ROLE OF SUBMUCOSAL TRAMADOL IN PAIN CONTROL AFTER MANDIBULAR THIRD MOLAR SURGERY

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ABSTRACT

Objective: The objective of this study was to find the analgesic effects of sub mucosal tramadol after 3rdmolar extraction.

Study Design: Study design was randomized, double-blind and placebo-controlled.

Place and Duration of Study: The study was conducted in Armed Forces Institute of Dentistry, Rawalpindi for a period of 4 months from 23rd February 2015 up till 30th June 2015.

Material and Methods: Sixty patients underwent third molar extractions (Pell & Gregory class 2, Position B, mesioangular). They were divided into two groups. Surgical site was randomly assigned to sub mucosal 100mg/2ml tramadol injection (group T) or normal saline solution (group P) immediately after surgery. Time of intake and amount of analgesic rescue drug, and postoperative pain intensity were recorded immediately after anesthesia cessation and 4, 8, 24and 48hours after surgery.

Results: Anesthetic blockade duration between groups was similar. In comparison to group P, time elapsed before first intake of rescue drug was longer, and pain intensity was lower significantly in group T ($p = 0.000$).

Conclusion: The local administration of 100mg/2ml tramadolcontributes to provide a prolonged pain-free period post-operatively and thus helps in controlling the amount of analgesics (specifically NSAIDS) consumed, increase patient comfort and compliance resulting in better quality of life.

Keywords: Analgesics, Third molar, Tramadol.

INTRODUCTION

Impacted mandibular third molar surgical removal causes swelling, trismus, and moderate to severe pain[1].Abetter pain control after oral surgery leads to an improved recovery in terms of quality of life[2]. Currently the most commonly used analgesics after dentoalveolar surgery arenon-steroidal anti-inflammatory drugs (NSAIDS)[3]. Use of NSAIDS is contraindicated in patients with peptic ulcers or bleedingdisorders, allergy to aspirin-like drugs and those taking anticoagulants or corticosteroids[4]. Tramadol may be an alternative for such patients. Different studies showed that tramadol is a safe analgesic for post-extraction pain relief with minimal side effects and provides prolonged analgesia hence proving it's effectiveness over ketorolac[4-6].

Tramadol is preferred over other opioids because it lacks serious side effects like respiratory depression[7]. Tramadol Hydrochloride being a narcotic analgesic which produces its effects through central actions. Tramadol and its active metabolite,M1, exhibits weak and selective affinity for opioidreceptors, acting as central analgesics[7]. Tramadol also exerts indirect action on monoaminergic receptors through norepinephrineand serotonin reuptake inhibition, thus blocking nociceptiveinputs at the spinal cord[7, 8]. Supra-additive anti-inflammatory effects produced by combination of tramadol andibuprofen has better efficacy for treating postsurgical dentalpain[8].

The present prospective placebo-controlled studywas designed to determine the analgesic

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and adjuvant anesthetic effects of tramadol administered locally by submucosal injection, immediately after impacted mandibular third molar removal.

Injecting tramadol submucosally is an easy and suitable method considered to be an additional therapeuticoption, available to dentists because it can be performed directly in the operative field[9].

MATERIAL AND METHODS

A randomized, double blind, placebo-controlled trial study was conducted in Armed Forces Institute of Dentistry, Rawalpindi, for a period of 4 months from 23rd February 2015 up till 30th June 2015. A total of 60 patients underwent surgical removal of one of their impacted mandibular 3rd molars in the department of oral and maxillofacial surgery.The inclusion criteria comprised of healthy individuals of any sex, age 25 to 35 years, with bone-impacted mandibular thirdmolars requiring surgical removal withequivalent surgical difficulty (Pell & Gregory class 2, Position B, mesioangular) andhaving no historyof psychiatric illness or allergy to NSAIDS or opioids.A single surgeon extracted all the third molars under local anesthesia containing lignocaine with adrenaline.

Exclusion criteria comprisedof the use of analgesic orana-inflammatory drugs 24 hours afore treatment, patients having seizure disorders, pregnancy or lactation, peptic ulcer, asthma, chronic opioid abuse or any other contraindication to NSAIDS or opioids. Patients were explained of the purpose, procedure and risks of the study and an informed consentwas taken on preoperative visit.An independent observer collected the preoperative interviews, subsequent observations and recordings after the surgery. Neither the observer nor the patients were aware of the rescue drug given. Teeth were extracted using standard envelope incision, removal of bone and wound closure. Patients (n=60) were divided into two groups randomly by using lottery method, Group-T received 100mg/2ml tramadol (TRAMAL 100® Grunenthal Ltd Pharmaceuticals , Pakistan) injected into the buccal mucosa adjacent to the third molar alveolus immediately after extraction and Group-P received 2ml normal saline solution in the same manner.

Patients were asked to note the intensity ofthepostoperative pain on a numerical scale of 0 to 10,where 0 meant no pain, 1-3 mild, 4-6 moderate,7-9 severe and 10 worst conceivable pain. Augmentin 625mg orally every 8 hours for 5 days was given as a standardized postoperative medicationto prevent any postoperative infection. A dose of 400 mg ibuprofen (Brufen) was prescribed as a rescue drug for moderate and severe postoperative pain as per need. Patients were instructed to record the number of analgesic pills (Brufen 400mg orally) taken by them, if any, and the time at which they took them. Patients were also instructed to return to hospital in case of unimaginable pain.Anesthetic cessation perception was noted by the moment of lip numbness cessation realized by patients.The readings were taken immediately after anesthesia cessation and at interval of 4, 8, 12, 24 and 48 hours after surgery. The patients were also asked to report the side effects of tramadol such as vomiting, nausea, dizziness, dry mouth and sweating.

Analgesic efficacy was assessed based on four end points: pain intensity (VAS); mean time elapsed before first intake of rescue medication; total dose of analgesic consumed during the first 48 hours; and overall evaluation of pain experience.

Data had been analyzed by using statistical software, SPSS version 20. Mean + S.D was calculated for qualitative variables like age and pain intensity(VAS) and categorical variables like gender and efficacy of drugs were presented by frequencies and percentages. Statistical test Chi-Square test was applied to measure the efficacy of drugs between groups T and P. A *p*-value of <0.05 was considered as a significant value

RESULTS

Out ofa total of 60 patients, 39 (65%)were male and 21(35%)were female. Their ages ranged from 25 to 35 years (Mean age 30.17+2.532 years). Mean ages of both groups were approximately same (Group – T=30.26 + 2.664 years and Group – *p*= 30.06+ 2.434 years), genders(Group – T= Males 73.3% and Females 26.7% and Group – P= Males 56.6% and Females 43.4%). Tables-1 and 2 show statistics of the above mentioned variables, along with the mean time elapsed before intake of first recue medication, for tramadol and normal saline respectively and table-3 shows the demographic data showing Chi-Square tests and P-value of both groups with reference to frequency of medication (efficacy of drugs).

Table-1: Frequency and time for medication of Tramadol.

Characteristics	Visual analogue scale (Mean)	Mean time for 1st medication (Hrs)	Frequency of medication
Mean	4.73	5.633 Hrs	4.20
Std Deviation	+0.640	+0.8503	+0.714
Minimum	4	5.0 Hrs	3
Maximum	6	7.0 Hrs	5

Table-2: Frequency and time for medication of Normal Saline.

Characteristics	Visual analogue scale (Mean)	Mean time for 1st medication (Hrs)	Frequency of medication
Mean	6.0	2.417 Hrs	5.17
Std Deviation	+0.947	+0.7437	+0.648
Minimum	4	1.5 Hrs	4
Maximum	7	4.0 Hrs	6

Table-3: The demographic data showing Chi-Square tests and *p*-value of both groups with reference to frequency of medication (efficacy of drugs).

Groups		Frequency of medication				Total	*p*-value
		3	4	5	6		
Tramadol or saline	Tramadol	5	14	11	0	30	<0.001
	Normal saline	0	4	17	9	30	
Total		**5**	**18**	**28**	**9**	**60**	

The results clearly show the effectiveness of tramadol as a potent analgesic. The patients in Group-T who were injected tramadol submucosally, had less pain intensity (average 4.73on VAS), longer time elapsed till first intake of rescue medication (Ibuprofen) and took less number of analgesic pills (128 in first 48 hours, Mean=4.26) post extraction as compared to patients in Group-P (145 in first 48 hours, Mean=4.83) who were injectednormal salinesubmucosal after 3rd molar extraction (average6.0on VAS) and a *p*-value of <0.001 (significant value).

DISCUSSION

Tramadol developed by a German pharmaceutical company in the early 1960s is commonly used as an analgesic for the relief of mild to moderate pain. Structurally it resembles codeine and morphine. Parenteral and oral are the most common administration routes, and it is very effective in managing moderate to severe postoperative painin both indoor and outdoor patients[10]. Tramadol is less likely to cause anypsychological dependence[11,12].

Tramadol has been proven to be an effective analgesic which is well tolerated by adults and children[13]. It isa safe drug which lacks side effects like respiratory depression and constipation. The

clinical use of tramadol in dental practice is less documented in Pakistan[14]. Tramadol is a good alternative to NSAIDs for postoperative pain after dentoalveolar surgery and is shown to besignificantly superior to placebo[14, 15]. Superior analgesic effect of tramadol by submucosal application is most probably due to the achievement of a higher drug concentration at the site of wound without loss, due to its body distribution and elimination[16].

An important finding of this study was that in comparison to group P,the mean time until intake of the first dose of rescuemedication was longer in group T, submucosal tramadol resulted in the decrease of postoperative analgesics use which is also in accordance with the other studies[5,17], providing evidence of the analgesic effectiveness of this kind of intervention.The peripheral mechanism of action of this otherwise centrally acting analgesic drug remains unclear. Some theories suggest that tramadol is an atypical opioid that acts on voltage-dependent sodium channels (as do local anesthetics) and adrenergic pathways (as do vasoconstrictors)[18], while someclaim that nonspecific voltage-dependent potassium channels and the nitric oxide system influence the antinociceptive effect of tramadol[17].

Tramadol has weak anti-inflammatory properties not involving arachidonic acid pathway[19, 20]. Tramadol has independent systemic and peripheral mechanisms of action, because itimproves the quality of postoperative analgesia when both routes are used in combination[21]. Between local and systemic mechanisms of action a synergistic effect is also conjectured[22].The submucosal route of administration is advantageous over systemic analgesics or NSAIDS because it reduces the risk of side effects[16]. In the present research, no major adverse effects were observed with tramadol.

CONCLUSION

The present study suggests that localadministration of 100mg/2ml tramadol providesa prolonged pain-free period (approx. 5 to 6 hours)with rare adverse effects as compared to other oral analgesics like NSAIDS and is a safe drug to be used for postoperative analgesia after dentoalveolar surgery.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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