

Pre-Emptive Analgesic Effect of Tramadol and Ibuprofen After Impacted Mandibular Third Molar Extraction

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الخلاصة

الأهداف: تقييم الفعالية لتسكين الآلام الناتجة عن إعطاء الترامادول أو الايبوبروفين قبل إجراء عملية رفع سن العقل جراحيا: **المواد وطرائق العمل:** تم إجراء القلع الجراحي لأسنان العقل السفلى لثلاثين مريضا، تم تقسيم المرضى إلى ثلاثة مجاميع، كل مجموعة تحتوي على عشرة مرضى، المجموعة الأولى تم إعطائهم ١٠٠ ملغ ترامادول قبل العملية زرقا عضليا، المجموعة الثانية تم إعطائهم ٨٠٠ ملغ ايبوبروفين عن طريق الفم، المجموعة الثالثة: لم يتم إعطائهم أي علاج قبل العملية (مجموعة السيطرة). تم تقييم الألم بعد العملية بعدة طرق مثل معيار الشبيه المرئي، معيار الألم اللفظي، اقتناع المريض، عدد حبوب البار استول ووقت أخذها خلال ٢٤ ساعة بعد العملية **النتائج:** وجدت فروق معنوية واضحة بين مجموعة الترامادول ومجموعة السيطرة في كل من معييير الألم المستخدمه لصالح مجموعة الترامادول. كما وجدت فروق معنوية في كل من معيار الشبيه المرئي وعدد الحبوب ووقت تناولها خلال ٢٤ ساعة بين مجموعة السيطرة ومجموعة الايبوبروفين لصالح مجموعة الايبوبروفين. وكذلك توجد فروقا معنوية واضحة بين مجموعتي الترامادول و الايبوبروفين في كل من معيار الشبيه المرئي ومعيار الألم اللفظي لصالح مجموعة الترامادول. **الاستنتاجات:** استخدام الترامادول أو الايبوبروفين استباقيا هو طريقة فعالة للسيطرة على الألم بعد عمليات القلع الجراحي لسن العقل المظمور.

ABSTRACT

Aims: to evaluate the efficacy of analgesia produced by preoperative administration of tramadol or ibuprofen on surgically extracted mandibular 3rd molars. **Materials and Methods:** surgical removal of lower 3rd molar was performed in 30 patients, they were divided into three groups of ten patient for each. Group I: preoperative 100mg tramadol IM injection; Group II: preoperative 800 mg Ibuprofen orally; Group III: control group with no preoperative treatment. Analgesia was assessed by visual analogue scale (VAS), Verbal pain Scale (VPS), patient satisfaction (PS), amount of analgesic consumption and time elapsed before first intake were recorded after 24 hours. **Results:** There was significant differences between tramadol and control group in all types of pain scales in favor of tramadol group. There was significant difference in the visual analog scale (VAS), number and time of tablets needed during 24 hours between Ibuprofen and control group. There was significant difference between Tramadol and Ibuprofen groups in both of (VAS) and (VPS) in favor of Tramadol group. **Conclusions:** The use of tramadol or ibuprofen preemptively is effective method of postoperative pain control in impacted lower 3rd molar surgery.

Key words: preemptive analgesia, impacted mandibular third molar

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INTRODUCTION

The removal of impacted lower third molar is the most common oral surgical operation, and the postoperative course can be complicated ⁽¹⁾. post-operative

complications may include swelling, bruising and limited mouth opening but patients are most often concerned about postoperative pain which may be severe ^(2,3). The post-operative pain severity may be anticipated from the nature of surgery.

Patients who require bone removal will experience severe pain. The patient should be advised before surgery for the anticipated postoperative pain and also the planned strategy to manage it. So, post operative pain management should be planned⁽²⁾. Despite major progress in pain management, post operative pain remains a clinical problem, that may extend the recovery period and predispose patients to expensive, time-consuming complication⁽⁴⁾. Poorly managed post operative pain contribute to patient dissatisfaction with their surgical experience, and yet pain management is frequently suboptimal⁽²⁾.

Preemptive analgesia concept was introduced by Crile at the beginning of the last century⁽⁵⁾. It was noted that blocking the transmission of pain before surgical incision reduced post operative mortality⁽⁶⁾. Preemptive analgesia is the administration of an analgesic before a painful stimulus, that occurs due to tissue damage during surgery, in an attempt to obtain better pain relief compared with when the same analgesic is used after the painful stimulus^(7, 8).

Tramadol has been found to be a suitable analgesic for use in moderate pain after oral surgery⁽³⁾. Tramadol, a centrally acting opioid analgesic, is agonist of μ opioid receptor⁽⁹⁾. On the basis of its potency, tramadol has comparatively few disadvantage associated with other opiates,

such as cardiovascular reactions, respiratory depression and physical dependency⁽¹⁰⁾.

Tramadol is a narcotic (opioid) used to control moderate and severe pain. Vertigo, nausea, vomiting, headache and xerostomia are the reported side effects of this drug⁽¹¹⁾. Non-steroidal anti-inflammatory drugs (NSAIDs) provide effective analgesia in patient with acute pain after surgery, either as a substitute or as an adjunct to opioid analgesia. The major advantage of NSAIDs is relatively well tolerability in selected patients for short term postoperative analgesia⁽¹⁰⁾. Ibuprofen as a NSAIDS drug was reported to control pain and is more tolerable than other drugs of the group⁽¹¹⁾. This study was performed to compare the preemptive analgesic effect of ibuprofen (non opioid) and tramadol (opioid) in patient undergoing surgical removal of impacted lower third molar.

MATERIALS AND METHODS

This study performed in department of oral and maxillofacial surgery of dentistry college, Mosul university, Iraq. The study was approved by the scientific committee of the department. The inclusion criteria consider healthy subjects of any sex, >18 years of age, with impacted mandibular third molar requiring surgical removal, and with no history of psychiatric illness or allergy to the drugs used in this study. Exclusion criteria included the use of analgesic or anti-

inflammatory drugs 24 hours before the surgical treatment, patient with gastritis or peptic ulcer.

Patients grouping: A double blind randomized study was carried out on a total number of thirties patients who included in this research. randomization were done by another surgeon.

The study comprise of three groups of 10 patients each. One group(control group) consist of patients receiving nothing in the preoperative setting (prior to surgery) followed by paracetamol 500mg tablets in the postoperative setting at need only (when there is intolerable pain) for 24 hours. Second group had patient receiving Ibuprofen 800 mg in the preoperative setting (one hour prior to surgery) and post operative setting of paracetamol 500 mg tablets at need. the third group consist of patients receiving 100 mg tramadol i.m injection 1 hour preoperatively, and post operative setting of paracetamol at need.

Surgical procedure: The same surgeon performed the surgical removal of impacted teeth of all the patients. Surgery was carried out under local anesthesia, using a maximum of 3 1.8 mL cartridges of 2% xylocain with 1:180, 000 adrenalin. A mucoperiosteal flap was elevated distally to the second molar providing access to the lower 3rd molar from the buccal aspect. Bone removal was achieved using new round bur with rotary hand piece under

copious continuous sterile saline irrigation. when it is needed, sectioning of crown and roots was performed with a fissure bur hand piece. After removal of the tooth, the socket was inspected and irrigated with sterile normal saline irrigation. Suturing was achieved by single stitch 3-0 black silk suture.). post operatively all patients received 500mg amoxicillin every 8 hours for 5 days or azithromycin 500 mg orally daily for 5 days to prevent post operative infection.

Pain scale measurement: Patients were given routine post operative instructions and were asked to fill a 4 parts questionnaire:1) evaluation of the pain intensity using of a 100 mm visual analog scale (VAS) at 24 hours post operatively, with 0 anchored by no pain and 100 is a very intense pain. ;2)evaluation of pain intensity with the use of the 5- points verbal pain scale scoring as 0 no pain 1: mild pain, 2: moderate pain, 3: severe pain and 4: as a very severe pain; 3)amount of analgesic consumption and time elapsed before first intake; 4) patient satisfaction as (yes) or(no).

Statistical analysis: Data were loaded on Pentium IV computer and analyzed using Statistical Package for Social Sciences (SPSS) Program Version 13.0. Analysis included descriptive statistics (frequency and percentages for non-parametric data, and mean and standard deviation for parametric ones); and analytical statistics

(Mann–Whitney Test for non–parametric data, and Duncan's Multiple Range Test for parametric ones). Differences between groups were considered statistically significant when $p \leq 0.05$ level

RESULTS

1- Comparing Tramadol and Control

group:

Using Mann- Whitney test there was significant differences between tramadol and control group in all of visual analog scale (VAS) , verbal pain scale (VPS) and patient satisfaction in favor of tramadol group as in table (1).

Table (1): tramadol versus control group

	VAS	VPS	Satisfaction
Mann-Whitney U	2.500	3.500	30.000
Z	-3.853	-3.696	-2.179
p–value	0.000*	0.000*	0.029*

Using Duncan's Multiple Range Test there was significant differences between the tramadol and control groups in number of

tablets (table 2) and time of tablets needed during 24 hours as in table (3)

Table (2): No. of Tablets

Group	No.	Duncan's Grouping	
		A	B
Tramadol	10	1.50	
Ibuprofen	10	2.30	
Control	10		3.60

Table (3): Time for Tablets to be Taken

Group	No.	Duncan's Grouping	
		A	B
Control	10	2.20	
Ibuprofen	10		4.70
Tramadol	10		4.88

1- Comparing Ibuprofen and Control groups

Using Mann-Whitney Test there was significant difference in the visual analog scale (VAS) between

Ibuprofen and control group but there was no significant differences regarding verbal pain scale (VPS) and patient satisfaction .as in table (4).

Table (4) :Ibuprofen vs. Control

	VAS	VPS	Satisfaction
Mann-Whitney U	27.500	27.500	45.000
Z	-2.033	-1.849	-0.457
p-value	0.042*	0.064	0.648

Using Duncan's Multiple Range Test there was significant differences between the Ibuprofen and control groups in number of tablets as in (table 2) and time of tablets needed during 24 hours as in table (3).

2- Comparing Tramadol versus Ibuprofen groups

Using Mann-Whitney Test there was

significant difference between Tramadol and Ibuprofen groups in both of (VAS) and (VPS) in favor of Tramadol group , but there was no significant difference in patient satisfaction , as in table (5).

Table (5): Tramadol vs. Ibuprofen

	VAS	VPS	Satisfaction
Mann-Whitney U	9.500	21.500	35.000
Z	-3.454	-2.374	-1.831
p-value	0.001*	0.018*	0.067

Using Duncan's Multiple Range Test there was no significant differences between the tramadol and Ibuprofen groups in both number of tablets, as in (table 2) and time of tablets needed during 24 hours, as in table (3).

3- Operation time of all the groups:

Using Duncan's Multiple Range Test there was no significant differences between the tramadol, Ibuprofen and control groups in time of the operation (in minutes from beginning of incision to the last stitch of suturing), as in table (6).

Table (6): Operation Time

Group	No.	Duncan's Grouping
		A
Control	10	16.80
Ibuprofen	10	19.00
Tramadol	10	19.50

DISCUSSION

Third molar extraction represent a standard model for predicting the clinical efficacy of analgesic⁽¹²⁾. Severe pain and average pain were related to the depth of tooth and the difficulty of extraction⁽¹⁾. Because 3rd molar surgical pain is so predictable, it has been suggested that prevention of pain is a better management strategy than treating pain once it has occurred⁽¹²⁾.

The topic of preemptive analgesia is controversial, with reports in favor of it as well as against it. therefore some guidelines have been developed to assess the quality of reports of randomized clinical trials in pain research⁽¹³⁾. Transmission of pain signals evoked by tissue damage leads to sensitization of the peripheral and central pain pathways. Preemptive analgesia is a treatment that is initiated before the surgical procedure in order to reduce this sensitization. consequently, immediate postoperative pain may be reduced and the development of chronic pain may be prevented⁽¹⁴⁾.

Pain receptors may be stimulated by mechanical damage, extremes of temperature, or by irritating chemical substances. When pain receptor in peripheral tissues (such as mucosa) are

stimulated, the nociceptive (pain) impulses are transmitted by two types of neurons to the spinal cord in the dorsal horn. The second order neurons, arising from the dorsal horn and pass via the spinothalamic tract to terminate in the thalamus, from which neuronal relays are sent to other CNS centers and the sensory cortex. These higher centers are responsible for the perception of pain and the emotional components that accompany it. There are four distinct processes in the sensory pathway: transduction, transmission, modulation and perception. Each of these processes presents a potential target for analgesic therapy⁽⁵⁾. So in this study Ibuprofen which is peripherally acting and Tramadol which is centrally acting analgesics were used to be assessed and compared as a preemptive analgesia.

From a conceptual standpoint, local anesthesia in itself is a preemptive analgesia, as it block the nerve impulse before starting the surgical incision. Thus we must consider that local anesthetic inhibits pain sensation both during and at the first hours after surgery⁽⁶⁾. Accordingly in this study, a placebo was not given for the control group.

This study shows that intramuscular

tramadol has a better analgesic efficacy in the prevention of post operative pain than oral ibuprofen and that of local anesthesia alone , however ibuprofen provide relatively good analgesia. This is agree with Ong et al in their study when they found that intra venous tramadol give better post operative analgesia than oral tramadol ⁽¹⁵⁾. Josh et al were use ibuprofen, paracetamol, codeine , diclofenac and placebo as a preemptive analgesia, they reach an interesting finding that patients who had taken placebo reported similar results to the preemptive analgesic groups ⁽¹⁶⁾.

It should be emphasized that VAS scores and other measures of pain may be influenced by side effects of the drug and other confounding variables, and may not be reliable as the sole measure in the study of preemptive analgesia ⁽¹⁴⁾ . the visual analogue scale is widely used in the measurement of both acute and chronic pain, as it simple to use and provides an accurate indication of the extent of pain ⁽²⁰⁾.accordingly in this study more than one scale were depended.

Regarding time elapsed before first need or intake of analgesic, in this study, the median time to rescue medication was 4.88 hours in the tramadol group, 4.7 hours in the Ibuprofen group and 2.2 hours in the control (local anesthesia) group. This results was coordinated with duration of action of tramadol, Ibuprofen and xylocain. It has been suggested that most patients would require analgesics 1-3

hours postoperatively following 3rd molar surgery using a conventional local anesthetic , this trend was further reflected by the significantly increased paracetamol consumption of rescue analgesics in the control group ⁽¹⁵⁾ .However, it should be noted that pain for 3rd molar surgery usually peaks at 6-8 hours after surgery⁽¹⁵⁾. thus the analgesic effects of intramuscular tramadol and that of ibuprofen would be decreasing just at the time when the post operative pain should be expected to peak, Hence additional rescue analgesics are required for good postoperative pain management ⁽¹⁵⁾.

Regarding number of analgesic tablets required postoperatively during 24 hours , in this study the control group required a mean of 3.6 tablets, Ibuprofen group required a mean of 2.3 tablets while tramadol group need a mean of 1.5 tablets. This indicated that the consumption of analgesics was significantly reduced in the preemptive groups.

Kaczmarzyk, et al, in 2010 reached that ketoprofen administered after third molar surgery provide more effective pain control than ketoprofen administered before the surgery^(21,22). Shaik MM concluded that tramadol is a suitable and safe analgesic for the relief of post operative pain and is more effective than ketorolac with prolonged analgesia and minimal side effects ⁽¹⁷⁾ , whereas Close BR concluded that Tramadol does not offer any particular benefits over existing analgesics and just recommended when

NSAIDs are not allowed to be administered for a patient⁽¹⁸⁾.

More refined studies are needed to establish whether the timing of administration and the mode of application (local anesthetic alone, NSADs alone, Opioid or combination) will be more effective, keeping in mind the possible rare adverse effects⁽¹⁹⁾.

CONCLUSIONS

The main finding in this study is that in patient undergoing surgical removal of an impacted mandibular 3rd molars, preemptive treatment with intramuscular tramadol did not result in a predictable decrease in postoperative pain compared with 800mg ibuprofen tablet, whereas both preemptive groups were significantly superior in pain reduction than control group. So the use of tramadol or ibuprofen preemptively is economical, effective, easy and safe method of postoperative pain control in impacted lower 3rd molar surgery.

REFERENCES

- 1- Yuasa H and Sugiora M. Clinical Postoperative Finding After Removal of Impacted Mandibular Third Molars: Prediction of Postoperative Facial Swelling and Pain Based on Postoperative Variables. *British Journal of Oral and Maxillofacial surgery*.2004;42:209-214.
- 2-Coulthard P.Post-operative oral surgery pain: areview : *oral surgery*. 2008 (1) ; 167- 177.
3. Cecheti MM, Negrato GV, Peres MP, Deboni MC and Naclerio Homem MD,. Analgesic And Adjuvant Anesthetic Effect Of Submucosal Tramadol After Mandibular Third Molar .Surgery.*Oral Surg Oral Med Oral Path Oral Radiol* .2012 ;xx (x): e1-e6.
- 4- Mobilio N, Gremigni P, pramstraller M, Vecchiadini R, Calura G and Catapano S. Explaining Pain After Lower Third Molar Extraction by Preoperative Pain Assessment. *J Oral Maxillofac Surg* .2011; 69: 2731- 2738.
- 5- Kelly DJ, Ahmed M and Brull SJ. Preemptive Analgesia I: Physiological Pathways And Pharmacological Modalities. *Can J Anesth*. 2001; 48(10): 1000-1010.
- 6- Liporaci Junior JLJ . Assessment Of Preemptive Analgesia Efficacy In Surgical Extraction Of Third Molars. *Rev Bras Anesteol*.2012; 62 (4) :502-510.
- 7- Hariharan S, Moseley H, Kumer A and Raju . The Effect Of Preemptive Analgesia In Postoperative Pain Relief- A Prospective Double- Blind Randomized Study: *American academy of pain medicine*: 2009; 10 (1) : 49- 53.
- 8- Jung YS, Kim MK, Um YJ, Park HS, Lee EW and Kang JW. The Effects On Postoperative Oral Surgery Pain By Varying NSAID Administration Times: Comparison On Effect Of Preemptive Analgesia . *Oral Surg Oral Med Oral Path Oral Radiol Endod* ,2005; 100 : 559- 563.
- 9- Hassan SS, Ahmed A, Rai M and Kalapa TM. Analgesic Efficacy of Tramadol and Butorphanol in Mandibular Third Molar

- Surgery. A Comparative Study. *The journal of contemporary dental practice*. 2012; 13 (3) :364-370.
- 10- Kirdemir P, Marsan A.comparing efficacy of preemptively used lornoxicam and tramadol for postoperative pain in patients underwent laparoscopic cholecystectomy. *Journal of clinical and experimental investigation*.2010; 1 (1): 1-6.
- 11- Zamiri B, Mousavizadeh K, Tajoddini M, Mohammadinezhad C and Arabi AM. Comparison of Ibuprofen, Celecoxib and Tramadol in Relief of Pain After Extraction of Mandibular Third Molar Teeth. *Iranian Red Crescent Medical Journal*.2009; 11 (4) :431-436.
- 12- Pozos-Guillenui A, Martinez-Rider R, Aguirre-Banuelos P and Perez-Urizar J. Pre-emptive Analgesic Effect of Tramadol After Mandibular Third Molar Extraction: A Pilot Study. *J Oral Maxillofac Surgery*.2007; 65:1315-1320.
- 13- Isiordia-espinoza , sanchez-prieto M, Tobaias- azua F, and Reyes-Garcia JG.Pre-emptive Analgesic Effectiveness of Meloxicam Versus Tramadol After Mandibular Third Molar Surgery: A Pilot Study.*J Oral Maxillofac Surg*. 2012;70:31-36.
- 14- Dahl JB and Moiniche S. pre-emptive analgesia .*British Medical Bulletin*.2004; 71: 13-27.
- 15- Ong CKS, Lirk P, Tan JM and SowBW. The Analgesic Efficacy of Intravenous Versus Oral Tramadol for Preventing Postoperative Pain After Third Molar Surgery. *J Oral Maxillofac Surg*.2005; 63:1162-1168.
- 16- Joshi A, Parara E, Macfarlane TV. A double-blind randomized controlled clinical trial of the effect of preoperative ibuprofen, diclofenac,paracetamol with codeine and placebo tablets for relief of postoperative pain after removal of impacted third molars. *British Journal of oral and maxillofacial surgery*.2004; 42: 299-306.
- 17- Shaik MM, Kumar J, Mobina N, et al. Comparative study of tramadol and ketolorac in the pain management of third molar tooth extraction. *J Coll Med Sci Nepal*.2010; 6(1): 35-43.
- 18- Close BR. Tramadol: does it have a role in emergency medicine?. *Emerg Med Australas*. 2005; 17:73-83.
- 19- Kaufman E,Epstein JB, Gorsky M,et al. Preemptive analgesia and local anesthesia as a supplement to general anesthesia: A Review. *Anesth Prog*.2005; 52. 29-38.
- 20- Nayyar MS and Yates C. Bupivacaine as pre-emptive analgesia in third molar surgery: Randomised controlled trial. *British journal of oral and maxillofacial surgery*. 2006;44:501-503.
- 21- Kaczmarzyk T, Wichlinski J, Stypulkowska J, Zaleska M, Woron J. Preemptive effect of ketoprofen on postoperative pain following third molar surgery. A prospective, randomized, double- blinded clinical trial. *Int J Oral Maxillofac Surg*. 2010;

- 39:647-652.
- 22- Shah R, Mahajan A, Shah N and Dadhania AP. Preemptive Analgesia in Third Molar Impaction Surgery. *National Journal of Maxillofacial Surgery*.2012 ; 3 (2):144-147.