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Comparison of Local Anesthetic Effects of Tramadol Hydrochloride with Adrenaline versus Plain Tramadol Hydrochloride

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ABSTRACT

Background: Tramadol with Adrenaline has been shown to have a local anaesthetic effect when used as infiltration/block. Purpose: Assess the efficacy of tramadol hydrochloride with and without adrenaline in the extraction of maxillary premolar teeth. **Methods:** A double-blinded study was conducted involving 50 patients. The study participants were randomly allocated to 2 groups: in group A (n = 25), each patient received an initial dose of drug A (tramadol HCl 50 mg and adrenalin 0.0225 mg diluted to 1.8 mL by distilled water); in group B (n = 25), each patient received an initial dose of drug B (tramadol HCl 50 mg diluted to 1.8 mL by distilled water). The outcomes measured were degree of pain during tooth extraction, duration of surgery, and total numbers of cartridges used were recorded intraoperatively. Postoperatively, patients were instructed to record any adverse effects, such as nausea or vomiting, on the first day of the operation and report telephonically. **Results:** Significant differences were observed in the number of cartridges used and the degree of intraoperative pain. However, there was no significant difference in duration of surgery or side effects. **Conclusion:** The results of this study suggest that tramadol HCl in combination with adrenaline can be used as an alternative local anaesthetic in dental and oral surgical procedures.

Keywords: Tramadol, Local Anaesthesia, Adrenaline, Maxillary Premolar.

INTRODUCTION

Tramadol hydrochloride, 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 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] 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] However, there is very less literature providing the evidence of local anaesthesia effect of tramadol. Therefore, we conducted this study comparing local anaesthetic effects of tramadol hydrochloride with adrenaline versus plain tramadol hydrochloride in extraction of upper maxillary premolar teeth.

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MATERIALS AND METHODS

A total of 50 ASA 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. Exclusion criteria included a history of compromised medical status, a history of allergy or hypersensitivity to the drugs used in this trial, pregnant or lactating women, and patients who refused to be involved in the study. The participants were randomly divided into two groups of 25 each.

Group A

Each patient received an initial dose of 1 dental cartridge (1.8 mL) of drug A (mixture of tramadol HCl 50mg and adrenalin 0.0225 mg diluted to 1.8 mL by distilled water).

Group B

Each patient received an initial dose of 1.8 mL of drug B (tramadol HCl 50 mg diluted to 1.8 mL by distilled water).

The study drugs for the 2 groups were prepared by an independent investigator in the Department who was not involved in the surgical procedure

(Anaesthetist). Cartridges of drugs A and B had a similar appearance and were coded and blinded to the investigator and the participants. The same investigator performed all surgical procedures without having any idea about the type of drug to be used.

Gingival separation was performed 4 minutes after administration of the anaesthetic agent. The patient was instructed to inform the investigator about the degree of pain at any time during extraction by raising the hand. The degree of pain was evaluated using visual analog scale (VAS).[5] The VAS consisted of an interval scale ranging from 0 (no pain or discomfort) to 10 (maximum pain).

The mean of the VAS scores during the extraction was calculated and recorded. During the extraction, when the VAS exceeded 3 points, an additional half-cartridge (0.9 mL) of the same drug was injected into the extraction site.

Nausea and vomiting are common adverse effects of tramadol HCl.9 Persistent nausea (defined as an urge to vomit lasting >30 minutes) and at least 2 episodes of vomiting were treated with an intravenous injection of metoclopramide 10 mg. Nausea and vomiting were recorded using a 3-point ordinal scale (0, none; 1, nausea; 2, vomiting). Patients were reviewed after 24 hours and information about adverse effects was recorded telephonically.

Statistical analysis

SPSS 20.0 was used to analyze the obtained data. Independent-sample t tests were used to compare parametric variables (degree of pain, number of cartridges used, patient's age, and duration of extraction); the Mann-Whitney U test was used to compare nonparametric variables (nausea and vomiting, patient's gender).

RESULTS

The study was conducted in 50 patients (35 female and 15 male; age range, 18 to 32 yrs). There were no significant statistical ($p > 0.05$) differences in patient age, patient gender, and duration of tooth extraction between the 2 groups. In addition, all teeth were extracted simply by conventional methods without root fracture.

Two patients in group A required 1 additional injection (0.9 mL). In group B, 10 patients required additional injections: 9 patients required 1 additional injection and 6 patients required 2 additional injections (1.8 mL). The highest mean for cartridges used (1.33) was recorded in group B, whereas the lowest mean (1.15) was found in group A. [Table 1]

For intraoperative pain, the highest mean (0.87) was recorded in group B, whereas the lowest (0.22) was found in group A. [Table 1]

Regarding adverse effects, which were recorded in the first 24 hours after tooth extraction, the study showed only 1 case of nausea in group B and 2 cases of nausea and 1 of vomiting in group A. Statistical analysis of these data showed no difference in adverse effects (P = .417), whereas there were significant differences between the 2 study groups in cartridge numbers (P = .015) and intraoperative pain (P = .015) [Table 1].

Table 1: Mean number of cartridges used and intraoperative pain among groups

Variables	Groups	Mean +SD	P Value
Used cartridges	A	1.15 + 0.019	.015
	B	1.33 +0.282	
Intraoperative pain	A	0.22 +0.68	.015
	B	0.87 +1.70	

DISCUSSION

It was pointed out by Bennett that LA activity resides in various structural configurations other than those of local anaesthetics, vizaviz , compounds like antihistamines, analgesics, tranquillizers and antiarrhythmic drugs may have LA 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 local anesthesia efficacy of tramadol was first reported by Pang etal 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. 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.

The evidence obtained in this study shows that tramadol HCl with adrenaline (1:100,000) exhibits a local anesthetic effect that enables the surgeon to perform painless extraction of uppermolar teeth when it is infiltrated and injected to susceptible neurons by a supraperiosteal infiltration technique. In contrast, supraperiosteal infiltration of tramadol HCl provides weak local anesthesia (in relation to the large volume). This difference may be due to the presence of adrenaline in combination with tramadol HCl (group A), which produces vasoconstriction and confines the tramadol HCl locally to produce its effects on the nerve perfectly. In this study, there was a significant difference between groups A and B in the volume of local anesthetic solution administered to produce local anesthesia and in levels of intraoperative pain using VAS. Drug A (tramadol HCl with adrenaline) produced perfect local anesthesia and allowed painless extraction of upper premolar teeth.

CONCLUSION

In conclusion, tramadol HCl in combination with adrenaline was shown to be a very effective local anesthetic for the extraction of upper premolar teeth and can be used as an alternative local anesthetic in dental and oral surgery.

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