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Efficacy of Tramadol as Pre-emptive Analgesia in Mandibular Impacted Third Molar Surgery

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Abstract **Original Research Article**

Introduction: The pre-emptive analgesia is an alternative for treating postsurgical pain. It is given before the painful stimulus begins to prevent or reduce the development of any ''memory'' of the pain stimulus in the nervous system. ***Objective:*** To investigate the existence of pre-emptive analgesic efficacy of Tramadol for impacted mandibular third molar surgery. ***Materials and methods:*** This was a prospective study carried out in Oral & Maxillofacial Surgery Department; Dhaka Dental College & Hospital.100 patients were included and were randomly divided into two groups. Study group received injection Tramadol 50mg, 20 minutes before surgery. Control group did not receive pre-emptive analgesic. Study parameters included (1) Pain intensity scores, (2) Time to 1st rescue analgesia and (3) Total number of analgesics consumed during the 5 post-operative days. ***Results:*** Study group reported considerable pain relief in the day of surgery at hours 1, 3 and 5 with significantly lower pain intensity scores. When the mean time to first rescue analgesic was assessed, study group reported a longer pain free interval with the mean time being 7.46±1.11 hours for study and 2.43±1.72 hours for control group. Patients in the control group consumed maximum number of rescue analgesics during the 5 post-operative days and Tramadol proved more efficient by consuming fewer rescue analgesics [p<0.001]. ***Conclusion:*** Tramadol has significant pre-emptive analgesic efficacy.

Keywords: Preemptive analgesia, Impacted third molar.

INTRODUCTION

Pre-emptive analgesia may be defined as an antinociceptive treatment that prevents establishment of altered central processing of afferent inputs from injury sites. Conditions are establish an appropriate blood level of analgesic before the surgical injury, and continuation of this effective analgesic level to prevent central sensitization during the inflammatory phase [1]. This concept was introduced by Crile at the beginning of the last century which is an alternative for treating postsurgical pain [2, 3].

Impacted third molar surgery is a common model for evaluating the efficacy of analgesics. Postoperative pain of this surgery ranges between moderate to severe during the first 24 hours, with the major pain intensity occurring between 6 to 8 hours [3]. The pain is so predictable, it has been suggested that prevention of pain is a better management strategy than treating pain once it has occurred [4].

Tramadol hydrochloride, (1RS,2RS)-2-[(dimethyl amino)-methyl]-1-(3-methoxyphenyl)-cyclohexanol hydrochloride, is clinically effective in the treatment of moderate to moderately severe pain with a relative low addiction potential [5]. It acts at opioid receptors and also seems to modify transmission of pain impulses by inhibition of monoamine reuptake. Tramadol is administered as a racemic mixture of two enantiomers, (+)-tramadol and (-)-tramadol, that are

metabolized by the liver [6]. The (+)-enantiomer has a moderate affinity for the opioid μ receptors, and inhibits serotonin reuptake, and the (-)-enantiomer is a norepinephrine reuptake inhibitor. In addition, biotransformation of tramadol in the liver results in many metabolites. O-desmethyl tramadol (M1) is the only active metabolite with a greater affinity for the μ receptors [7].

There are descriptions of the analgesic efficacy of Tramadol in different dentistry procedures. Clinically, studies have shown that tramadol may have local anesthetic-type properties but there are few studies that evaluated the pre-emptive analgesic effect of Tramadol [4]. The objective of the study was to assess the pre-emptive analgesic efficacy of Tramadol for impacted mandibular third molar surgery so that patient can have better comfort with less analgesic requirement.

MATERIALS AND METHODS

This prospective study was carried out in Oral & Maxillofacial Surgery Department of Dhaka Dental College & Hospital from 1st January 2016 to 30 June 2017. After approval by the Ethical Committee and signing the informed consent, total 100 patients presented with vertically placed impacted mandibular third molar (asymptomatic) requiring surgical extraction, under local anaesthesia were randomly divided into study and control group. Inclusion criteria were age group of 16 to 25 years, both sex, with vertical impaction (Pederson Difficulty index: 5-7), with no medical records, not using concomitant medication and not showing any sign of local infection at the time of surgery. Exclusion criteria includes local sign of infection, medically compromised, pregnancy, on steroid therapy, metabolic disorder and who had taken any type of analgesic in the past 48 hours. Patient confidentiality was strictly maintained.

All patients were given morning appointment. Preoperative measurement of pain was done by Visual Analogue Scale (VAS). In deltoid muscle, injection Tramadol 50mg was applied for study group before 20 minutes of incision. No pre-emptive analgesic was received by control group. In this study Tab Diclofenac sodium 50mg used as rescue analgesic and Tab Domperidone 10mg was antiemetic drug. Any adverse events like pain on injection of the study drug, nausea, vomiting or other complication were noted.

Postoperative pain assessment was done on day-1(Day of surgery) at hours 1,3,5,8 & 12 using a Numerical Rating Scale which was categorized as [0]-no pain, [1-3]-mild pain, [4-6]-moderate pain & [7-10]-severe pain. Time to 1st rescue analgesia (Diclofenac 50mg) and Total number of analgesics (Diclofenac 50mg) consumed during the 5 postoperative days was recorded. Data were compiled in a check list and was analysed by SPSS, Version 12.

Surgical procedure:

With all aseptic precaution under LA (Two 1.8ml cartridge of 2% Lignocaine with 1:100000 Adrenaline) clean and meticulous envelop incision was made. Mucoperiosteal flap was raised without damaging periosteum. Low speed micro motor straight hand piece (below 30000 rpm) was used for guttering of the bone on buccal and distal portion with surgical round and fissure bur. Adequate cooling arrangement was ensured. Sectioning of the third molar was done as per the standard methodology of impacted teeth surgery. After surgery, socket was inspected, irrigated with normal saline and the flap was closed with 3-0 silk suture. 2-3mm gap was kept distal to the second molar during suturing. Post-surgical instructions were explained.

RESULTS

Total 100 patients [48 males & 52 females] were divided into two equal groups as study & control. Both the groups were statistically balanced for the demographic variables and compared pre-emptive analgesic efficacy in terms of the following parameters: (1) Pain intensity scores on day 1 at Hours 1, 3, 5, 8 & 12; (2) Time to first rescue analgesia & (3) Total number of rescue analgesics consumed during 5 post-operative days. During the statistical analysis, p value of <0.05 or <0.01 were considered as significant, while p<0.001 suggested a highly significant value & p>0.05 was considered statistically not significant. The overall findings are presented in tables and figures.

Table I: Demographic variables

Variable	Study Group (n=50)	Control Group (n=50)	p value	Remarks
Age(mean±SD)	20.6±1.48	20.69±1.54	p > 0.05	Not Significant * Unpaired t test
Sex (male/female)	27/23	24/26	p > 0.05	Not Significant. X^2= 0.09
Weight (mean±SD)	60.72±8	57.1±8	p > 0.05	Not Significant *
Duration of Surgery (Hours)	0.88±0.2	0.89±0.22	p > 0.05	Not Significant *

* Unpaired t test

Table II Comparison between Study Group and Control Group in terms of pain intensity score in day of surgery

Pain Score	Control Group (Mean±SD)	Study Group (Mean±SD)	Mean Difference	p* Value	Significance
Hour 1	1.83±1.65	0.42±0.45	1.41	p 0.001	Highly Significant
Hour 3	3.11±1.26	1.37±0.54	1.74	p 0.001	Highly Significant
Hour 5	3.34±1.71	1.65±0.79	1.69	p 0.001	Highly Significant
Hour 8	3.64±1.98	3.14±1.08	0.5	p>0.05	Not Significant
Hour 12	2.69±1.47	2.33±0.94	0.36	p>0.05	Not Significant

*Wilcoxon's signed rank test

Table II shows that patients when treated with Tramadol reported of a considerable pain relief at Hours 1, 3 & 5 with significantly lower pain intensity scores but at hour 8 & 12 the difference was not statistically significant [p>0.05] .

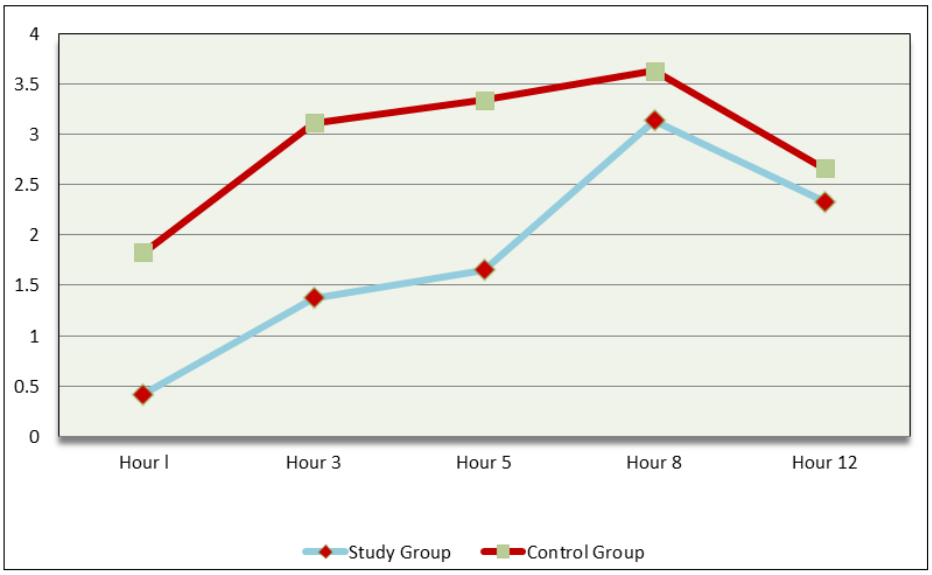

Fig I: Mean pain intensity score comparing between Study and Control Group

Fig I Showed patients when treated with Tramadol reported a lower pain intensity score then control group at all the time interval.

Table III: Mean time to first rescue analgesic and Total analgesics consumption

	Mean±SD		Mean Difference	p Value	Significance
	Control Group	Study Group			
Time to 1st Rescue Analgesic (Hours)	2.43±1.72	7.46±1.11	-5.03	p<0.001	Highly Significant*
Total No. of Analgesics consumed during 5 postoperative days	10.78±3.01	7.09±1.91	3.69	p<0.001	Highly Significant#

*Paired t test

#Wilcoxon's signed rank test

Table III shows, in terms of first rescue analgesic, patients in the study group reported a longer pain free interval than the control group with the mean time being 7.46±1.15 hours for study and 2.43±1.72 hours for control group. Patients in the control group consumed maximum number of rescue analgesic during the 5 post-operative days as against the study group and statistically highly significant value was noted. Tramadol proved more efficient by consuming fewer rescue analgesics [p<0.001].

DISCUSSION

An impacted tooth is one that has failed to erupt into the oral cavity within its expected developmental period of time and most common is mandibular third molar [8]. 18-40% of all extracted impacted third molars are asymptomatic and prophylactically removed in order to prevent the anticipated various complications [9]. Tramadol is a novel opioid drug having potency similar to that of

pathidine and shown to be effective for the treatment of moderate to severe postoperative pain following a variety of surgical procedures [10].

In this study both the study & control groups did not differ in their demographic characteristics & the surgical factors including the operating time; both of which can potentially affect the outcome measures. Any significant difference between both the study & the control groups in terms of pain, is thus attributable to the drug effect.

Present study shows, in terms of pain intensity score, study group achieved a better pain relief at all assessment levels. In a study Pozos Guillen *et al*., found statistically significant pain score while applied Tramadol as pre-emptive analgesia over non pre-emptive group for mandibular third molar surgery [4].

When the mean time to first rescue analgesic was assessed, patients in the study group reported a longer pain free interval than the control group with the mean time being 7.46±1.11 and 2.43±1.72 hours respectively, which is statistically highly significant [p<0.001]. Ashwin V. Shah *et al*., in their study found that pre-operative Tramadol produced post-operative analgesia for 7.43 hours which is consistent with this study [9]. Pozos Guillen *et al*., also concluded in his study about longer pain free interval up to 10.3 hours while applied intramuscular 100mg Tramadol as pre-emptive analgesia [4]. The longer duration to first rescue analgesic may be due to pre-emptive analgesic effect.

Patients of control group consumed maximum number of rescue analgesic during the 5 post-operative days and statistically significant value was noted [p<0.001]. Ashwin V. Shah *et al*., found that after application of pre-operative Tramadol for mandibular third molar surgery, mean value of post-operative analgesic consumed was 8.92±1.91 which supports this study [9]. Pozos Guillen *et al*., also found lesser number of rescue analgesic consumption while applied Tramadol as pre-emptive analgesia for mandibular third molar extraction [4]. In a study Dikhit P S *et al*., found mean number of rescue analgesic was 3.72±1.86 while applied 50mg Tramadol orally which is fair then us [11].

Ameury *et al*., found in their trial that pre-emptive Tramadol did not result in a perceptible decrease in post-operative pain compared with postoperative instant treatment group with the same dose but a longer time to rescue medication & lesser total post-operative analgesic consumption in the pre-treatment group was clinically significant suggestive of pre-emptive analgesic effect of tramadol [4]. Vittorio *et al*., in their study rated Tramadol as a better drug when compared to ketorolac which was used for post-operative pain management following nasal surgeries [12]. Putland *et al*., also observed better post-operative pain relief with tramadol as against to ketorolac following day case laparoscopic sterilization.[10] Present study is consistent with all of them.

In contrast to this study, a systematic review and meta-analysis demonstrated by Isiordia-Espinoza MA *et al*., showed that a single dose of tramadol has a significantly inferior analgesic effectiveness and safety profile than NSAIDs in oral surgery [13]. Unlugenc H *et al*., suggest that presurgical exposure to systemic opioid analgesia may not result in clinically perceptible benefits [14].

The side-effect profile of Tramadol may be more favourable than that of equipotent doses of other opioids, particularly in the context of day surgery and it has been shown to be associated with decreased sedation, a lack of clinically significant respiratory depression, and minimal effect on gastrointestinal function [10]. However, nausea and vomiting are the major side effect of Tramadol [9]. In our study only 3 patients complained of nausea. None of the patient in study group showed any other difficulties.

CONCLUSION

According to this study, Tramadol may be considered as an adjunctive before surgical procedures, which will reduce requirement of NSAID. However, more prospective studies should be encouraged for a much extensive, qualitative as well as quantitative assessment of the ideal pre-emptive analgesic.

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