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RESEARCH ARTICLE

TRAMADOL - A LOCAL ANAESTHETIC WITH A DIFFERENCE

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ABSTRACT

Objectives: The synthetic opioid, tramadol is useful in a wide range of acute and chronic pain states. Of late, in addition to its systemic action, the local anaesthetic effect of tramadol on peripheral nerves has been shown in both: clinical and laboratory studies. We conducted a study to evaluate the effect of tramadol as a local anaesthetic and postoperative analgesic when compared with lignocaine for minor surgeries.***Methods:*** 40 ASA I-II adult patients aged 18-60 years, who were to undergo elective day care minor surgeries under local anaesthesia were randomly assigned to receive either 2mg/kg of tramadol with 1:2,00,000 adrenaline (Group T) or 1mg/kg of lignocaine with 1:2,00,000 adrenaline (Group L). Visual analogue score (VAS), pulse rate, respiratory rate & blood pressure were recorded at various times intraoperatively. Side effects were assessed. The total dose of rescue analgesic (oral paracetamol) consumed by the patient over the immediate 24 hours postoperatively was noted. ***Results and conclusion*:** After statistical analysis of the data, it was concluded that tramadol is a good local anaesthetic cum postoperative analgesic for minor surgical procedures and can be used as an adjunct or option to other commonly used local anaesthetics.

Key words: tramadol; lignocaine; local anaesthetic; postoperative analgesia.

INTRODUCTION:

The efficacy of tramadol in a wide range of acute and chronic pain states is well known[1]. It has been used in myocardial emergencies, in trauma and obstetric pain to supplement balanced anaesthesia and to treat postoperative pain[2]. It is an effective and well tolerated agent for the management of chronic pain of malignant or non-malignant origin, particularly neuropathic pain[3]. Of late, in addition to its systemic action, the local anaesthetic effect of tramadol on peripheral nerves has been shown in both: clinical and laboratory studies [4,5]. Nevertheless, we planned and conducted a study to evaluate the effect of tramadol as a local anaesthetic and postoperative analgesic when compared with lignocaine for minor surgeries.

METHODS:

Forty ASA-I-II adult patients aged 18-60 years were included in the study. All patients were to undergo elective day-case excision procedures on the trunk and extremities under local anaesthesia (e.g. lipoma excision, corn excision, sebaceous cyst excision). The exclusion criteria included patients with lesion on the face, incision >4cm, lesions with extensive tissue undermining, patients with history of sensitivity to the study drugs i. e. lignocaine / tramadol, obstetric patients and patients with risk of seizures.

After approval of the Ethical Committee of our hospital, written informed consent was obtained from all the subjects. The patients were divided into two, small, fixed and equal size groups of 20 each by simple random sampling as below –

Group L, n = 20 – received 1mg / kg lignocaine with 1:2,00,000 adrenaline for local infiltration.

Group T, n = 20 – received 2mg/kg tramadol with 1:2,00,000 adrenaline for local infiltration.

The sample size of 20 was decided in consultation with our statistician.

The solutions were diluted to 5ml. No preoperative sedation was given. The drug was prepared in a labelled syringe by the anaesthesiologist doing the study and was given for injection to the surgeon who was aware of the contents of the syringe. At the time of injection, pain was scored using visual analogue score VAS (0-10). Also, pulse rate, respiratory rate and B.P were recorded. After 2

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minutes, the surgeon was instructed to make the incision. At this time, VAS, pulse rate, respiratory rate and blood pressure were again noted. In case the VAS was more than 4 at incision, an additional dose of 0.5mg/kg of either drug was injected simultaneously. VAS, pulse rate, respiratory rate and B.P were noted again during surgery at 15 minutes and 30 minutes. If at any time, VAS was found to be >4, an additional 0.5mg/kg of Tramadol was given. Bleeding during surgery, local reactions, side effects like nausea and vomiting, dizziness were assessed and noted. The patient was shifted to the ward/discharged home and instructed to take 1 gm paracetamol twelve hourly orally only when he experienced pain. The patients were called on telephone or asked to visit our department on the next day, i.e. 24 hours after surgery and the total dose of analgesic consumed in 24 hours was noted. Also, questions related to the occurrence of side-effects like nausea, vomiting, dizziness, dry mouth postoperatively were asked.

Statistical analysis of data:

Student's 't' test was applied for parametric data analysis. P<0.05 was considered as statistically significant. Fisher's exact test was used for comparison of incidence of complications between the study groups. 95% confidence intervals (C.I) were calculated.

RESULTS:

Table 1: Patient demographics

Groups	Age(yrs) Mean ± SD	Sex (M/F)
Group L (n=20)	27.7 ± 8.14	10/10
Group T (n=20)	24.75 ± 8.19	11/9

L = lignocaine, T = tramadol, SD = standard deviation

It shows patient demographics. The patients were comparable in age and sex.

Table 2: Comparison of vas score

TIME (Min) (After study drug injection)	0	2	15	30
Group L VAS (Mean ± SD)	1.6 ± 0.60	0.95 ± 0.69	0.95 ± 1.15	0.75 ± 0.55
Group T VAS (Mean ± SD)	2 ± 1.08	0.5 ± 0.76	1.15 ± 1.14	1.20 ± 0.95

VAS = visual analogue score, L = lignocaine, T= tramadol, SD = standard deviation

It shows comparison of mean VAS scores at 0, 2,15 and 30 minutes following study drug injection. On applying Student's't' test, p>0.05 at 2,15 and 30 minutes, 95% C.I being 0.4±2.88. There was no statistically significant difference between the VAS scores of the two groups. At '0' minutes (time of injection), the VAS score was significantly high (p>0.001) in tramadol group compared to ligncocaine group.

Figure 1: Comparison of vas score

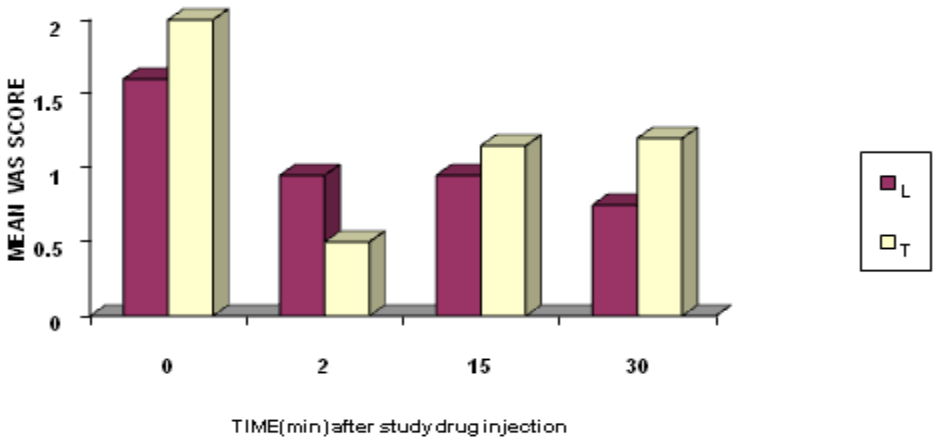


Table 3: comparison of 24hr post operative analgesic requirement {oral paracetamol (grams)}

Group	TOTAL 24HR ANALGESIC REQUIREMENT(Grams) Mean ± SD
Group L (n = 20)	1.71 ± 0.47
Group T (n = 20)	1.15 ± 0.38

L = lignocaine, T = tramadol, SD = Standard Deviation

It shows 24 hours postoperative analgesic requirement (oral paracetamol). Student's t-test was applied. It was found that tramadol group patients showed a significantly lower analgesic requirement compared to lignocaine group patients. ($p<0.001$, 95% C.I=0.56± 8.28).]

Figure 2: comparison of 24hr post operative analgesic requirement {oral paracetamol (grams)

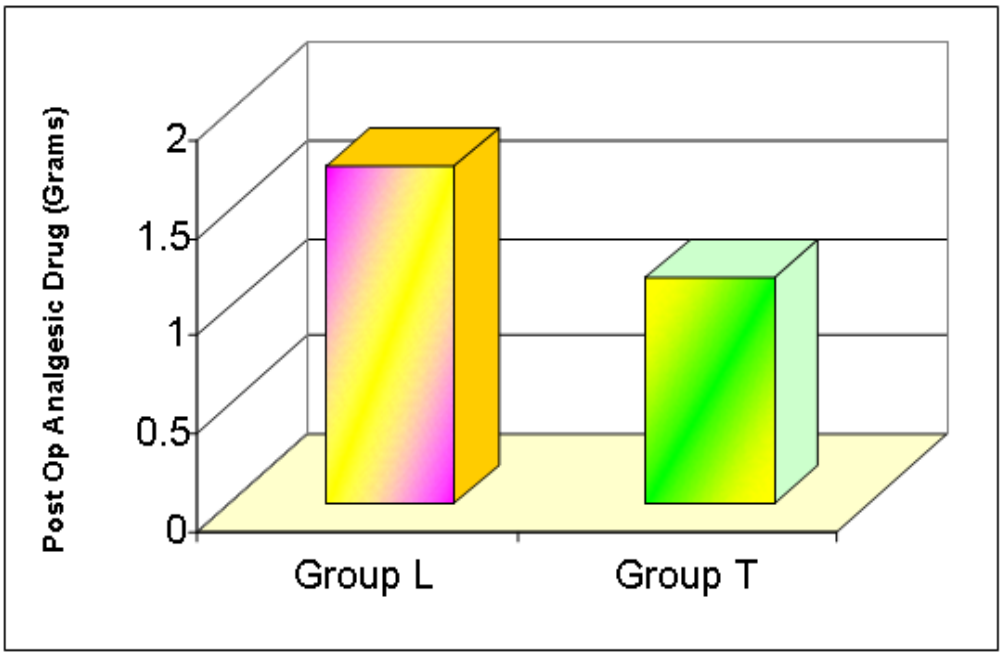


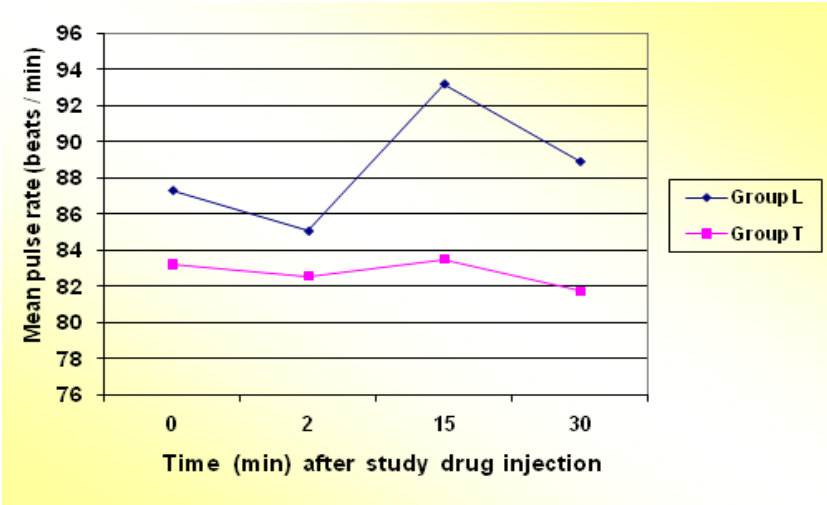
Table 4: comparison of mean pulse rate (beats / min)

TIME(MIN) (After study drug injection)	GROUP L Mean ± SD	GRPOUP T Mean ± SD
0	87.35 ± 3.12	83.25 ± 7.09
2	85.1 ± 6.44	82.6 ± 8.29
15	93.25 ± 9.68	83.5 ± 5.91
30	88.95 ± 6.85	81.8 ± 6.22

L = lignocaine, T = Tramadol, SD = Standard Deviation

It shows that haemodynamic parameters (pulse rate and mean arterial pressure) at post injection times (two,15 and 30 minutes) were comparable between the two groups except for a significant increase in heart rate and decrease in pulse rate at 15 & 30 minutes compared to baseline in lignocaine group and tramadol group respectively.

Figure 3: comparison of mean pulse rate (beats / min)



L = lignocaine, T = Tramadol

5% & 15% patients in tramadol group had nausea intra- operatively and post-operatively respectively whereas only 5% patients in lignocaine group had intraoperative nausea. 10% of patients in tramadol group had intraoperative giddiness. 5% tramadol group patients had significant intraoperative bleeding. However, there was no significant difference in the incidence of all these adverse effects on applying Fisher's exact test.

DISCUSSION:

The subcutaneous infiltration of local anaesthetic is effective for minor procedures or after surgery where it reduces postoperative analgesic requirements. Clonidine, opioids such as diamorphine, meperidine, fentanyl, sufentanil and antiarrhythmics like diltiazem, mexiletine have local anaesthetic effects in vitro studies[6,7]. Tramadol, a weak opioid selective for 'μ' receptors has been shown to have a local anaesthetic action on peripheral nerves[4].

Some investigators have compared the local anaesthetic effect of 5% tramadol 1ml with 1ml of 2% prilocaine injected intradermally for excision of lesions smaller than1cm [4]. They have reported a local anaesthetic effect with tramadol similar to that of prilocaine but with increase in the incidence of local reactions. In another study by the same authors[8], the subcutaneously administered tramadol 2mg/kg was found to provide local anaesthesia equal to lignocaine 1mg/kg with an extended postoperative pain free period. 2mg/kg tramadol has been used safely in intramuscular injections for analgesia. Hence, we used the same dose for local infiltration in our study. We did not observe any significant difference in VAS score for pain at incision at 2minutes, 15 minutes and 30 minutes after local injection between the tramadol and lignocaine groups thus proving that the local anaesthetic efficacy of tramadol equals that of lignocaine.

Regarding the intra-operative haemodynamic parameters, the mean arterial pressure and pulse rate remained stable in both groups. However, in lignocaine group, there was a significant rise in pulse rate at 15th and 30th minutes intraoperatively. This could be attributed to a possibility of increasing levels of patient anxiety. In this context, tramadol offers the added advantage of having sedation as one of its common adverse effects and stable haemodynamics resulting thereby [9].

The 24 hours postoperative analgesic requirement was significantly low in Tramadol group patients compared to lignocaine in our study. This shows that tramadol has the added advantage of providing postoperative analgesia.

Nausea and vomiting have been major side effects of tramadol used for postoperative analgesia[1]. Neverthless in our study, only 5% patients in tramadol group had nausea intraoperatively and 15% had nausea postoperatively. This incidence was less in lignocaine group, though the difference was not statistically significant.

Common adverse effects of tramadol include sedation, dizziness, nausea and dry mouth[9,10]. Drowsiness, constipation and sweating have also been reported[11].Compared with narcotics; tramadol does not induce significant respiratory depression. However, respiratory depression and convulsions have been noted occasionally with overdose of tramadol [12]. Except for 10%

of tramadol group cases having giddiness we did not encounter any of these side effects in our study.

Tramadol, a synthetic opioid of the aminocyclohexanol group is a centrally acting analgesic with weak opioid agonist (mu receptor) activity and effects on noradrenergic and serotonergic transmission. The opioid and non-opioid modes of action appear to act synergistically[2]. Regarding its local anaesthetic action, tramadol is said to affect sensory and motor nerve conduction by a similar mechanism to that of lidocaine which acts on the voltage dependant sodium channel leading to axonal blockage[12]. However, some authors have proposed that tramadol might have a mechanism different from that of lidocaine for producing conduction blocks wherein, the presence of a large Ca^{+2} concentration in the external medium increases activity of tramadol whereas decreasing activity of lidocaine [13.]
In our study, the sample size was limited to 20 each. Also, there was no blinding. Nevertheless, we propose to conduct a larger double blind study in the future for better statistical relevance. We compared tramadol with lignocaine because lignocaine is the most commonly used drug for local infiltration in our institute. Nevertheless, bupivacaine would have been another choice for drug comparison particularly because of its longer duration of action contributing to postoperative analgesia.

Adding tramadol as an adjunct to lignocaine for local infiltration could have been another option to choose. Application of tramadol locally preoperatively over the surgical site could be yet another future perspective. Here it could serve the dual purpose of preemptive analgesia cum local anaethesia. Nevertheless, it would not be surprising if in the near future, the manufacturers of tramadol would present it as a formulation for local application – a gel/cream/patch.
Local anaesthetics like lignocaine are directly myotoxic[14]. This effect is dose dependent and increased by repeated injection, increased concentration of agent and the concomitant use of epinephrine[14]. Local anaesthetic agents like lignocaine, bupivacaine, mepivacaine and ropivacaine can produce direct neurological damage and can be neurotoxic. They can produce morphological changes in growing neurons[15]. Commonly used local anaesthetic agents like lignocaine are vasoactive, being constrictor in low concentrations[14]. This may potentially lead to demyelination or local neuronal damage due to ischemia secondary to constriction of the nerve blood supply [14]. Understanding the mechanism of local anaesthetic action and the physical and pharmacological characteristics of currently available local anaesthetics enables the clinician to select the best drug for each clinical situation[15]. Thus for patients with a history of hypersensitivity to lignocaine or bupivacaine and in patients with leprous neuritis, motor neuron disease and multiple sclerosis where commonly used local anaesthetics may prove toxic to the nerves, tramadol could be a well chosen alternative. As the science of local anaesthesia evolves, better agents will edipse those currently available[16].
We conclude that tramadol is a good local anaesthetic cum postoperative analgesic for minor surgical procedures. Our study shows that tramadol can share or even challenge the position of existing local infiltration anaesthetics. Lignocaine, bupivacaine and other local anaesthetics out there, are you listening?

REFERENCES:

1 Shipton EA. Tramadol: present and future. Anesth Intensive care 2000;28:363-74.
2 Lehmann KA. Tramadol in acute pain. Drugs 1997;53 (2): 25-33.
3 Grond S, Sablotzki A. clinical pharmacology of tramadol. Clinical pharmacokinetics 2004; 43(13): 879-923.
4 Altunkaya H, Ozer Y, Kargi E, Babuccu O. Comparison of local anaesthetic effects of tramadol with prilocaine for minor surgical procedures. BJA 2003; 90(3) : 320-2
5 Pang WW, Huang PY, Chang DP, Huang MH. The peripheral analgesic effect of tramadol in reducing propofol injection pain: a comparison with ligocaine. Reg Anesth Pain Med 1999; 24:246-249.
6 Gissen AJ, Gugino LD, Datta S,Miller J, Covino BG . Effects of fentanyl and sufentanil on peripheral mammalian nerves. Anesth Analg 1987;66:1272-6.
7 Power I, Brown DT, Wildsmith JAW. The effects of fentanyl, meperidine and diamorphine on nerve conduction invitro. Reg Anesth 1991;16:204-8.
8 Altunkaya Hanife, Ozer Y, Kargi E, Ozkocak I, Hosnuter M, et al. The postoperative analgesic effect of tramadol when used as a subcutaneous local anaesthetic. Anesth Analg 2004;99:1461-4.
9 Lewis KS, Han NH. Tramadol : a new centrally acting analgesic. Am J Health Syst Pharm 1997. Mar 15; 54(6):643-52.
10 Katz WA. Pharmacology and clinical experience with tramadol in osteoarthritis. Drugs 1996; 52(3):39-47.
11 Smith Carolyn M, Colvin John R. Control of acute pain in postoperative and posttraumatic situations. Anaesthesia and Intensive care medicine 2005;61:2-6.

(availableat:www.sciencedirect.com/ science /journal /14720299/6/1)

12 Jou IM, Chu KS, Chen HH, Chang PJ, Tsai YC. The effects of intrathecal tramadol on spinal somatosensory evoked potentials and motor evoked responses in rats. Anesth Analg 2003; 96(3): 783-8.

13 Tufan Mert , Gunes Y, Guven M, Gunay I, Ozcengiz D et al. Comparison of nerve conduction blocks by an opioid and a local anesthetic. Eur J Pharmacol 2002;439:77-8.

14 Ian Melonachie, Janet Barrie. Regional anaesthesia techniques. In: Wylie and Churchill Davidson's A practice of Anaesthesia, seventh edition. Arnold 2003:599-629.

15 Inas A.M. Radwan, Shigeru Saito, Fumio Goto. The neurotoxicity of local anaesthetics on growing neurons: mepivacaine and ropivacaine. Anesth Analg 2002,94:319-24.

16 Saifudin Rashiq , Brendan T Finucane. Nerve conduction and local anaesthetic action. In: Wylie and Churchill Davidson's A practice of Anaesthesia, 7th edition. Arnold 2003: 267-77.

