

Efficacy of Tramadol Hydrochloride as Local Anaesthetic and Analgesic Agent for Extraction of Maxillary Teeth

U SIVA KALYAN¹, NVV SATYA BHUSHAN², KC CHIANG³, D APARNA⁴, T SUNIL⁵



ABSTRACT

Introduction: To make the extraction experience pain-free administering local anaesthesia before dental extraction is standard protocol worldwide. Over the years, the concept of local anaesthesia and anaesthetic agents has evolved. Apart from conventional esters and amides, opioids have also shown the local anaesthetic property. In circumstances, where the patients are allergic to esters and amides or when they are unavailable or unobtainable the need for an alternative local anaesthetic agent arises.

Aim: To assess the efficacy of 1 mL of 50 mg tramadol hydrochloride as a local anaesthetic agent when given as buccal infiltration for extraction of maxillary teeth. Also, assess its analgesic effect.

Materials and Methods: A prospective, non-randomised, non-blinded study was done from October 2017 to August 2019 in 90 patients who required extraction of maxillary teeth. A 1 mL of 50 mg tramadol hydrochloride was given via buccal infiltration as a local anaesthetic-agent and its efficacy was evaluated by assessing the onset of action, peak effect, the

intensity of pain during extraction, duration of anaesthesia and postoperative analgesic intake. No palatal injection was given. The data was analysed using SPSS v. 20. Descriptive statistics were represented in percentages. Statistical tests used were unpaired t-test and chi-square test. The level of significance was considered to be statistically significant when the p-value was ≤ 0.05 .

Results: A 1 mL of 50 mg tramadol hydrochloride, when given as a buccal infiltration has been effective in providing local anaesthesia for extraction of maxillary teeth. It also provides a good postoperative analgesia within the first 24 hours post-extraction. It was noted that patients undergoing extraction of posterior maxillary teeth experienced more pain when compared to those undergoing extraction of anterior maxillary teeth with a significant p value of < 0.001 .

Conclusion: Tramadol hydrochloride was good in first 24 hours of post-extraction as analgesic. Buccal infiltration of tramadol hydrochloride was an effective local anaesthesia for extraction of anterior maxillary teeth.

Keywords: Amide, Buccal infiltration, Ester, Opioid

INTRODUCTION

Over the years, the concept of local anaesthesia and anaesthetic agents have evolved. Apart from conventional esters and amides, opioids have also shown the local anaesthetic property [1,2]. It also has an additional analgesic effect which the esters and amides do not possess, thereby decreasing the postoperative analgesic intake.

Tramadol hydrochloride (HCl) is a 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol, which relates to morphine and codeine structurally and is centrally acting in nature. Its use to relieve pain in conditions like post-surgical pain, obstetric pain, terminal cancer pain and pain of coronary origin is well established by the literature [3]. It also has been used as adjuvant therapy in anaesthesia to either prolong the duration of action of local anaesthetic or to achieve postoperative analgesia [4,5].

Many researchers over the past twenty years have documented that tramadol has a local anaesthetic effect similar to lignocaine [6]. It was used as a local agent for excision of soft tissue lesions [1], circumcision procedure [2] and tendon repair surgery in hand injuries [7]. Another study in 2010 found that tramadol HCl 5% plus adrenaline could provide safe and effective local anaesthesia during circumcision procedures and postoperative periods in children [2].

In Oral and Maxillofacial Surgery, two studies were done in the years 2013 [3] and 2019 [8] to evaluate the efficacy of tramadol as a local anaesthetic agent. Both studies did not throw sufficient light on its ability to provide pulpal anaesthesia, mechanism of action and properties which bring about the local anaesthetic effect [8].

This study was undertaken to unravel the efficacy of tramadol hydrochloride as a local anaesthetic and an analgesic agent extraction of maxillary teeth.

MATERIALS AND METHODS

A prospective non-randomised, non-blinded study was done in 90 patients at GITAM Dental College and Hospital, Visakhapatnam. The study sample was determined by taking the time period into account and all the patients who visited the Department of Oral and Maxillofacial Surgery for the extraction of maxillary teeth between October 2017 to August 2019 were included in the study. The approval for the study was taken from the Institutional review board and the Ethical Committee of GITAM Dental College and Hospital. Informed consent was taken from all the patients before they underwent the procedure.

Inclusion criteria: Healthy patients of ASA 1 category. Patients between the age 20 and 80 years who required the extraction of maxillary teeth due to dental caries i.e., chronic irreversible pulpitis were included in the study. Patients who are willing to participate in the study by signing the informed consent.

Exclusion criteria: Medically compromised patients, patients who are not willing to participate in the study, patients with acute infections, patients with previous history of allergy to tramadol, complicated and traumatic extractions were excluded from the study.

Before the study, all patients were checked for typical vital signs. Detailed medical history was also obtained by conducting clinical examinations. All patients in a non-blinded manner were submitted

to a standardised extraction procedure performed under local anaesthesia by one Oral Surgeon with experience in dentoalveolar surgery who performed all of the extraction procedures. 1 mL of 50 mg of plain Tramadol HCl (Tramazac injection manufactured by ZydusCadila) was given as a buccal infiltration using a 27 gauge needle for the tooth to be extracted.

Patients were asked for the need of additional anaesthesia and pain, especially in the palate when peak effect was assessed. If they required an extra dose of anaesthesia, it was planned that these patients were excluded from the study.

The parameters assessed were the onset of action, peak effect, duration of anaesthesia, the intensity of pain during extraction and the number of postoperative analgesics taken within 24 hours. 90 teeth were extracted, 27 anterior and 63 posterior teeth.

Onset of Action

Immediately after injection to the time, that patient felt numbness in the area of administration; the time interval was recorded using a stopwatch [9].

Peak Effect

Peak effect or induction time is defined as a period from the deposition of the anaesthetic solution to complete conduction blockade [10]. After the buccal infiltrative anaesthesia injection, the attached gingiva and labial mucosa corresponding to the injection site were subjected to a pinprick test using Mallieffer exploratory probe. The time at which the patient perceived neither pain nor stinging was noted as it indicated complete sensory blockade [11].

Pain During Extraction

The degree of pain during extraction was assessed using a 10-cm Visual Analog Scale (VAS) ranging from 0 to 10. For pain degree, while '0' described 'no pain' on the Wong Bakers VAS scale, '10' was defined 'the worst pain' [8].

Total Duration of Anaesthesia

After the extraction, the patient was evaluated every 5 minutes by pricking with a Mallieffer probe at the injection site until the return of normal sensations in the area of injection [8].

Postoperative Analgesic Intake

A telephonic interview was performed 24 hours after the extraction to enquire about the intake of analgesics (diclofenac sodium 50 mg + Paracetamol 325 mg tablets) [8]. Side effects if any were jotted down after the telephonic interview. Six patients required analgesics in this study, so a total of 84 patients were assessed for the analgesic effect of tramadol.

STATISTICAL ANALYSIS

The data entered in MS Excel under the heading MASTER CHART was analysed using SPSS v.20. Descriptive statistics were represented in percentages. The statistical tests used were an unpaired t-tests and Chi Square tests. The level of significance was considered to be statistically significant when the p-value was ≤ 0.05 .

RESULTS

Out of the 90 subjects included in study 37 were male and 53 were female, which accounted for 41.11% and 58.88%, respectively with the mean age being 45.43 ± 12.74 years.

The [Table/Fig-1] shows the mean time for onset, peak, duration of action for 1 mL of 50 mg tramadol hydrochloride to be 4.5, 12.13, 40.14 minutes, respectively.

The [Table/Fig-2] represents the mean pain score during extraction to be 0.41, 2.54 and respectively, when the scores for extraction of anterior and posterior teeth were compared. An unpaired t-test showed a substantial difference in the pain score between the

patients undergoing the extraction of anterior and posterior teeth with a p-value of 0.000 where $p < 0.001$, hence significant. The p-value was ≤ 0.05 was considered to be statistically significant. It can be inferred that the extraction of anterior maxillary teeth was less painful than posterior maxillary teeth when 1 mL of 50 mg tramadol hydrochloride, was given as a buccal infiltration for extraction of teeth.

Variable	Mean (min)	SD (min)
Time of Onset	4.5	1.309
Peak	12.13	2.381
Duration of action	40.14	3.136

[Table/Fig-1]: Mean of onset, peak and duration of action in minutes.

Teeth		Pain score		
		Mean	t-value	p-value
Region	Anterior	0.41	6.627	<0.001*
	Posterior	2.54		

[Table/Fig-2]: Comparison of pain score between anterior and posterior teeth. Unpaired t-test, *statistically significant

From the [Table/Fig-3], the analgesics taken within the first 24 hours of extraction when compared with 96.3% of patients undergoing extraction of anterior tooth and 92.1% of those undergoing posterior tooth extraction did not require any analgesic within 24 hours with a p-value of 0.461. When various age groups were compared 100%, 96%, 88.5%, 100%, 71.4% of patients in the age groups 20-30 years, 31-40 years, 41-50 years, 51-60 years and above 60 years respectively did not require analgesic within the first 24 hours after extraction, p-value being 0.062.

Characteristics of subjects		Analgesics taken within 24 h		Chi square value	p-value
		Not taken	Taken		
Gender	Males	35 (94.6%)	2 (5.4%)	0.161	0.689
	Females	49 (92.5%)	4 (7.5%)		
Region	Anterior	26 (96.3%)	1 (3.7%)	0.544	0.461
	Posterior	58 (92.1%)	5 (7.9%)		
Age groups	20-30 years	13 (100%)	0 (0%)	8.961	0.062
	31-40 years	24 (96%)	1 (4%)		
	41-50 years	23 (88.5%)	3 (11.5%)		
	51-60 years	19 (100%)	0 (0%)		
	Above 60 years	5 (71.4%)	2 (28.6%)		

[Table/Fig-3]: Analgesics taken within 24 hours post extraction.

Out of 90 patients in the study population, 3 patients experienced dizziness and nausea post-injection; in 2 patients, erythema at the site of injection was observed.

The results of the present study have shown that 1 mL of 50 mg tramadol hydrochloride, when given as a buccal infiltration has been effective in providing local anaesthesia for extraction of maxillary teeth. Tramadol HCL also provides a good postoperative analgesia within the first 24 hours post-extraction. It was noted that extraction of posterior maxillary teeth was more painful when compared to anterior maxillary teeth.

DISCUSSION

Efficacious anaesthetics and anaesthesia techniques can provide pain control. However, despite the use of adequate anaesthesia in dentistry, prejudice against dental treatment due to possible pain continues to prevail. To perform a painless minor oral surgical procedure, the use of local anaesthetics is a must. The ideal local anaesthetics used in dentistry have a good anaesthetic action. There are no local anaesthetics that have both anaesthetic and analgesic action. Hence, there is a need to ascertain a drug that gives excellent local anaesthesia along with good postoperative analgesia [9].

Opioids have been successfully used for pain management for many decades. Some of the opioids are known to have local anaesthetic action also [3].

In recent experimental and clinical studies, the peripheral local anaesthetic effect of tramadol was elucidated. Of all the opioids which have local anaesthetic potential, tramadol is known to have a low addiction rate [3]. When combined with mepivacaine, tramadol increases the blockage of the brachial plexus [5]. Injection of 5% tramadol in soft tissue lesions via intradermal route proved to have a local anaesthetic effect similar to 2% lidocaine [12].

Besides, the combination of tramadol with adrenaline was found to be more effective than their single-use; the use of 5% tramadol was safer and equally effective like lidocaine for local anaesthesia in the circumcision of children [2].

The effect of tramadol anaesthesia has also been investigated in dentistry where Jaber L et al., demonstrated the presence of mu-opioid receptors in human coronal and radicular pulp tissue of human teeth, which indicates that peripheral anaesthetic effects of opioid agonists are induced by interaction with peripheral opioid receptors [13]. Danic P et al., the mechanism of local anaesthesia of tramadol after reviewing various articles as follows [14]. Weak peripheral agonism over peripheral mu-opioid receptors whose number is heightened in hyperalgesia and inflammatory conditions, favouring the opening of nonspecific voltage-dependent potassium channels, acting in the nitric oxide pathway, agonistic action on vanilloid receptor one that apart from local analgesic effect, exerting undesired local side effects, such as burning pain and erythema, with a high concentration of tramadol blockade of the N-methyl-D-aspartate receptors and direct blocking of voltage-dependent sodium channels explains the local anaesthetic effect of tramadol.

Tramadol was used to extract teeth in this study because although limited literature shows that it has both local anaesthetic and postoperative analgesic action which can be used to avoid additional intake of analgesics in patients undergoing simple extraction of maxillary teeth. There are also studies showing that tramadol can be used as a single local anaesthetic agent to achieve local anaesthesia.

Ege B et al., reported in a non-invasive study that the anaesthetic onset of 0.5 mL of 25 mg tramadol was delayed as compared to lignocaine when given as buccal infiltration anaesthesia in the maxilla; however, tramadol provided statistically more effective anaesthesia in the gingiva and the skin than lidocaine [11].

Ege B et al., did a study to differentiate between the anaesthetic efficacy of tramadol and lignocaine for the extraction of maxillary premolar teeth. The authors concluded that tramadol, besides its analgesic property is a harmless alternative to existing local anaesthetics when given in conjunction with adrenaline [15].

Jendi SK and Talathi A had done a double-blind study to document gingival anaesthesia produced by tramadol hydrochloride in the maxilla. Every patient was given 0.5 mL of 50 mg tramadol hydrochloride over the cuspid in one quadrant as a buccal infiltration while in the other quadrant 0.5 mL of 20 mg lignocaine. The local anaesthetic effect of tramadol and lignocaine on soft tissues were indistinguishable according to the authors [8].

Alsandook TA and Al-Haideri YA used combinations of 1.8 mL of lidocaine (36 mg lidocaine) and 1.8 mL of tramadol (50 mg tramadol) with epinephrine in minor oral surgeries as a nerve block for procedures such as tooth extraction and periapical surgery in lower molar teeth, where they did not find difference in the onset of anaesthesia between the groups [9]. They further emphasised that surgeries can be performed using a combination of tramadol and adrenaline and that tramadol may be an alternative to lidocaine [1].

The preparation of tramadol with adrenaline requires a specific protocol and a separate manufacturing unit which is not available in this institution. Hence, plain tramadol, which is readily available,

was used in this study.

When this study was embarked in 2017, there was no research published on the feasibility of administering a nerve block using plain tramadol HCL alone for the extraction of maxillary teeth which lead to apprehension of using it as a nerve block, hence buccal infiltration was chosen in this study.

In the present study, extraction of upper teeth was carried out using a single buccal injection given as local infiltration. It was done by Isik K et al., and Somuri AV et al., who reported that the extraction of maxillary teeth was possible by administering a single buccal injection without the necessity of a palatal injection when articaine was used as local anaesthetic [16,17]. Ali W et al., demonstrated the same using 2% lignocaine with epinephrine [18]. Hence this study was done to explore the feasibility of single buccal injection of tramadol, since the standard anaesthetics like lignocaine and articaine proved that palatal injection was not necessary to extract maxillary teeth.

The present study used a dose of 50 mg of 1 mL tramadol HCL for buccal infiltration, per the studies done previously by Atunkaya H et al. [1], Al-Haideri YA [3], Ege B et al. [11,15], Alsandook TA and Al-Haideri YA [9]. In terms of the ideal dosage of tramadol, Kakagia D et al., reported that the maximum safe dose for local infiltration should not exceed 2 mg/kg [12]. The 50 mg dose used in this study is way within the maximum recommended safe dose of 2 mg/kg.

In this study, the mean onset was found to be 4.5 minutes which is comparable with 3.41 minutes of Alsandook TA and Al-Haideri YA [9] and contrary to 2.86 minutes by Jendi SK and Talathi A [8]. In the studies by Ege B et al., mean onset was faster when compared to the studies mentioned above with values of 43.91 seconds and 43.26 seconds, respectively, due to the addition of vasoconstrictor to the solution of tramadol which limits the drug to the periphery and enables the faster onset [11,15]. Studies have also shown that tramadol when compared with lignocaine has a slower onset [8,11,15].

Dalkilic N et al., mentioned that the Na⁺ channels of fast conducting fibers are more susceptible to tramadol when compared to that of the slow conducting fibers. It might be the reason for more delayed onset of tramadol in the oral cavity when compared to its onset on skin [19].

The mean of peak effect for 1 mL of 50 mg plain tramadol was observed to be 12.13 minutes in this study, which is coherent with the peak achieved between 15-20 minutes by Ege B et al., [11]. In another study, the peak effect when compared between lignocaine and tramadol at the 5th-minute postinjection showed that lignocaine had better anaesthetic efficacy than tramadol when used intraorally [15].

The mean duration of action ascertained in the study was 40.14 minutes, which are in congruence with 45.70 minutes and 42.83 minutes stated in the reviews by Jendi SK and Talathi A and Ege B et al., respectively [8,11]. Alsandook TA and Al-Haideri YA and Ege B et al., conducted two studies where they compared the duration of the action of tramadol with adrenaline to lignocaine with adrenaline and found the mean duration of tramadol to be 148.6 minutes and 117.38 minutes respectively [9,15]. They also stated that when given in conjunction with adrenaline, tramadol had a similar duration of action to lignocaine with adrenaline with no statistically significant difference.

On comparison, the mean pain score during extraction in anterior and posterior teeth were found to be 0.41 and 2.54, respectively. The current study inferred that patients undergoing extraction of posterior maxillary teeth experienced more pain when compared to those undergoing extraction of anterior maxillary teeth which might be due to the multirooted nature of posterior teeth. Extraction of teeth is supposed to be a painless procedure and hence, use of tramadol for extraction of posterior teeth is not recommended. It

is contrary to the study by Alsandook TA and Al-Haideri YA where they elucidated no difference in pain scores between lignocaine and tramadol when used in minor oral surgical procedures as a nerve block [9]. In another study, Al-Haideri YA compared 1.8 mL of 50 mg tramadol with tramadol and adrenaline combination in the extraction of maxillary molar teeth and investigated their anaesthetic activity and deduced that the combined use is more effective and has lower VAS values, thereby, recommended the use of tramadol-adrenaline combination in oral surgeries [3].

On the contrary, studies by Polat F et al., and Mannion S et al., showed that tramadol has no local anaesthetic effect [20,21].

Tramadol is an atypical opioid act selectively on the mu-opioid receptors. In terms of analgesic effects, it increases the inhibition of pain transport through both opioid and mono-aminergic mechanisms. Moreover, it has a non-opioid Cl_2 -agonistic and serotonergic pain inhibitory effect, acting like a five hydroxytryptamine and norepinephrine inhibitor for nerve endings [22]. Kapral S et al., suggested that tramadol interacts with receptors in the posterior horn of the spinal cord to bring about the analgesic action on peripheral nerves [5].

In the present study, to assess the postoperative analgesic effect of tramadol, a telephone interview was performed 24 hours after the extraction to enquire about the intake of analgesics (diclofenac sodium 50 mg+Paracetamol 325 mg tablets) [8]. In this study, 93% of the study population, that is 84 out of 90 patients did not take analgesics within the first 24 hours after injection of tramadol hydrochloride which can be attributed to its postoperative analgesic effect. The results of the postoperative analgesic efficacy of tramadol in the present study are concurrent with the investigations of Kargi E et al., Ege B et al., Kaakagia D et al., Ege B et al., Cecchetti MM et al., Madan HK et al., Mert T et al., [2,7,11,12,15,23-25]. However, these results are contrary to the conclusions drawn by Mannion S et al., where they emphasise that tramadol does not exhibit any significant peripheral analgesic property [21].

Out of 90 patients in the study population, three patients experienced dizziness and nausea post-injection; in 2 patients, erythema at the site of injection was observed which is congruent with the observations made in the studies by Al-Haideri YA, Pang WW et al., Ege B et al., and Kakagia D et al., [3,6,11,12]. Apart from these, tramadol has a disadvantage that it cannot be used in patients on medications ailing with systemic diseases apart from nausea, dizziness and erythema at the site of injection. Tramadol can be best used for extraction of anterior maxillary teeth.

Limitation(s)

The limitations of this study are that it has not considered teeth with acute infections, complicated extractions, mandibular teeth. In this study, the only infiltration was given for extraction, but the nerve block was not administered using tramadol. Comparison with another drug was not done.

CONCLUSION(S)

In conclusion, this study undertaken in 90 patients to assess the efficacy of tramadol HCL as a local anaesthetic agent for extraction of maxillary teeth has shown that 1 mL of 50 mg plain tramadol hydrochloride, when given as a buccal infiltration has been effective in providing local anaesthesia for extraction of anterior maxillary teeth and is also providing good postoperative analgesia for the first 24 hours post-extraction. Further studies are advised with

significant number of cases.

REFERENCES

- [1] Altunkaya H, Ozer Y, Kargi E, Babucco O. Comparison of local anesthetic effects of tramadol with prilocaine for minor surgical procedures. *Br J Anaesth*. 2003;90(3):320-22.
- [2] Kargi E, İşıkdemir A, Tokgöz H, Erol B, İşıkdemir F, Hancı V, Payaslı C. Comparison of local anesthetic effects of tramadol with prilocaine during circumcission procedure. *Urology*. 2010;75(3):672-75.
- [3] Al-Haideri YA. Comparison of local anesthetic efficacy of tramadol hydrochloride (with adrenaline) versus plain tramadol hydrochloride in extraction of upper molar teeth. *J Oral Maxillofac Surg*. 2013;71(12):2035-38.
- [4] Pozos AJ, Martinez R, Aguirre P, Perez J, Potosi SL. The effects of tramadol added to articaine on anesthesia duration. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102(5): 614-17.
- [5] Kapral S, Gollmann G, Waltl B, Likar R, Sladen RN, Weinstabl C, et al. Tramadol added to mepivacaine prolongs the duration of an axillary brachial plexus blockade. *Anesth Analg*. 1999;88(4):853-56.
- [6] Pang WW, Mok MS, Chang DP, Huang MH. Local anesthetic effect of tramadol, metoclopramide and lignocaine following intradermal injection. *Regional Reg Anesth Pain Med*. 1998;23(6):580-83.
- [7] Kargi E, Babucco O, Altunkaya H, Hosnuter M, Ozer Y, Babucco O, et al. Tramadol as a local anesthetic in tendon repair surgery of hand. *J Int Med Res*. 2008;36(5):971-78.
- [8] Jendi SK, Talathi A. Tramadol hydrochloride: An alternative to conventional local anaesthetics for intraoral procedures- A preliminary study. *J Oral Biol Craniofac Res*. 2019;9(1):111-14.
- [9] Alsandook TA, Al-Haideri YA. A pilot double blinded clinical trial to compare between tramadol HCL and Lidocaine HCL as local anaesthesia amongst hospital-outpatient adult dental attendees Mosul-Iraq. *Journal of Oral and Dental Research*. 2013;23(1945):01-05.
- [10] Stanley F Malamed. *Handbook of local anesthesia*. 6th edition. India: Elsevier India;2014.20.
- [11] Ege B, Calisir M, Al-Haideri Y, Ege M, Gungormus M. Comparison of local anesthetic efficacy of tramadol hydrochloride and lignocaine hydrochloride. *J Oral Maxillofac Surg*. 2018;76(4):744-751.
- [12] Kakagia D, Vogiatzaki T, Eleftheriadis S, Trypsiannis G, Iatrou C. Local infiltrative anesthetic effect of tramadol compared to lidocaine for excision of cutaneous lesions: Pilot randomized double-blind clinical trial. *J Cutan Med Surg*. 2012;16(2):101-06.
- [13] Jaber L, Swaim WD, Dionne RA. Immunohistochemical localization of mu-opioid receptors in the human dental pulp. *J Endod*. 2003;29(2):108-10.
- [14] Danic P, Salarić I, Macan D. New findings on local tramadol use in oral surgery. *Acta Stomatol Croat*. 2017;51(4):336-44.
- [15] Ege B, Ege M, Kopal M, Alan H. Comparison of anesthetic efficiency of tramadol hydrochloride and lignocaine hydrochloride in orthodontic extractions. A split-mouth, prospective, randomized, double-blind study. *J Oral Maxillofac Surg*. 2019;78(1):52-62.
- [16] Isik K, Kalayci A, Durmus E. Comparison of depth of anesthesia in different parts of maxilla when only buccal anesthesia was done for maxillary teeth extraction. *Int J Dent*. 2011;5:575-874.
- [17] Somuri AV, Rai AB, Pillai M. Extraction of permanent maxillary teeth by only buccal infiltration of articaine. *J Oral Maxillofac Surg*. 2013;12(2):130-32.
- [18] Ali W, Kazmi SS, Mirza KS, Chaudhry R, Yaseen S. Use of only buccal infiltration of 2% lignocaine with epinephrine for the removal of maxillary teeth. *Biomedica*. 2018;34(1):44-47.
- [19] Dalkilic N, Tuncer S, Bariskaner H, Kiziltan E. The effect of tramadol on the rat sciatic nerve conduction: A numerical analysis and conduction velocity distribution study. *Yakugaku Zasshi*. 2009;129(4):485-93.
- [20] Polat F, Tuncel A, Balci M, Aslan Y, Sacan O, Kisa C, et al. Comparison of local anesthetic effects of lidocaine versus tramadol and effect of child anxiety on pain level in circumcission procedure. *J Pediatr Urol*. 2013;9(5):670-74.
- [21] Mannion S, Callaghan SO, Murphy DB, Shorten GD. Tramadol as an adjunct to psoas compartment block with levobupivacaine 0.5%: A randomized double-blind study. *Nerve block*. *Br J Anaesth*. 2005;94(3):352-56.
- [22] Bamigbade TA, Davidson C, Langford RM, Stamford JA. Actions of tramadol, its enantiomers and principal metabolite, O-desmethyl tramadol, on serotonin (5-HT) efflux and uptake in rat dorsal raphe nucleus. *Br J Anaesth*. 1997;79(2):352-56.
- [23] Cecchetti MM, Negrato GV, Peres MP, Deboni MC, Naclerio-Homem. Analgesic and adjuvant anesthetic effect of submucosal tramadol after mandibular third molar surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2014;117(3):e249-54.
- [24] Madan HK, Singh R, Sodhi GS. Comparison of Intravenous Lignocaine, Tramadol and Keterolac for Attenuation of Propofol Injection Pain. *Journal of Clinical and Diagnostic Research: JCDR*. 2016;10(7):UC05-UC08.
- [25] Mert T, Gunes Y, Gunay I. Local analgesic efficacy of tramadol following intraplantar injection. *European Journal of Pharmacology*. 2007;558(1-3):68-72.

PARTICULARS OF CONTRIBUTORS:

1. Reader, Department of Oral and Maxillofacial Surgery, Gitam Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India.
2. Professor and Head, Department of Oral and Maxillofacial Surgery, Gitam Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India.
3. Reader, Department of Oral and Maxillofacial Surgery, Gitam Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India.
4. Postgraduate Student, Department of Oral and Maxillofacial Surgery, Gitam Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India.
5. Professor, Department of Oral and Maxillofacial Surgery, Gitam Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

D Aparna,
Department of Oral and Maxillofacial Surgery, Gitam Dental College and Hospital,
Gandhi Nagar Campus, Rushikonda, Visakhapatnam-530045, Andhra Pradesh, India.
E-mail: datlaaparna87@gmail.com

PLAGIARISM CHECKING METHODS: [\[Jan H et al.\]](#)

- Plagiarism X-checker: Jan 31, 2020
- Manual Googling: Apr 20, 2020
- iThenticate Software: May 22, 2020 (14%)

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. NA

Date of Submission: **Jan 30, 2020**Date of Peer Review: **Mar 06, 2020**Date of Acceptance: **Apr 22, 2020**Date of Publishing: **Jun 01, 2020**