DOI: 10.7860/JCDR/2023/61356.17650

Research Protocol

Dentistry Section

Efficacy of Lignocaine Hydrochloride with Adrenaline, Clonidine and Dexmedetomidine for Surgical Removal of Impacted Mandibular Third Molar: A Research Protocol for a Randomised Clinical Trial

AKASH YOGESH DOSHI[1], NITIN DHARMPAL BHOLA[2]

ABSTRACT

Introduction: In human dentition, the most common impacted teeth are Mandibular Third Molars (M3M). Removal or extraction of these teeth leads to anxiety in the patients oweing to the perception of pain. Thus, pain control mechanism like anaesthesia needs to be executed appropriately. Using newer local anaesthetic drugs minimises side-effects and drug interactions. Adrenaline is traditionally used vasoconstrictor along with Lignocaine. Dexmedetomidine and Clonidine are alpha agonists which in combination with Lignocaine provide a prolonged duration of anaesthesia thus decreasing the need for rescue analgesics.

Need of the study: This research will assist in assessing and establishing the duration of anaesthesia and postoperative analgesia after the administration of lignocaine hydrochloride with adrenaline, clonidine and dexmedetomidine in third molar surgery. This will eventually lead to less consumption of analgesics owing to the delay in ingestion of rescue analgesics.

Aim: To evaluate and compare the safety and efficacy of adrenaline, clonidine and dexmedetomidine as an adjuvant to lignocaine hydrochloride for perineural inferior alveolar nerve block in cases of Impacted Mandibular Third Molars (IM3M) surgeries.

Materials and Methods: This is a prospective, triple-blind, randomised, controlled, parallel arm study. The study will be conducted at the Department of Oral and Maxillofacial Surgery, Sharad Pawar Dental College and Hospital, Sawangi (M), Wardha, India, from February 2023 to June 2024. A total of 45 consecutive systemically healthy patients requiring unilateral surgical extraction of impacted M3M with similar orientations will be divided into three groups randomly. The first group will receive lignocaine with adrenaline, the second group will receive lignocaine with clonidine and third group will receive lignocaine with dexmedetomidine during the extraction procedure which will be compared on following parameters like the onset of anaesthesia, depth of anaesthesia, haemodynamic parameters and duration of postoperative analgesia. 'One-way Analysis of Variance (ANOVA)' will be used to analyse and evaluate.

Keywords: Epinephrine, Impacted lower third molars, Precedex and catapres, Xylocaine

INTRODUCTION

Third molar surgery is the most frequently performed surgical procedure by Oral and Maxillofacial Surgeons [1]. The surgical extraction of the Impacted Mandibular Third Molars (IM3M) frequently results in considerable postoperative discomfort. Irrespective of its status of impaction complete or partial, it has been well-acknowledged that these are associated with several complications including regional pain, pericoronitis, dental caries, periapical abscess, trismus, cysts and tumours. Early removal of such impacted teeth to prevent complications is a widely accepted dental practice. The surgical extraction of IM3M creates a considerable amount of insult to soft and hard bony tissue surrounding the tooth resulting in significant inflammatory reaction leading to complications, like pain, oedema and trismus that unfavourably effects physical, functional and psychological well-being that bear direct repercussions over patients' quality of life [2-4].

Pain management is key to any successful surgical procedure. It is defined as "an unpleasant sensory and emotional experience linked to or defined in terms of tissue destruction, whether actual or potential" [5]. It is a complex, personal and perceptual experience involving all domains of an individual life. It is a subjective phenomenon varying from individual to individual and differing in the same individual at different times [6]. The commonly practiced modalities to alleviate pain are use of analgesics, corticosteroids, enzymes, muscle relaxants, improved instrumentation, closure techniques, various irrigant solutions, cryotherapy, physiotherapy, ozone therapy and Low Level Laser Therapy (LLLT). In general practice, pain is generally controlled through a variety of approaches, including removing the cause, blocking the pain impulse channel, elevating the pain threshold, and cortical depression, which inhibits pain perception [7]. Pre-emptive analgesia can be administered through various methods such as: by injecting local anaesthesia resulting in the prevention of nociceptors, by Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) resulting in the inhibition of inflammation and peripheral sensitisation. A successful combination of these techniques may be able to alleviate postoperative discomfort [8,9].

Local anaesthetic agents are the main tenets in the management of pain control in dentistry and they act by preventing the transmission of pain impulse to the Central Nervous System (CNS), where it gets interpreted as such. The history for local anaesthetics started with the invention of cocaine, by Niemann [10]. Lignocaine is conventionally used local anaesthetic having intermediate duration of action. Lignocaine has shown dose dependent side-effects as high plasma levels can be induced by an overdose, quick absorption, or an unintentional intravascular injection, or they can be caused by a patient's hypersensitivity, idiosyncrasy, or decreased tolerance. Dose dependent side-effects of lignocaine constitute hypertension,

tachycardia, arrhythmia, headache, drowsiness and dizziness. Multitude of studies demonstrated to overcome the limitations and new adjuvants was derived [11].

An adjuvant is a drug, another substance, or a mixture of chemicals that is used to boost the efficacy or potency of a drug. Various adjuvants such as vasoconstrictors, opioids, and alpha-2 agonists have been utilised to lessen the chance of local anaesthetic side-effects and extend the duration of intraoperative and postoperative analgesia [12].

Clonidine, alpha-2 adrenergic agonist acts as a central and peripheral agonist for lowering anxiety. Central stimulation of the presynaptic alpha-2 adrenoreceptor lowers blood pressure and cause mild sedation. The activation of postsynaptic alpha-2 adrenoreceptors causes vasoconstriction of peripheral blood arteries. Clonidine has also been shown to release enkephalin-like compounds, which have a peripheral analgesic effect. It acts by stabilising the membrane, affecting neurons. However, the exact mechanism is still unknown. Studies have demonstrated by combining clonidine with lignocaine to treat neurological deficit to produces effective analgesia [13]. Brummett CM and Wagner DS have shown an increased duration of anaesthesia when combined with short and intermediate local anaesthetics [14].

Dexmedetomidine is an agonist for the alpha-2 adrenergic receptor that is extremely selective. Dexmedetomidine effects of hypnosis and supraspinal analgesia are mediated by noradrenergic neuron hyperpolarisation, which reduces neuronal firing in the locus ceruleus while also inhibiting norepinephrine release. This inhibition of inhibitory control increases neurotransmitters that reduce histamine release resulting in hypnosis that resembles normal sleep without ventilatory depression. It has neuroprotective properties and reduces postoperative pain without producing cardiorespiratory depression, allowing for faster neuromuscular recovery and sedation. It has a modulation that protects the heart. It extends the duration of local anaesthetics' sensory block [15]. It has also shown its efficacy in providing analgesia in the postpartum period [16].

Previous studies suggest the comparison and evaluation of two drugs as adjuvants to lignocaine [13,16,17]. As per our knowledge, there is a lacuna in available literature regarding the comparison between adrenaline, clonidine and dexmedetomidine when used as an adjuvant to lignocaine hydrochloride for perineural inferior alveolar nerve block for IM3M surgeries. To the best of our knowledge, no earlier studies attempted to evaluate and compare the effects of adrenaline, clonidine and dexmedetomidine along with lignocaine hydrochloride on onset and depth of anaesthesia, haemodynamic parameters and postoperative analgesia in lower third molar surgery. Thus, in the present study comparison of anaesthetic efficacy among two alpha-2 agonists i.e., clonidine and dexmedetomidine and adrenaline as additive will be done to analyse the postoperative analgesia following the removal of IM3M. Similar studies have been demonstrated in upper limb surgery and have shown better anaesthetic efficacy of dexmedetomidine as compared to clonidine [18,19].

The aim of the study is to evaluate and compare the safety and efficacy of adrenaline, clonidine and dexmedetomidine as an adjuvant to lignocaine hydrochloride for perineural inferior alveolar nerve block in cases of IM3M surgeries.

The objectives of the study:

- To evaluate and compare the time of onset of mandibular anaesthesia following classic inferior alveolar nerve block with Lignocaine hydrochloride with adrenaline, clonidine and Dexmedetomidine.
- To evaluate and compare the depth of anaesthesia following classic inferior alveolar nerve block with Lignocaine hydrochloride with adrenaline, clonidine and Dexmedetomidine.
- To evaluate and compare the duration of postoperative analgesia with lignocaine hydrochloride with adrenaline, clonidine and dexmedetomidine.
- To evaluate and compare the haemodynamic changes associated with the use of Lignocaine hydrochloride with adrenaline, clonidine and dexmedetomidine.

REVIEW OF LITERATURE

Pain control after M3M surgery has been a challenge due to the variable amount of inflammatory response. There is a continual burgeoning search for a pharmacological agent with optimal therapeutic efficacy and minimal side-effects. The present study is deliberated to compare and evaluate the anaesthetic efficacy of dexmedetomidine, clonidine and adrenaline in IANB for surgical removal of M3M. In the present study, authors will be selecting a homogenous sample having well-controlled determinants of postoperative pain and inflammation in the extraction of M3M, viz., age, gender, asymptomatic, similarly oriented M3M, surgeon's experience and the quantity of the local anaesthetic used [20].

Epinephrine is conventionally used as an additive to local anaesthetics. 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 [21]. In animal models of spinal anaesthesia and sciatic nerve block, dexmedetomidine did not show toxicity and was potentially neuroprotective when combined with lignocaine and bupivacaine. Hence, based on the available literature dexmedetomidine appears to be a viable option as an additive to local anaesthetics, especially where bradycardia and hypotension is an issue [21].

Dexmedetomidine is a promising pharmacologically active dextro-isomer of medetomidine that shows specific and selective α2 adrenoceptor agonism. Clinically, it not only prolongs the duration of anaesthesia but also helps reduce anxiety and induce arousable sedation and analgesia [22]. When used as an adjunct to local anaesthetic shortens the latency period and prolongs the duration of local anaesthetic, maintains homeostasis which induces haemostasis and helps to provide better subject satisfaction [22].

Clonidine, alpha-2 adrenergic agonist acts as a central and peripheral agonist for lowering anxiety. Central stimulation of the presynaptic alpha-2 adrenoreceptor lowers blood pressure and causes mild sedation [23]. The activation of postsynaptic alpha-2 adrenoreceptors causes vasoconstriction of peripheral blood arteries. Clonidine has been shown to release enkephalin-like compounds, which have a peripheral analgesic effect. It acts by stabilising membrane, affecting neurons. However, the exact mechanism is still unknown. Studies have demonstrated by combining clonidine with lignocaine to treat neurological deficits to produces effective analgesia [24].

Dcruz TM et al., conducted the study which a group of 40 healthy people who needed their lower third molars out because they were impacted on both sides [16]. One side of the patients were assigned as the test side, with lignocaine with dexmedetomidine (2% lignocaine+dexmedetomidine 1 μg/mL) as the local anaesthetic, whereas other side was assigned as the control side, with lignocaine with adrenaline as the local anaesthetic (2% t lignocaine in 1:80,000 adrenaline). Both surgical extractions were done over for atleast two weeks in two consecutive appointments. The onset of action and duration of action were the primary outcome variables, while pain and haemodynamic changes associated with the action were secondary outcomes. When the alpha-2 agonist drug dexmedetomidine was used as an adjuvant to lignocaine, the local anaesthetic was found to have a quicker time to action as well as a longer duration of effect (p-value <0.05) when assessed to the classic combination of lignocaine and adrenaline. Following the injection of dexmedetomidine, in comparison to baseline, there

was no substantial difference in cardiovasular haemodynamic parameters. When lignocaine is injected locally into the oral mucosa, combining dexmedetomidine and lignocaine boosts the local anaesthetic power of lignocaine without creating significant systemic effects, according to the study.

Rajkumar V et al., assessed the effectiveness of clonidine as a vasoconstrictor replacement [13]. This was done on ten individuals who were having bilateral third molar operations. In comparison to the epinephrine group, the haemodynamic alterations in the clonidine group were steady, and the postoperative analgesic impact was better in the epinephrine group. The study concluded that clonidine, when added to the local anaesthetic solution, stabilises haemodynamic parameters while also lowering anxiety. In terms of haemodynamic parameters and commencement of action, however, there was little change.

Chatrath V et al., conducted a study on sixty patients receiving upper limb surgery [18]. Intravenous (i.v.) regional anaesthesia was achieved using 3 mg/kg 0.5 percent lignocaine diluted with saline to a total volume of 40 mL, to which 1 µg/kg clonidine in group 1 and 1 µg/kg dexmedetomidine in group 2 were added. All demographic data variables, operation time, and during and after surgery haemodynamic variables were all identical in both groups. According to the findings, combining 1 µg/kg clonidine or 1 µg/kg dexmedetomidine with 3 milligram/kilogram 0.5 percent lignocaine is efficacious, equivalent in terms of sensory and motor blockage onset and recovery, and haemodynamically stable and free of side-effects and problems.

Pachore PJ et al., conducted a study in bier block to assess the effects of clonidine added to lignocaine vs. dexmedetomidine added to lignocaine [19]. Forty ASA I and ASA II subjects who were scheduled for upper limb surgery were given lignocaine with either dexmedetomidine (Group-D) 1 µg/kg or clonidine (Group-C) 1 µg/kg. The number of subjects needing analgesia and the quantity ingested were considerably lesser in the Group-D (0 percent and 0 µg/kg, respectively) than in the Group-C (40 percent and 27±43 µg/kg, respectively) intraoperatively. The number of patients seeking analgesia and the amount ingested were considerably lower in the Group-D (5 percent and 2.5±11 µg), respectively, when compared to the Group-C (35 percent and 32±24.5 µg) and the Group-D (5 percent and 2.5±11 µg). The quality of anaesthesia in the Group-D was considerably higher than in the Group-C. During the brief postoperative period, patients in the Group-D were more sedated. According to the findings, in Bier's block, adding dexmedetomidine to lignocaine is preferable to adding clonidine.

Tilkar Y et al, conducted a study to determine equipotent dosages and compare the efficacy of two 2 agonists, clonidine and dexmedetomidine, as adjuvants in supraclavicular block [24]. Ninety subjects from the American Society of Anaesthesiologists (ASA) I and II, ranging in age from 20 to 50 years, were divided into three groups for elective upper limb procedures under supraclavicular block: Bupivacaine 0.5 percent 15 mL injection+injection was given to Group-N. A 15 mL lignocaine with 2% adrenaline+0.5 mL normal saline 1 µg/kg dexmedetomidine in Group-D. In Group-C, instead of normal saline, 1.5 µg/kg clonidine was used as the study medication. Onset, sensory and motor blockade duration, duration of analgesia, VAS score, haemodynamics, sedation, and other side-effects are all factors to consider. Postoperative VAS was found low in dexmedetomidine group.

MATERIALS AND METHODS

This parallel arm, triple blind, randomised clinical trial (CTRI No. CTRI/2022/12/048281) was conducted at the Department of Oral and Maxillofacial Surgery, Sharad Pawar Dental College and Hospital, Sawangi (M), Wardha, India, from February 2023 to June 2024. The Ethical clearance was obtained on 15/02/2022 by the Institutional Ethical Committee (IEC) of Datta Meghe Institute of Medical Sciences; Ethical approval number is Ref.No.DMIMS(DU)/IEC/2022/776. After receiving a written consent for the procedure from the patient, the patient will be taken up for the surgery and prepared according to the protocols.

The sample size was calculated with Statistical Package for the Social Science (SPSS) 27.0V, GraphPad Prism 7.0V. A total of 45 consecutive systemically healthy patients requiring unilateral surgical removal of IM3M with similar difficulty (moderate to very difficult according to Modified Pederson's Index) will be selected [25].

Inclusion criteria:

1. Individuals with ASA I status.
2. Individuals between 18 to 40 years.
3. Presence of atleast one asymptomatic IM3M having moderate to very difficult, difficulty index (Modified Pederson's Scoring).

Exclusion criteria:

1. History of drug dependence.
2. Patients with systemic disease such as hypertension, diabetes, blood dyscrasias, immunocompromised status.
3. Chronic smokers.
4. Patients on cardio-selective antihypertensive drugs.
5. Patients with allergy to local anaesthetic agents used in the study.
6. Pregnant and nursing mothers.
7. Females on oral contraceptives.
8. Patients undergoing treatment with antibiotics, anti-inflammatory drugs.
9. Presence of any local infection like pericoronitis/pterygomandibular space infection.
10. Presence of any chronic facial pain on the side of intervention.
11. Radiologic evidence of inferior alveolar canal approximation.
12. Patients with congenital heart disease.
13. Patients with any psychiatric illness.

Methods: Assignment of interventions (for controlled trials)

- **Allocation:** Computer generated table of random numbers will be used to allocate study population equally into three different groups (n=15).
- **Implementation:** Independent observer.
- **Blinding (masking):** Triple Blinding.

A total of 45 consecutive systemically healthy patients requiring unilateral surgical removal of IM3M with similar difficulty (moderate to very difficult according to Modified Pederson's Index) from February 2023 to June 2024 are to be included in the study.

Simple Randomisation of 45 patients will be done into three groups based on electronically generated table of random figures in a sealed opaque envelope (n=15 each) irrespective of age, gender and type of impaction.

Group A: Subjects (n=15) requiring impacted third molar surgery with 2% lignocaine hydrochloride with 1:1,00,000 adrenaline as the local anaesthetic agent.

Group-B: Subjects (n=15) requiring impacted third molar surgery with 2% lignocaine hydrochloride with 15 µg/mL clonidine [17] as the local anaesthetic agent.

Group-C: Subjects (n=15) requiring impacted third molar surgery with 2% lignocaine hydrochloride with 1 µg/mL dexmedetomedine [26] as the local anaesthetic agent.

Procedure

All the subjects will be asked to gargle with 2% w/v betadine solution 10 minutes prior to the start of the procedure. Surgical site will be prepared under standard aseptic conditions by applying over the perioral region with 7.5% betadine solution the site of

injection to be administered will be dried by using a cotton gauze. All the nerve blocks and surgical procedure were administered by a single experienced surgeon. IANB will be administered using Fischer 123 method.

IANB will be said to be successful when the patient experienced numbness along the distribution of the inferior alveolar nerve. This will be objectively confirmed by using a blunt moons probe. Ward I/Modified Ward's I incision will be given in all subjects. A sharp tip of periosteal elevator will be used to reflect the full thickness mucoperiosteal flap in the sub-periosteal plane, without breaching the periosteum. The mucoperiosteal flap will be retracted by using Austin's retractor providing good access and preventing its injury from burs and instruments. Once the mucoperiosteal flap reflected, tooth will be exposed and the bone partly encasing the crown of the LITM will be removed by making an outline through the round bur (No: 702) around tooth and the bone guttering done by a fissure bur (No: 701).

During bone guttering copious 0.9% saline irrigation will be used to dissipate the heat and to flush the bone particles preventing in obstruction of the bur. Following extraction of the tooth, the extraction socket will be compressed with the help of gauze to achieve initial haemostasis and examination for the existence of any foreign particle will be done. In case of any sharp bony margins around the socket they were trimmed with the help of a round bur and were smoothened by using a bone file. Any lacerated margins of the flap will be removed with sharp scissors. The surgical site then sutured with simple interrupted sutures using 3-0 blacksilk.

Around 2-3 sutures were given, of which the first suture will be given behind the second molar distally followed by the two sutures will be given distally to first one over the surgical site. Each patient will be given similar standard postoperative instructions and will be instructed to defer the consumption of any analgesic until the time a pain score ≥4 on Visual Analog Scale (VAS) experience by the subject as the anaesthesia of the lower lip weaned off completely. The sutures will be removed after seven days on recall.

Postoperative Care

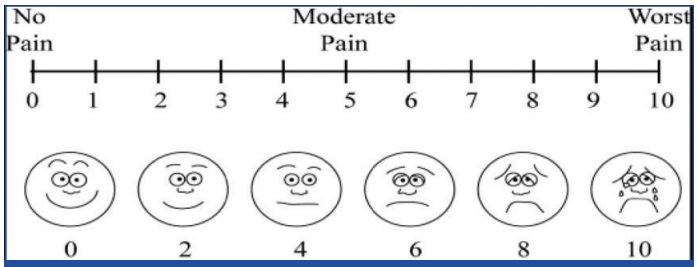
After the procedure and the necessary assessment and evaluation, the patient will be advised postoperative instructions and necessary medications will be prescribed. {Analgesic-Tab. aceclofenac 100 mg 12 hourly (Hifenac®, Intas Pharmaceuticals, India) and antibiotic-Cap. amoxicillin 500 mg 8 hourly Almox®, Alkem Pharmaceutical, Indian)}.

The patient will be given a printout card with the VAS printed on it for further assessment (at 30 minutes, 60 minutes, 90 minutes and till the first bout of pain is experienced) and will be relieved.

The patient will be asked to reciprocate about the reading of the VAS over a telephonic conversation when the first bout of pain is experienced postoperatively thereby assessing the pain intensity and the duration of postoperative analgesia.

The patients will be evaluated on the following parameters:

1. **Latency/Onset of anaesthesia:** It will be measured from the time of deposition of solution to the time when the first symptom of anaesthesia occurs. The onset of mandibular anaesthesia will be assessed by the subjective signs of lower lip and partial tongue numbness and will be confirmed objectively by using a blunt atraumatic probe [27].
2. **Profoundness/Depth of anaesthesia:** It will be determined by determining the severity of pain experienced during the following events of surgery (incision, flap reflection, bone guttering, tooth sectioning/elevation) to be recorded immediately when surgical procedure will be completed and is to be measured on 10 units VAS [28]. It uses faces to interpret expressed pain [Table/Fig-1].
3. **Haemodynamic parameters:** It will include Non Invasive Blood Pressure (NIBP) measurement of SBP, DBP in all patients. The basal measurement will be obtained prior to administration of local anaesthetic solution, with additional recordings taken at intervals of 15,30,60,90 and 120 minutes after the first anaesthetic injection during and after the procedure. Heart rate will be measured using a pulse oximeter.
4. **Duration of postoperative analgesia:** Postoperatively each patient will be asked to record the pain intensity on VAS. The duration is recorded from the completion of surgical procedure to the point of time when the first bout of pain is experienced postoperatively followed by which the patient consumes an analgesic (First Rescue Analgesic) and is to be considered as the end point of the study.



[Table/Fig-1]: Visual Analogue Scale (VAS).

The study is a triple blinded in design wherein the clinician administering the local anaesthetic solution, the patient and the evaluator, will be unaware of the solution being administered. The auxiliary staff will ensure randomisation and will load the local anaesthesia into a syringe to the clinician.

STATISTICAL ANALYSIS

The values evaluated will be represented in number and mean±standard deviation. The statistical test used for analysis will be standard: Chi-square test, one-way ANOVA, Tukey multiple comparison test and to find out various results based on the aim and objectives of study.

REFERENCES

[1] Mercier P, Precious D. Risks and benefits of removal of impacted third molars: A critical review of the literature. Int J Oral Maxillofac Surg. 1992;21(1):17-27.
[2] McGrath C, Comfort MB, Lo EC, Luo Y. Changes in life quality following third molar surgery-the immediate postoperative period. Br Dent J. 2003;194(5):265-68.
[3] Oginni FO, Ugboko VI, Assam E, Ogunbodede EO. Postoperative complaints following impacted mandibular third molar surgery in Ile-Ife, Nigeria. Sadj. 2002;57(7):264-68.
[4] Deepti C, Rehan HS, Mehra P. Changes in quality of life after surgical removal of impacted mandibular third molar teeth. J Maxillofac Surg. 2009;8(3):257-60.
[5] Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised IASP definition of pain: Concepts, challenges, and compromises. Pain. 2020;161(9):1976.
[6] Spacek A. Modern concepts of acute and chronic pain management. Biomedicine & Pharmacotherapy. 2006;60(7):329-35.
[7] Glowacki D. Effective pain management and improvements in patients' outcomes and satisfaction. Critical Care Nurse. 2015;35(3):33-41.
[8] Liporaci Junior JL. Assessment of preemptive analgesia efficacy in surgical extraction of third molars. Revista Brasileira De Anestesiologia. 2012;62:506-10.
[9] Shah R, Mahajan A, Shah N, Dadhania AP. Preemptive analgesia in third molar impaction surgery. Natl J Maxillofac Surg. 2012;3(2):144.
[10] Calatayud J, González Á. History of the development and evolution of local anaesthesia since the coca leaf. The Journal of the American Society of Anaesthesiologists. 2003;98(6):1503-08.
[11] Goodwin K. Development of a greener synthesis of Lidocaine (Doctoral dissertation, California State University, Sacramento).
[12] De Pinto M, Cahana A. Medical management of acute pain in patients with chronic pain. Expert Review of Neurotherapeutics. 2012;12(11):1325-38.
[13] Rajkumar V, Sequeira J, Rao BS. Efficacy of lignocaine with clonidine and adrenaline in lower third molar extraction. Int J Sci Study. 2017;5(1):185-88.
[14] Brummett CM, Wagner DS. The use of alpha-2 agonists in peripheral nerve blocks: A review of the history of clonidine and a look at a possible future for dexmedetomidine. InSeminars in Anaesthesia, Perioperative Medicine and Pain. 2006;25(2):84-92. WB Saunders.
[15] Grewal A. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol. 2011;27(3):297.
[16] Dcruz TM, Patel C, Masih A, Shaik I. A comparative study evaluating the efficacy of lignocaine and dexmedetomidine with lignocaine and adrenaline in third molar surgery. J Maxillofac Surg. 2020;21(2):634-38.

[17] Chowdhury S, Singh M, Shah A. Efficacy of lignocaine with clonidine and adrenaline in minor oral surgical procedure. Contemporary Clinical Dentistry. 2012;3(2):227.
[18] Chatrath V, Sharan R, Bala A, Soni S. Comparative evaluation of adding clonidine v/s dexmedetomidine to lignocaine during Bier's block in upper limb orthopedic surgeries. J Evol Med Dent Sci. 2014;3(74):15511-21.
[19] Pachore PJ, Chaudhari SA, Alapure RG, Nikam GK. Comparative evalution of clonidine with lignocaine versus Dexmedetomidine with Lignocaine. Age (yrs.). 2015;36(14/40):4.
[20] Bhola N, Patil S. Comparative evaluation of 0.5% Levobupivacaine V/S 0.5% Levobupivacaine mixed with 20 µG Dexmedetomidine in mandibular lii molar surgeries-A double blind randomised controlled Trial. J Pharm Res Int. 2022:56-63.
[21] Dcruz TM, Patel C, Masih A, Shaik I. A comparative study evaluating the efficacy of lignocaine and dexmedetomidine with lignocaine and adrenaline in third molar surgery. J Maxillofac Surg. 2020:01-05.
[22] Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anaesthesia. 1999;54(2):146-65.
[23] Holaday JW. Cardiovascular effects of endogenous opiate systems. Annu Rev Pharmacol. 1983;23(1):541.
[24] Tilkar Y, Agarwal SB, Gupta R, Karmalkar S, Khatri P, Gupta N. The efficacy and safety of clonidine and dexmedetomidine as an adjuvant in supraclavicular brachial plexus block for elective upper limb surgery. Int J Med Sci Public Health. 2017;6(8):1314-20.
[25] Yuasa H, Kawai T, Sugiura M. Classification of surgical difficulty in extracting impacted third molars. Br J Oral Maxillofac Surg. 2002;40(1):26-31.
[26] Kumar P, Thepra M, Bhagol A, Priya K, Singh V. The newer aspect of dexmedetomidine use in dentistry: As an additive to local anaesthesia, initial experience, and review of literature. Natl J Maxillofac Surg. 2016;7(1):76.
[27] Donkor P. A clinical and an anatomical study of the closed mouth mandibular block technique (Doctoral dissertation).
[28] Crichton N. Visual analogue scale (VAS). J Clin Nurs. 2001;10(5):706-06.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Oral and Maxillofacial Surgery, Datta Meghe Institutes of Medical Sciences, Wardha, Maharashtra, India.
2. Professor and Head, Department of Oral and Maxillofacial Surgery, Datta Meghe Institutes of Medical Sciences, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Akash Yogesh Doshi,
Sharad Pawar Dental College and Hospital, Datta Meghe Institutes of Medical Sciences, Wardha, Maharashtra, India.
E-mail: akashdoshi23@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 22, 2022
- Manual Googling: Jan 10, 2023
- iThenticate Software: Jan 23, 2023 (22%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Nov 10, 2022**
Date of Peer Review: **Nov 24, 2022**
Date of Acceptance: **Jan 24, 2023**
Date of Publishing: **Apr 01, 2023**