in either of the sides. The rest of the results are shown in Table 1.

Discussion

Numerous studies have been carried out in the past in the quest to increase the duration of action of the local anesthetic along with reducing the systemic toxicity. Commonly used adjuvants include non-opioids like epinephrine, alpha-2 agonist clonidine, nonsteroidal anti-inflammatory drugs, $Mg2+$, and $NaHCO_3$ and opioids like fentanyl, sufentanil, and morphine [8]. However, most of them were invariably associated with some adverse effects.

Epinephrine is conventionally used as an additive to local anesthetics [9]. When administered in high doses, it can cause tachycardia and hypertension. Epinephrine compromises endoneurial blood flow and increase neurotoxicity, particularly in the setting of diabetic animal models, arguing against its use in patients with diabetic peripheral neuropathy [10]. In animal models of spinal anesthesia and sciatic nerve block, dexmedetomidine did not show toxicity and was potentially neuroprotective when combined with lignocaine and bupivacaine [11]. Hence, based on the available literature dexmedetomidine appears to be a viable option as an additive to local anesthetics, especially where bradycardia and hypotension is an issue.

Dexmedetomidine, a selective alpha-2 adrenoceptor agonist, with sedative, analgesic, anxiolytic, sympatholytic, and opioid-sparing properties is routinely used intravenously as a sedative in intensive care unit and for procedural sedation [12]. The addition of dexmedetomidine to

Table 1 Mean observations made before the procedure, during the first 15 min and after the procedure (n = 40 in each group)

	Lignocaine + Dexmedtomidine	Lignocaine + Adrenaline	P value
Onset of action (sec)	138	95	< 0.001
Duration of action (min)	132	70	< 0.001
VAS	3	4	< 0.001
Blood loss (ml)	8	10	< 0.001
Preoperative BP:			
Systolic	122	122	0.85
Diastolic	81	81	0.80
Intraoperative BP (first 15 min):			
Systolic	110	135	< 0.001
Diastolic	74	82	0.60
Postoperative BP:			
Systolic	121	120	0.86
Diastolic	80	80	0.90
Heart rate:			
Preoperative	84	84	0.74
Intraoperative (first 15 min)	73	97	< 0.001
Postoperative	83	85	0.91

**VAS* visual analogue scale, **BP* blood pressure, **ml* milliliters, * *sec* seconds *, *mins* minutes

local anesthetics has been employed for spinal and nerve blocks, and the beneficial effect of dexmedetomidine on local anesthetic action has been demonstrated [13–15]. Considering the fact that an intravenously administered dexmedetomidine induces sedation in patients and occasionally influences the cardiovascular system by causing hypotension and bradycardia, the safe use of dexmedetomidine as an adjunct to local anesthetic in minor oral surgical procedures needs thorough evaluation [16, 17].

Dexmedetomidine does not appear to have any direct effects on the heart [18]. It shows a biphasic response where there is an initial transient increase of the blood pressure and a reflex decrease in heart rate, especially in younger healthy individuals [19]. The initial response lasts for 5–10 min and is followed by a decrease in blood pressure below baseline and a stabilization of the heart rate, also below baseline values [20]. Dexmedetomidine undergoes almost complete biotransformation through direct glucuronidation and cytochrome P450 metabolism, all hepatic processes, with very little excretion of unchanged molecules in the urine or feces [17]. Metabolites of biotransformation are excreted in the urine. The elimination half-life is approximately 2 h [17].

The results of this study show that the onset and duration of effective anesthesia were considerably longer when dexmedetomidine is added to lignocaine than that of the conventional 2% lignocaine with adrenaline. These are in accordance with previous studies which showed that addition of dexmedetomidine to local anesthetic agents increases the onset and duration of action [13–15, 21]. Postoperative pain after third molar surgery usually reaches its maximum intensity within 6–8 h of operation as a result of the release of chemical mediators and are governed by numerous factors like the flap design, duration of surgery, and the cutting tool used [22, 23]. Literature shows that dexmedetomidine also provides intense analgesia during the postoperative period and that the postoperative analgesic requirements were reduced by 50% [24]. The results of this study are in accordance with previous studies. It was observed that the VAS score was lesser on the test side than the control side. During the postoperative period, the anesthetic effect starts fading off leading to a gradual increase in the perception of pain. This study assessed pain as an individual entity and did not relate it to other perceptions such a proprioception, temperature, and pressure, so the total duration of anesthesia and onset of pain during the postoperative period are not comparable. Considering the fact that it is a comparative evaluation, this study highlighted the fact that patients experienced some degree of sedation with dexmedetomidine which results in patients experiencing less pain during the procedure. Hence, in comparison with lignocaine + adrenaline, lignocaine + dexmedetomidine when injected to patients cause less pain to the patients during the surgical intervention. VAS score is a reflection of this hypothesis.

All local anesthetics currently available for dental use have some vasodilating activity. Adrenaline decreases the blood flow at the site of injection thereby decrease the rate of absorption, lower systemic blood flow, and reduce the incidence of systemic reactions to lignocaine [2]. However, the reduction of the blood pressure caused by dexmedetomidine compensates the effects of adrenaline. The decrease in cardiac output and the increase in systemic vascular resistance seen in response to dexmedetomidine do not seem to be related to a decreased contractility, relaxation, or intracellular calcium-channel block [18]. Instead, the hemodynamic changes can be attributed to the dexmedetomidine induced bradycardia, $\alpha 2$-adrenergic stimulation, and a decrease in oxygen requirements [25]. The blood loss encountered was easily manageable without any adjunctive procedures. The discomfort experienced by the patients was also less since adrenaline which reduces the pH of the solution was not used [2].

With regard to the hemodynamic changes, there was a transient increase in the systolic blood pressure and heart rate immediately after the administration of lignocaine with adrenaline. This transient increase can lead to arrhythmias in patients with compromised cardiovascular system. The effect of dexmedetomidine on hemodynamics remained relatively constant, with a mild transient increase in the second interval during the operation [16, 21]. These cardiovascular changes could probably be related to the surgical intervention and not as a result of dexmedetomidine.

Patients included in this study did not encounter any adverse effects with dexmedetomidine, but experienced efficient anesthesia and excellent residual analgesia with no cardiovascular or central nervous system complications. So, it is justified that dexmedetomidine is clinically useful as an additive to local anesthetics for enhancing local anesthesia for minor oral surgical procedures.

Based on the results of this study, it can be concluded that this combination can be used in routine dental setup and does not require a hospital setup. Evaluation of the plasma concentration would give more details about its effects on the cardiovascular system, as this study was confined only to evaluate the hemodynamic changes. The limitations of this study include lack of randomization and blinding in the study design. In addition to this, conducting the study on a small sample size and restricting the study design to only moderately difficult impacted tooth removals are the other notable limitations. Dexmedetomidine should further be used on larger samples in various other clinical scenarios pertaining to the scope of oral & maxillofacial surgery to evaluate its efficacy and versatility.

Conclusion

The results of this study show that dexmedetomidine produces sedation, analgesia, reduction in the blood pressure and bradycardia when combined with a local anesthetic agent which results is beneficial clinical effects when combined with lignocaine. The findings in our study suggest that dexmedetomidine is clinically useful as an additive to local anesthetics for enhancing local anesthesia for minor oral surgical procedures.

Compliance with Ethical Standards

Conflict of interest None.

Consent Patient consents obtained.

Ethical Approval Institutional ethical clearance obtained.

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