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Comparative Study Of Tramadol And Ketorolac In The Pain Management Of Third Molar Tooth Extraction

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Abstract:
Background: *Analgesia, One Of The Components Of Triad Of Anaesthesia, Has Now Extended To Relief Of Postoperative Pain Of Third Molar Extraction. In This Comparative Study Is Presenting To Compare The Analgesic Efficacy Of Preoperative Intramuscular (IM) Ketorolac Versus Tramadol In Preventing Postoperative Pain After Mandibular Third Molar Surgery.*
Materials And Methods*: In This Comparative Study, 50 Patients Of Age Group 16 To 40 Years Undergoing Third Molar Extraction Under Local Anesthesia. Patients Were Randomly Allocated 25 Patients Each Group, Group K(Ketarolac 30 Mg IM) & Group T (Tramadol 100mg IM).*
Results*: The Present Study Included Administration Of IM Ketorolac And Tramadol In 50 Patients Each Preoperative To Third Molar Surgery And Both Drugs Were Compared For Onset Of Analgesia, Duration Of Action, Sum Of Pain Intensity Scores For 2nd, 4th, 6th, 12th, And 24th Post-Operative Hour And Interpreted.*
Conclusion*: To Conclude, Though Both The Drugs Were Effective In Controlling Postoperative Pain In Patients Undergoing Third Molar Surgery, The Comparative Results Of This Study Clearly Demonstrate That Intramuscular Tramadol Is Significantly Better Than Intramuscular Ketorolac (P<0.05).*
Key Word*: Ketorolac, Pain, Third Molar Surgery, Tramadol*

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I. Introduction

Pain is one of the most commonly experienced symptoms in dentistry, as such, is a major concern to the surgeon. Pain defines as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1]. Accordingly, pain is that experience which associate with actual or potential tissue damage. One of the most important aspects of the practice of dentistry is the control or elimination of pain. After extraction of any tooth most commonly seen complication is pain, especially in surgical extraction of third molar. Post surgery pain control after third molar surgery may lead to improve regaining in terms of lifestyle and oral function [2,3]. For pain control raising the pain threshold is one of widely used method. It depends on the pharmacological actions of drugs possessing analgesic interface with pain reaction. It should be clearly understood that the pain threshold can be raised to limited degree, depending on the specific drugs.

Tramadol hydrochloride, which is a synthetic analog of codeine, has been proved clinically effective in treating moderate to moderately severe pain [4]. In humans, Tramadol causes minimal respiratory depression and few gastrointestinal effects, and has less potential for causing opiate like dependence than morphine [5]. Ketorolac is a member of pyrrolo-pyrrole group of non-steroidal anti-inflammatory drugs. It possesses analgesic, anti-inflammatory and anti-pyretic activity. The primary action of Ketorolac appears to be inhibition of cyclooxygenase enzyme that metabolizes Arachidonic acid to endoperoxide intermediates and prostaglandins that promote pain[6,7]. The purpose of this analysis is to comparatively assess the best post operative analgesia outcome in third molar surgery using doses of Ketorolac (30 mg IM) and Tramadol (100 mg IM).

II. Methods

This comparative analytical study was conducted at Kusum Devi Sundarlal Jain Dental Hospital & College between December 2022 and May 2023, included 50 patients who underwent removal of third molars under Local anaesthesia (LA). Patient's records were collected using visual analog scale (VAS). All procedures were performed by consultant oral and maxillofacial surgeons and their designated subordinates who were trained to extract third molars. All patients underwent standard surgical protocol.

The extraction technique involved the removal of third molars with or without mucoperiosteal flap elevation and lingual flap retraction, bone removal and tooth sectioning using surgical drills, elevators and/or forceps. After tooth extraction, the sockets were irrigated with chlorhexidine, bony irregularities were corrected and surgical wounds were closed using non-absorbable sutures. Following the procedure, detailed postoperative instructions were given to the patients and suitable antibiotics and analgesics were prescribed.

50 adult patients were randomized into two groups. The first group of patients (Group-K) was given Ketorolac 30 mg IM post-operatively. The second group of patients (Group-T) was given Tramadol 100 mg IM in the same manner. Pain was assessed on the basis of visual analogue scale (VAS) at the 2nd, 4th, 6th, 12th, and 24th post operative hour. The end points of the 100 mm VAS were 'no pain' and 'pain could not be worse'. The mean from VAS were classified as none/no pain 0–10 mm, mild pain 11–30 mm, moderate pain 31–60 mm and severe pain 61–100 mm. All the patients enrolled completed the study

III. Result

The present study included administration of IM ketorolac and tramadol in 50 patients each preoperative to third molar surgery and both drugs were compared for onset of analgesia, duration of action, sum of pain intensity scores for 2nd, 4th, 6th, 12th, and 24th post-operative hour and interpreted.

The mean age of ketorolac and tramadol was 16 and 40 , respectively, which were not significant statistically [Table 1].

Table 2 shows pain measurement in Group-K on the basis of VAS. The VAS values were recorded at the 2nd, 4th, 6th, 12th, and 24th post-operative hour and interpreted. There was a significant decrease in pain intensity from the 2nd to 24th post-operative hour (chi -test, $P<0.05$). The maximum pain recording belonged to moderate category and the maximum number of patients experiencing moderate pain was 11 during the 2nd post-operative hour, while at the 24th post-operative hour, 8 patients reported only mild pain while 17 patients were free of any pain. Table 3 shows pain measurement in Group-T on the basis of VAS at the 2nd, 4th, 6th, 12th, and 24th postoperative hour. There was a significant decrease in pain intensity from the 2nd to 24th post-operative hour (chi test, P\0.05). In this group also, the maximum pain recording belonged to moderate category but the maximum number of patients experiencing moderate pain was just 4 at the 2nd post-operative hour. All the patients were free of pain at the 24th post-operative hour.

Table 4 shows comparison of pain incidence between Group-K and Group-T. In both groups, the pain intensity was measured on the basis of VAS at the 2nd, 4th, 6th, 12th, and 24th post-operative hour, and the results were compared using x^2 -test (chi). Though both the drugs resulted in significant decrease in pain intensity from the 2nd to 24th post-operative hour, intramuscular tramadol always resulted in better pain control than intramuscular ketorolac at every post-operative hour ($P<0.050$).

Table 5 shows adverse events associated with Group-K and Group-T. There were only three adverse events (mild skin reaction, 2; sweating and nausea, 1) in patients taking intramuscular ketorolac while three adverse events (nausea, 2; nausea and vomiting, 1) were noted among those taking intramuscular tramadol.

Table no 1- Age-wise distribution between the groups

Age group (years)	Frequency (%)	Ketorolac	Tramadol	t test	P	Significance
16-24	87% (43.5)	27.37±6.19	25.73±5.72	1.945	0.299	Not significant
25-32	78(39.0)					
33-40	35(17.5)					
Total	200 (100.0)					

Age range: 16-40 years unpaired t-test, $P>0.05$, not significant

Table 2 Pain incidence in Ketorolac

Time of assessment (h)	No. of cases	Pain incidence		
		Mild pain N (%)	Moderate pain N (%)	No pain N (%)
2	25	14 (56%)	11 (44%)	----------
4	25	21 (84%)	4 (16%)	--------
6	25	25 (100%)	--------	--------
12	25	20 (80%)	-------	5 (20%)

24	25	8 (32%)		25 (100%)
Comparison (h)			Significance	
			X^2	P
2–4			4.67	<0.05
2–6			14.1	<0.01
2–12			17.1	<0.01
2–24			29.6	<0.01

Table 3 Pain incidence in Tramadol

Time of assessment (h)	No. of cases	Pain incidence		
		Mild pain N (%)	Moderate pain N (%)	No pain N (%)
2	25	19 (76%)	4 (16%)	2 (8%)
4	25	18(22%)	1 (4%)	6(24%)
6	25	8 (32%)	---------	17(68%)
12	25	3 (12%)	--------	22(88%)
24	25	----------	---------	25 (100%)
Comparison (h)			Significance	
			X^2	P
2–4			3.83	<0.05
2–6			20.3	<0.01
2–12			32.3	<0.01
2–24			42.6	<0.01

Table 4 Comparison of pain incidence between Ketorolac group (Group-K) and Tramadol group (Group-T)

Time (h)	Group	No. of patient	Pain incidence			K vs T	
			Mild pain N (%)	Moderate pain N (%)	No pain N (%)		
						X^2	P
2	K	25	14 (56%)	11 (44%)	-----	6.03	<0.05
	T	25	19(76%)	4(16%)	2(8%)		
4	K	25	21 (84%)	4(16%)	----	8.03	<0.05
	T	25	18(72%)	1(4%)	6(24%)		
6	K	25	25 (100%)	-------	-----	25.8	<0.01
	T	25	8(32%)	--------	17(68%)		
12	K	25	20 (80%)	--------	5(20%)	23.3	<0.01
	T	25	3(12%)	--------	22(88%)		
24	K	25	8(32%)	--------	17(68%)	9.5	<0.01
	T	25	--------	----------	25(100%)		

Table 5 Side effects seen in Tramadol and Ketorolac groups

Side effects	Group		Significance
	Ketorolac (%)	Tramadol (%)	
Mild skin reaction	2 (8.00%) N.S.	0 (0.00%)	N.S.
Nausea and vomiting	0 (0.00%)	1 (4.00%)	N.S.
Nausea	0 (0.00%)	2 (8.00%)	N.S.
Sweating and nausea	1 (4.00%)	0 (0.00%)	N.S.
Total	3(12%)	3(12%)	N.S.

IV. Discussion

Inspite of the spectacular advances in modern medicine, no single drug satisfied all the criteria of an ideal post extraction analgesic. Post extraction analgesia can increase the patients' comfort, decrease the pain and stress after tooth extraction.[8]. The tissue response to noxious stimuli due to injury results by reducing the threshold of nociceptive afferent nerve terminals and at the more central level, by increasing the excitability of the second order neurons in the spinal cord. Based on this the concept of preemptive analgesia has been evolved. Administration of analgesics before the painful stimulus, the development of pain hypersensitization may be reduced or abolished, thus resulting in less postoperative pain[9,10]. It has been postulated that the pain existing before surgery may have already achieved central sensitization, thus making preemptive analgesia ineffective; therefore, asymptomatic impacted mandibular third molars were included in the current study.

There is an increase in need for clinical models that accurately reflect the efficacy of various analgesics commonly used. Third molar surgery is the model commonly used to test the efficacy of analgesics since the procedure induces pain that generally is consistent in severity allowing for good discrimination between weak and strong analgesics [11].

The search for appropriate drugs to treat patients with moderate to severe pain has led to the development of Tramadol hydrochloride, a centrally acting synthetic analgesic with a novel mechanism of action: a complementary and synergistic interaction between an inhibition of neuronal monoamine reuptake and a weak affinity for opioid receptors [12]. On other side Ketorolac is a member of pyrrolo-pyrrole group of Non-steroidal anti-inflammatory drugs. It possesses analgesic, anti-inflammatory and anti-pyretic activity. The primary action of Ketorolac appears to be inhibition of cyclooxygenase enzyme that metabolizes Arachidonic acid to endoperoxide intermediates and prostaglandins that promote pain [13]. The best postoperative regimen is one that offers broad analgesic coverage, is easy to administer, and is safe and economical. The surgeons must do everything possible to eliminate postoperative pain without causing additional problems, such as respiratory or vascular depression, gastrointestinal and visceral motility disorders, coagulation anomalies, drug tolerance and dependence.

Excellent results were demonstrated with the use of intramuscular Tramadol for treatment of postoperative pain in maxillofacial surgery (Table 4). Tramadol provided effective pain relief in high percentage of cases than ketorolac at every scheduled post-operative VAS record (Table 4). It has been reported that intramuscular Tramadol 100 mg, given postoperatively, has an analgesic effect equivalent to 30 mg of Pentazocine but is less potent than 10 mg of morphine [13]. The maximum pain, as experienced by patients, was of moderate type in both the groups. In the Group-K, moderate pain was reported in 44% of patients at 2nd postoperative hour, and by 16% of patients at 4th postoperative hour, while in Group-T moderate pain was reported by 16% of patients, and by only 4% of cases at 4th postoperative hour. After that, pain was not reported by the patients of either group.

The use of Ketorolac is now contraindicated in patients with hemorrhagic diathesis and in patients undergoing surgery that is associated with a high risk of hemorrhage or with incomplete haemostasis, and the maximum permitted dosage has been reduced from 90 to 60 mg/d in elderly [14]. A recent retrospective trial of more than 20,000 patients showed that parenteral Ketorolac caused a higher incidence of both gastrointestinal and surgical site bleeding than did opioids [15]. Tramadol, on the other hand, causes no significant adverse cardiovascular or respiratory reactions, and has no effect on coagulation either. These advantages bring it closer to an ideal analgesic which would have a high level of activity and a reassuring safety profile [16,17]. There are several studies comparing the analgesic efficacy of parenteral Tramadol and Ketorolac and most of them are in favour of Tramadol with regard to postoperative pain control[18]. However, few authors have found Tramadol-induced vomiting to be significant which can be controlled by anti-emetics that have been found to be safe in normal healthy adults.

V. Conclusion

To conclude, though both the drugs were effective in controlling postoperative pain in patients undergoing third molar surgery, the comparative results of this study clearly demonstrate that intramuscular Tramadol is significantly better than intramuscular Ketorolac ($P<0.05$). However, both produced side effects that were minor but do not appear to influence the outcome. Future randomized placebo-controlled research trials need to be performed to determine rational dose–response curves, in order to minimize undesirable side-effects but maximize benefits, economically.

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