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ORIGINAL ARTICLE

Comparison of Local Anaesthetic Efficacy of Tramadol Versus Lignocaine for Extraction of Tooth Under Supraperiosteal Infiltration

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Abstract
Background Tramadol has been shown to have a local anaesthetic effect when used as infiltration anaesthesia.
Methods The local anaesthetic efficacy of tramadol was compared with that of lignocaine for the extraction of teeth in terms of their onset of action, duration of action, intra-operative pain, post-operative analgesic effect and adverse reactions. Apart from this, incidence of allergic reaction was also recorded for both the drugs. A total of 100 patients were divided into two groups randomly. Each patient was assigned to receive either a maximum of 2 ml of 5% tramadol (Supridol 50 mg, Neon laboratories), Group T ($n = 50$), as a local anaesthetic solution for extraction of maxillary premolar for orthodontic reason under supraperiosteal infiltration following strict aseptic precaution or a maximum of 2 ml of 2% lignocaine (Lox 2%, Neon laboratories), Group L ($n = 50$), in a double-blinded fashion.
Results In group T, the mean subjective onset of action was 33.66 s, while in group L it was 33.06 s ($p = 0.881$). In group T, the mean objective onset of action was 3.04 min, while in group L it was 3.18 min ($p > 0.05$). The mean duration of action in group T was 55.60 min, while in group L it was 57.50 min ($p = 0.432$). Only 2 patients in group T and 1 patient in group L had nausea ($p = 0.245$).
Conclusion We conclude that 5% tramadol has a local anaesthetic efficacy similar to 2% lignocaine but is comparatively a weaker agent.

Keywords Tramadol · Lignocaine · Local anaesthesia · Supraperiosteal infiltration

Introduction

Tramadol hydrochloride (HCl), a centrally acting opioid analgesic, was synthesized in 1962 by Grunenthal GmbH in Germany and was made available to use for pain management in Germany since 1977. It was registered in UK in 1994 while in USA in 1995. It is known to be effective in treatment of moderate to severe type of pain [1, 2]. Pang and colleagues in 1998 for the first time reported on the anaesthetic property of commercially available tramadol when injected intradermally [3]. Since then, a number of researchers have conducted both in vitro and in vivo studies to test the local anaesthetic (LA) effect of tramadol. In 2013, Al Haideri reported that tramadol alone or in combination with adrenaline can be used as a local anaesthetic for the extraction of upper molar tooth under supraperiosteal infiltration [4]. This is one of the studies of its kind conducted by Al Haideri in dentistry where tramadol was used as a LA agent for tooth extraction. Therefore, we conducted this study to compare the LA efficacy of tramadol HCl versus lignocaine HCl for therapeutic extraction of upper premolars under supraperiosteal infiltration. It was hypothesized that tramadol, an opioid analgesic, had a LA effect that could be compared to lignocaine.

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Materials and Methods

The study was approved by the institutional ethical committee. The purpose of the study was explained to all the participants and relevant data pertaining to the case history were recorded in a special proforma and written informed consent was obtained from all the participants. A total of 100 ASA physical status I patients, aged 18–32 years, both male and female were included in this study. The patients included in the study were those who required therapeutic extraction of maxillary premolars for orthodontic reasons. The patients excluded were pregnant or lactating females, medically compromised individuals, and those who were allergic to the drugs used in the study. The participants were randomly divided into two groups of 50 each. Each patient was assigned to receive either a maximum of 2 ml of 5% tramadol (Supridol 50 mg, Neon laboratories), Group T ($n = 50$), as a LA solution for extraction of maxillary premolar for orthodontic reason under supraperiosteal infiltration following strict aseptic precaution or a maximum of 2 ml of 2% lignocaine (Lox 2%, Neon laboratories), Group L ($n = 50$), in a double-blinded fashion.

All the patients were assessed for the following parameters in both the groups.

Incidence of allergic reaction

Every patient underwent drug allergy testing for those drugs which were to be injected as supraperiosteal infiltration anaesthesia. 0.1 ml of test dose was injected intradermally under all aseptic precaution on the forearm of right hand using sterile 1 mL tuberculin syringe with a short needle. The intradermal (intracutaneous) injection was performed by inserting the needle tip, bevel up, just underneath the surface of the skin and injecting 0.1 mL of the drug. The formation of "bleb" was an indication that the injection was performed properly.

Evaluation of the response

Each injection site was evaluated for 15–20 min.

The response was measured by the diameter of skin change or wheal, if present [5].

Scale: 0 = no reaction. 1 = mild rash. 2 = erythema. 3 = urticaria.

If there was no allergic reaction to the drug injected, then intraoral injection was performed. Each patient initially received 0.6 mL of either tramadol or lignocaine as supraperiosteal infiltration on buccal side and 0.1 mL on the palatal side.

Onset of anaesthesia

Immediately after injection was complete (considered as time zero) to the time that the patient felt numbness at the site of injection, this time interval was recorded as the subjective onset of supraperiosteal infiltration anaesthesia using a stopwatch as interpreted by the patient. Then, after 1 min of completion of injection procedure and at every 10-s interval, the objective onset of anaesthesia was checked with a dental probe that was pushed into the gingival crevice of the same tooth on buccal surface and pain was assessed using visual analogue scale (VAS) ranging from 0 to 10. Visual analogue scale was explained to each patient before the start of procedure. The time at which the patient felt no pain, i.e. VAS score of 0 was recorded as the objective onset of anaesthesia. If during extraction procedure the patient experienced pain and the pain score was less than 3 on VAS, then the extraction was carried out, and if it was more than 3, then an additional 0.6 mL of the same drug was injected using the same technique on the buccal side, and after waiting for about 5 min, the extraction procedure was proceeded. Again if the patient experienced pain during extraction and the pain score was less than 3 on VAS, then the extraction was carried, out and if it was more than 3, then an additional 0.6 mL of the same drug was injected using the same technique on the buccal side, and after waiting for about 5 min, the extraction procedure was proceeded. If the third time the patient experienced pain where the score was more than 3 on VAS, then that case was considered as failure. Then, they received conventional LA, 2% lignocaine with 1:80,000 adrenaline, as nerve block for the completion of the procedure.

Duration of Anaesthesia

The time interval between the appearance of numbness at the site of drug delivery and its disappearance, as reported by the patient, was recorded as the duration of anaesthesia. The patient was also evaluated every 5 min to check the disappearance of anaesthesia by pricking with a dental probe on the buccal soft tissue at the injection site. The patient was made to wait in the department for up to 3 h for which a written informed consent was obtained from all the patients.

Post-operative Analgesia

Patients were recalled after 24 h and were evaluated for the need of analgesic. They were instructed to take the prescribed analgesic tablets only if they experienced pain after the extraction of tooth. The duration from the extraction of tooth to the need of analgesic was measured as informed by

the patient and depended upon the patient. All the patients received a self-assessment chart and were explained about it. They were instructed to evaluate the pain experienced by them with the help of visual analogue scale every hour up to 12 h from the time of extraction and then every 6th hourly till 24 hours were complete from the time of extraction. All the patients submitted the self-assessment chart during the follow-up visit.

Adverse Reaction

The adverse effects of the drugs injected were also recorded when the patient was recalled for the follow-up after 24 h. We used the following scale to record the same:

0 = None
1 = Nausea
2 = Vomiting

Intraoperative Pain

The pain experienced by the patient during extraction of the tooth was recorded using visual analogue scale (VAS) ranging from 0 to 10 as interpreted by the patient, where 0 means no pain and 10 means the worst pain. This scale was explained to the patient before the start of the procedure.

The data obtained from the study were statistically analysed and compared using independent sample t test on IBM SPSS 21.0 version (2015) software.

Results

Of all the patients selected, 64 were female and 36 were male. Out of these, group 1 had 32 females and 18 males, while group 2 had 32 females and 18 males. All the patients ranged between 18 and 32 years of age. None of the patients in either group showed any untoward reaction to the drug injected. In group T, the mean subjective onset of action was 33.66 s with a range of 33.66 ± 5.204 s. In group L, the mean subjective onset of action was 33.06 s with a range of 33.06 ± 5.366 s (Fig. 1). The highest onset of action was recorded in group T which was 49 s, while the lowest was recorded in group L which was 26 s. The statistical difference for the onset of action was not significant between the two groups ($p = 0.881$). In group T, the mean objective onset of action was 3.04 min with a range of 3.04 ± 0.79 min. In group L, the mean objective onset of action was 3.18 min with a range of 3.18 ± 0.70 min (Fig. 2). The highest onset of action was recorded in group T which was 4 min 50 s (4.83 min), while the lowest was also recorded in group T which was 1 min 20 s (1.33 min). The statistical difference was not significant between the two groups ($p > 0.05$). About intraoperative pain, the maximum VAS score recorded was 4 in group T, while minimum VAS score recorded was 0 in both the groups. The mean intraoperative pain in group T was 0.4400 with a range of 0.4400 ± 1.01338. The mean intraoperative pain in group L was 0.2000 with a range of 0.2000 ± 0.45175. The statistical difference was significant between the two groups ($p = 0.04$). The mean duration of action in group T was 55.60 min, while in group L it was 57.50 min (Fig. 3). The highest duration of action recorded was 90 min in group L, and lowest was 45 min recorded in group T. The statistical difference was not significant ($p = 0.432$). The mean duration of analgesia was 11.92 h in group T, while in group L it was 2 h (Fig. 4). The highest duration of analgesia recorded was 24 h in group T, while the lowest was 2 h in group L. The statistical difference was significant between the two groups ($p = 0.000$). Regarding the adverse effects recorded for up to 24 h, only 2 patients in group T and 1 patient in group L had nausea. The statistical difference between the two groups was not significant ($p = 0.245$).

Discussion

Bennett pointed out that LA activity resides in various structural configurations other than those of local anaesthetics, viz., compounds like antihistamines, analgesics, tranquillizers and antiarrhythmic drugs may have LA

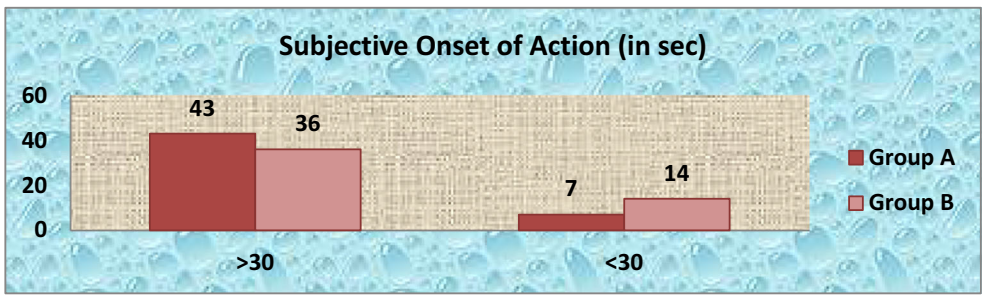

Fig. 1 Graph representing subjective onset of action in Group A (Tramadol) and Group B (Lignocaine) measured in seconds

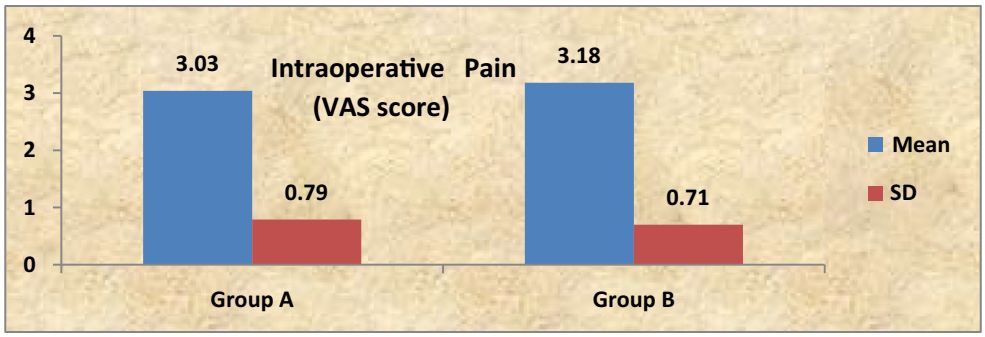

Fig. 2 Graph representing intraoperative pain (VAS score) in Group A (Tramadol) and Group B (Lignocaine)

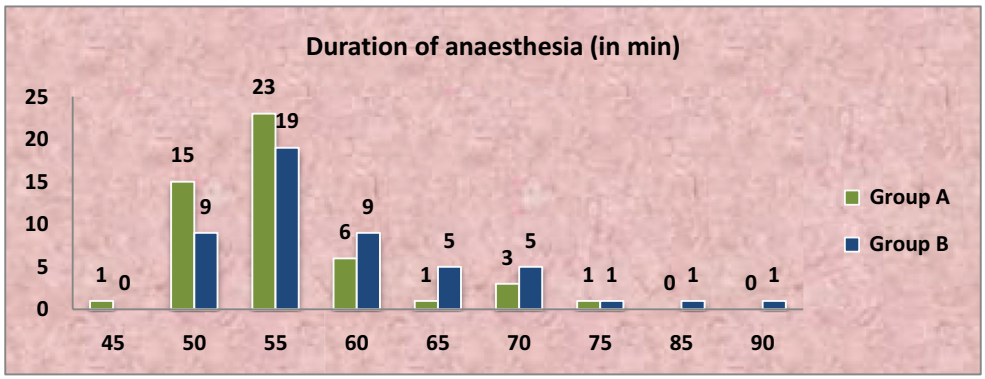

Fig. 3 Graph representing duration of anaesthesia in Group A (Tramadol) and Group B (Lignocaine) measured in minute

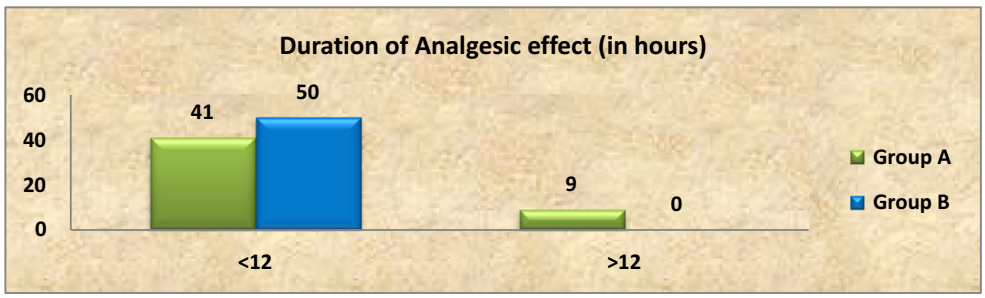

Fig. 4 Graph representing duration of analgesic effect in Group A (Tramadol) and Group B (Lignocaine) measured in hours

activity [6]. Even alcohols, anticonvulsants, barbiturates and narcotics can also produce conduction block in nerves [7]. Opioids have been shown to have a LA effect in both in vivo and in vitro studies. The LA property of opioids like meperidine, fentanyl, sufentanil, tramadol and others are well documented in the literature [8–12].

The LA efficacy of tramadol was first reported by Pang and colleagues in 1998. In their study, they found that tramadol produced a reduction in sensation to pinprick, touch and cold when injected intradermally on the forearm [3]. In 1999, it was shown by Pang et al. [13] that tramadol was effective in reducing propofol injection pain and it was postulated that tramadol has a peripheral analgesic activity. In 2001, Tsai et al. studied the effect of tramadol when applied directly to the sciatic nerves in rats. They found that tramadol inhibited nerve conduction in dose-dependent manner which was fully reversible and without deleterious neurological effects and this effect of tramadol was not reversed by naloxone [14]. Mert et al. [15] in 2001 demonstrated that tramadol has a LA effect which is similar to but weaker than lidocaine and an increase in the pH increased the conduction blocking potency of tramadol. Mert et al. [16] in an in vitro study found that tramadol has a LA effect similar to lidocaine, but it was relatively weaker and that tramadol may have a mechanism different from lidocaine for producing conduction blockade. Tramadol has a LA effect similar to prilocaine when used for the excision of skin lesions was shown by Altunkaya et al.

[5]. Tramadol provided local anaesthesia equal to lidocaine when injected subcutaneously for excision of skin lesions and provided benefit of prolonged post-operative analgesic effect, thereby reducing the analgesic requirement [17]. Guven et al. [18] showed that tramadol may produce conduction blockade by exerting a LA-like effect on the rat sciatic nerve by blocking Na^+ channels following a hydrophilic pathway like lidocaine. Tramadol as a LA for tooth extraction was first reported by Yahya Al- Haideri and Tahani Al-Sandook from Iraq in 2013 [4, 19].

Much confusion prevails among different researchers as how this opioid analgesic works as a LA. Mert et al. [15] proposed that tramadol may follow hydrophobic pathway like benzocaine by passing through the nerve membrane and blocking the sodium channels. In a study by Tsai et al. [14], it was shown that the changes in somatosensory evoked potential by tramadol were not reversed by naloxone, suggesting that the LA effect of tramadol is not mediated by opioid receptors. A similar finding was reported by Mert et al. [20]. Mert et al. [16] suggested that tramadol may have a LA effect with a different mechanism of action than that of lignocaine and the presence of Ca^+ concentrations increases this activity of tramadol. Mustafa G. and colleagues in 2005 suggested that tramadol may produce nerve conduction block by exerting a LA effect by blocking Na^+ channels following a hydrophilic pathway as lignocaine and it blocks K^+ channels more than lignocaine [18]. Mert et al. [9] proposed that the LA effect of tramadol may be due to the non-specific binding to membrane proteins or non-specific membrane effects. Nizamettin and his associates in 2009 suggested that Na^+ channels in fast conducting fibres are more susceptible to the effect of tramadol than Na^+ channels in slow conduction fibres [11]. In the past, it was shown that opioids can produce two distinct effects on membrane excitability: a non-specific LA-like effect in which both the specific increase in sodium conductance and the delayed increase in potassium conductance are depressed, and a selective decrease in sodium conductance alone due to activation of stereospecific opioid drug receptors [10].

True allergic reaction to amide type of LA is extremely rare and accounts for about less than 1% [21], while for opioids the allergic reactions account for about 0.1% [2]. True allergic reactions and systemic anaphylactoid reactions to opioids are rare [20]. Pang et al. [3, 13] in his study found that intradermal injection of tramadol produced erythema and/or wheal more than lidocaine. Altunkaya et al. [5] also reported local skin reaction (rash) with intradermal injection of tramadol. However, in the study of Kargi et al. [22] it was found that tramadol did not have any significant local side effects when injected as local infiltration on skin. Vahabi et al. [23] also showed that tramadol did not have any significant local skin reactions when injected subcutaneously. Pang et al. [3] reported that the sensations (pinprick, cold, touch) were significantly reduced at 1 min after the intradermal injection of tramadol. In a study by Al Tunkaya et al. [5], the anaesthetic effect of tramadol started within 1 min after intradermal injection of tramadol for excision of cutaneous lesions. A similar finding was shown by Kargi et al. [22] where they used tramadol as a local infiltration anaesthesia in tendon repair surgery of hand. The onset of action for tramadol as a LA using inferior alveolar nerve block has been reported to be about 2.95 min by Tahani Alsandook and co-workers. Lignocaine is the gold standard with which we can compare the LA effects of other new drugs [19]. Bennett [6] mentioned that the drug with a higher pK_a value provides relatively poor quality of local anaesthesia. The pK_a value for lignocaine is 7.9, while for tramadol it is 9.41 [1, 6, 24]. It has been shown that tramadol has a LA effect which is weaker than lignocaine [15, 16]. Therefore, owing to the relatively weaker anaesthetic property of tramadol there was a significant difference for intraoperative pain between the two groups in our study. The incidence of adverse events with tramadol is approximately 15% [25]. The most common adverse events with single or multiple dose oral or parenteral tramadol administration are nausea (6.1%) and vomiting (1.7%) [4, 25]. The incidence of adverse events depends on the mode of administration. If administered parenterally, then tramadol has relatively high initial plasma concentrations, particularly when injected too rapidly [2]. In a study conducted by Alsandook et al. [19], tramadol (with adrenaline) induced nausea in 6.45% and vomiting in 1.61% of patients, while lignocaine (with adrenaline) induced nausea in 2.23% of patients with no incidence of vomiting.

In conclusion, 5% tramadol has a LA property similar to 2% lignocaine but is a weaker anaesthetic as compared to lignocaine and it can be used as an alternative to lignocaine for extraction of tooth, like diphenhydramine, in situations where lignocaine cannot be used due to some unusual reason. However, it cannot be recommended as a first choice drug due to its weaker anaesthetic effect.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in this study (involving human participants) were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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