Pre– and post– operative effectiveness of naproxen and ibuprofen on pain, swelling, and trismus following surgical removal of impacted mandibular third molar

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ABSTRACT

This study focused on the clinical evaluation of naproxen and ibuprofen efficacy on pain, swelling and trismus after surgical removal of impacted mandibular third molar, whether they used only pre–operatively or pre– and post–operatively. The number of patients included in the present study was 40, divided into four groups: Each group is 10 patients, the first group received naproxen as sodium 1hour pre-operatively followed by three times daily for five days post–operatively. Whereas the second group received naproxen as sodium three times daily for five days begins 1hour post–operatively. However, the third group had been given ibuprofen 1hour pre–operatively followed by three times daily for five days post–operatively. The fourth group administered ibuprofen three times daily for five days begins 1hour post–operatively.

The pain was evaluated by the number of paracetamol tablets taken by the patients recorded on the pocket chart, whereas the swelling was measured subjectively. The trismus was evaluated by measuring the maximum mouth opening between the incisal edges of the maxillary and mandi-bular central incisors using the graduated vernier.

The results showed that the use of naproxen as sodium 1hour pre–operatively minimized the pain, swelling and trismus significantly compared to ibuprofen.

Key Words: NSAIDs, naproxen, ibuprofen, impaction.

الخلاصة

إن هذه الدراسة ركزت على التقييم السريري لفعالية النابروكسين و الآيبوبروفين على الألم والورم والضزز بعد إزالة الأضراس السفلية الثالثة المطمورة فيما إذا استخدم العقار فقط قبل أجراء العملية أو قبل وبعد أجراء العملية . وكان عدد المراجعين المشاركين ٤٠ مريض قسموا إلى أربعة مجاميع لكل مجموعة ١٠ مرضى، وكالآتي:

المجموعة الأولى: يتناولون النابروكسين ساعة واحدة قبل العملية ثم ٣ جرعات يوميا لمدة خمسة أيام بعد العملية.

المجموعة الثانية: يتناولون النابروكسين ٣ جرعات يوميا لمدة خمسة أيام ابتداءً من ساعة واحدة بعد إنهاء العملية.

المجموعة الثالثة: يتناولون الأيبوبروفين ساعة واحدة قبل العملية ثم ٣ جرعات يوميا لمدة خمسة أيام بعد العملية.

المجموعة الرابعة: يتناولون الآيبوبروفين ٣ جرعات يوميا لمدة خمسة أيام ابتداءً من ساعة واحدة بعد إنهاء العملية.

قيم الألم بواسطة عدد حبوب الباراسيتامول التي يتناولها المريض والتي تسجل على بطاقة جيب، بينما قيم الورم نظريا وقيس الضزز بأعلى فتحة للفم ما بين الحافة القاطعة للقاطع الأول العلوي و السفلي بواسطة آلة لقياس الكسور الرقمية.

أثبتت النتائج بان استخدام النابروكسين ساعة واحدة قبل العملية له تأثير معنوي على الألم والورم والضزز مقارنة بالآيبوبروفين.

INTRODUCTION

Removal of either partially or completely impacted third molars involve trauma to soft tissue and bone, which results in post–operative inflammation, significant pain, swelling and trismus. The pain is generated by the release of endogenous mediators, such as bradykinine, serotonine and certain types of prostaglandin, beside that raising in tissue tension within the inflamed area is another cause. Pain also lead to continuation of trismus.[1] The main factor responsible for swelling is local edema caused by accumu-lation of fluid exudates in interstitial tissue spaces. The cause of trismus is due to inf-luence on the muscle by post–operative edema developed in adjacent tissue[2] and also surgical trauma to masticatory mus-cles mainly the masseter one.[3] Many approaches have been made to overcome or at least to reduce the severity of post-operative problems and localize the extend of inflammatory process. So that trials were made to achieve such goals either by using medicaments as antibiotics[4] or glucocorticosteroids which found to exert universal effect on inflammatory process,[5] antihistamine was showed to reduce the extend of inflammatory process,[6] also non–steroidal anti–inflammatory drugs (NSAIDs) were used.[7,8]

Vogel *et al*.[9] reported that the NSAIDs, are now becoming part of preoperative analgesic regimens to reduce post surgical pain and swelling, in that giving single dose immediately before an invasive procedure rather than prescribing the NSAIDs only after the pain become significant. Sevelius *et al*.[10] reported that a single dose of 550mg of naproxen sodium has greater analgesic activity than 650mg of aspirin with low incidence of side effect.

Sindet–Pedersen *et al.*[11] compared 500mg of naproxen, 650mg of aspirin twice daily for three days following oral surgery and showed greater efficacy and fewer side effects of naproxen. Prostaglandin E2 plays an important role in the inflammatory process and immune response causing long lasting vasodilatation accompanied by increased vascular permeability.[12] Prostaglandin are not stored in large amount in the body in contrast to other biologically active compounds but rather are synthesized immediately before they release. Prostaglandin concentration does not peak until 4 hours or more following surgical trauma. When ibuprofen is given following surgery, their blood level will be reached before peak prostaglandin level.[13]

Troullos *et al*.[14] compared the ibuprofen and flurbiprofen with methyl predinsolone and placebo for suppression of acute pain, swelling and trismus. Their subjects were out patients undergoing surgical removal of lower third molar (M_3). They found that NSAIDs produce earlier analgesia than do steroid, and combined use of steroids and NSAIDs in the pre–operative periods would be more effective than either one used alone in the control of post–operative pain, swelling and trismus.

Trismus can be evaluated post–operatively by different methods, such as the Boley gauge to measure the degree of trismus developed post–operatively.[6, 15, 16] A graduated vernier is used to measure the distance between upper and lower central incisor edges at maximal unaided mouth opening.[2, 8, 17]

This study focused on the clinical evaluation of naproxen and ibuprofen efficacy on pain, swelling and trismus after surgical removal of impacted mandibular third molar, whether they used only pre–operatively or pre– and post–operatively.

MATERIALS AND METHODS

This clinical trial comprised 40 out patients attending the Department of Oral and Maxillofacial Surgery, College of Dentistry, University of Mosul complaining of partially erupted lower third molar.

The patient selection

As far as the medical history was concerned the patient should be healthy without any medical complaints, no contra–indication to NSAIDs. All the cases op-erated on in the present study were ex-amined clinically to be partially erupted, free of symptom at the day of operation with mesioangular impaction in

relation to standing second molar and roentgenography determine the depth and direction of impaction and relation of the roots to inferior dental canal. The cases followed these criteria were accepted and treated and considered as data to present study. A specific case sheet was designed (Figure 1).

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Case No. ……

Drug Tested ……..

Patient's Name: …….. **Occupation: ……**

Age: …….. **Date: …….**

Sex: …… **Address: …….**

- **Chief Complain: ……**
- **Medical History:**

  Hospital admission . . . . . Drug use . . . . . Visit physician . . . . . .
- **Direction of Impaction:**

  Vertical . . . . Mesioangular . . . . . .Distoangular . . . . . Horizontal . . . . . .
- **Depth of Impaction :**

  Partially erupted ….. Covered by soft tissue . . . .Covered by hard tissue . . . .
- **Pre-Operative Assessment:**

  Mouth opening…….. mm

  Surgical Procedure:

  Operative time……min.

  Surgical trauma Mild [1] Moderate [2] Severe [3]

Follow up after 3 days

No pain [0] Mild [1] Moderate [2] Severe [3] Very severe [4]

Trismus was recorded …….mm

Swelling was recorded Grade 1… 2… 3… 4….

Follow up after 7 days

Suture Removal

No pain [0] Mild [1] Moderate [2] Severe [3] Very severe [4]

Trismus was recorded ……mm

Swelling was recorded Grade 1… 2… 3… 4….

Figure (1): Case sheet

The patients included in the present study were divided into four groups as follows:

- **NTG^{A}:** This group comprise 10 patients received naproxen as sodium 250mg (Naproxen as sodium HIKMA Pharmaceutical Jordan) one tablets 1hour pre–operatively followed by 3 tablets/ day for each 8 hours post–operatively for 5 days to be administered 1hour following surgical procedure.
- **NTG^{B}:** This group comprise 10 patients received naproxen as sodium 250mg (Naproxen as sodium HIKMA Pharmaceutical Jordan) 3 tablets/ day for each 8 hours post–operatively for 5 days to be administered 1hour following surgical procedure.
- **BTG^{A}:** This group comprise 10 patients received ibuprofen (ibuprofen 200mg SAMMERA Iraqi) one tablets 1hour pre–operatively followed by 3 tablets/ day for each 8 hours post–operatively for 5 days to be administered 1hour following surgical procedure.
- **BTG^{B}:** This group comprise 10 patients received ibuprofen (ibuprofen 200mg SAMMERA Iraqi) 3 tablets/ day for each 8 hours post–operatively for 5 days to be administered 1hour following surgical procedure.

NTG^{A}: Naproxen treated group pre– and post–operatively.
BTG^{A}: Ibuprofen treated group pre– and post–operatively.
NTG^{B}: Naproxen treated group post-operatively only.
BTG^{B}: Ibuprofen treated group post-operatively only.

Surgical instruments and tools used in the surgical operation room are shown in Figure (2).

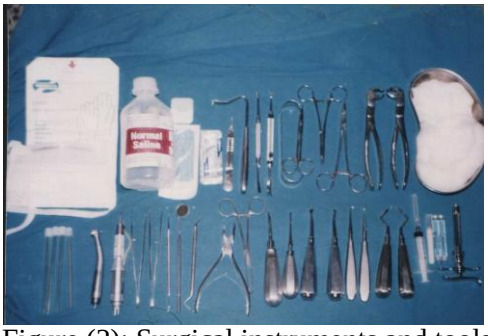

Figure (2): Surgical instruments and tools

Upper row (left to right): Surgical gloves, mask, normal saline, 3/0 black silk suture, dental film, blade no. 15, scalpel handle, flap retractor, Howarth's muco-periosteal elevator, bone file, cheek retractor, scissors, Extraction forceps lower wisdom (left and right), kidney dish with cotton.

Lower row (left to right): Disposable sucker tip, high speed turbine, low speed handpieces with surgical round bur no. 2, tweezers, dental probe, mouth mirror, curette, Roenger, toothed tissue forceps, straight elevator, chisel no. 1, Cryers elevators (left and right), Warwick James elevator (left and right), disposable hydrodynamic syringe, dental needle, xylocaine anesthesia carpules, dental syringe.

- **Operation technique**

All the surgical operations performed by the same researcher under local anesthesia which obtained by inferior alveolar, lingual and long buccal nerve block, using 2.2 ml lidocaine with 1:80000 adrenaline (Septodent–France). Standard surgical technique was used for all patients described by Killey *et al*.[18] Following reflection of mucoperiosteal flap, bone removal was done if needed. The degree of surgical trauma was recorded as follows:

- **Mild:** Only reflection of muco-periosteal flap and creation of point of application of elevator.
- **Moderate:** It needs reflection of mucoperiosteal flap and the bone removal by creating gutter on the buccal side of the tooth. Tooth sectioning if needed.
- **Severe:** It needs reflection of mucoperiosteal flap, bone removal from occlusal, buccal and the distal sides together with sectioning of the tooth.

As far as delivery of the tooth, the socket irrigated with at least 10 ml of normal saline for debridement of socket and only one stitch was done just distal to standing second molar and all post–operative instructions were recorded on the back of the chart as a guide line to patient

post–operatively.

- **Assessment of post–operative pain**

The pain was assessed subjectively according to the criteria developed by Al–Ani *et al*.[19] as follows (Figure 3):

Score 1: 0 Tablet.…….No pain .
Score 2: 1 Tablet …….Mild pain.
Score 3: 2 Tablets ……Moderate pain.
Score 4: 3 Tablets and over ….Severe pain.

Operation date:……..

Number of paracetamol tablets intake in week

Days	1st Tablet	2nd Tablet	3rd Tablet	Others
Satur.				
Sun.				
Mon.				
Tues.				
Wednes.				
Thurs.				
Fri.				

Figure (3): Pocket chart

- **Assessment of post–operative swelling**

The post–operative swelling were ass-essed subjectively by criteria developed by Sabur[16] as follows:

Score 0: No swelling.
Score 1: Edema that involves the alveolar mucosa buccally and /or lingually (intraorally).
Score 2: Edema that involves the alveolar mucosa buccally and /or lingually, and involves the cheek (extraorally) to the lower border of the mandible.
Score 3: Edema that involves the alveolar mucosa buccally and/or lingually and involves the cheek (extraorally) below the lower border of the mandible (Figures 4 and 5).

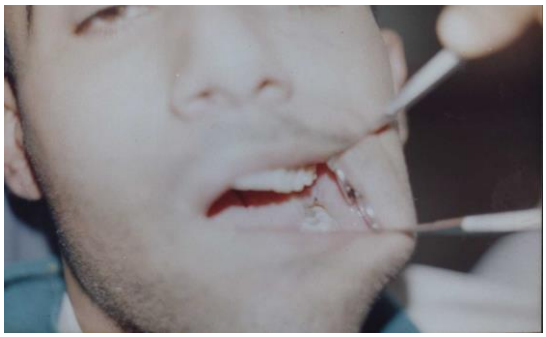

Figure (4): Intraoral swelling on buccal mucosa

- **Assessment of post–operative trismus**

The limitation of mouth opening was measured by using vernier between the incisal edges of upper and lower central incisors. The degree of trismus was assessed by subtracting the post–operative from the pre–operative measurements[8] (Figure 6).

The statistical analysis prepared in the present study was chi–square test (χ^2) for the direct statistical comparison of pain and swelling between ibuprofen treated groups (post–operative only or pre– and post–operatively) and naproxen treated groups (post–operative only or pre– and post–operatively), while t–test was used for the trismus. Paired sample t–test was used for statistical comparison between naproxen and ibuprofen treated groups for pain, swelling and trismus.

Figure (5): Extraoral swelling on buccal mucosa

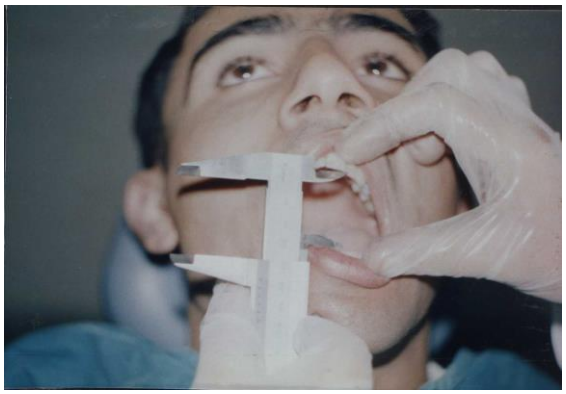

Figure (6): Using vernier to assess post–operative trismus

RESULTS

The number of patients operated on was 43. Of these, 3 cases were excluded because lacking the follow up data, so that the remaining 40 cases were introduced for statistical analysis.

1- The sex distribution and the mean age of patients in naproxen treated group (NTG):

In NTG^A there were 7 cases male and 3 cases female. The age range 22–28; the mean is 24.4. In NTG^B there were 3 cases male and 7 cases female. The age range 17–34; the mean is 23.9 as shown in Table (1).

2- The sex distribution and the mean age of patients in ibuprofen treated group(BTG):

In BTG^A there were 3 cases male and 7 cases female. The age range 18–33; the mean is 24.3. In BTG^B there were 5 cases male and 5 cases female. The age rang 17–30; the mean is 23.3 as shown in Table (2).

Table (1): Sex distribution and mean age of naproxen treated group

Group Tested	Sex		Age Range	Mean Age
	Male	Female		
NTG^A	7	3	22-28	24.4
NTG^B	3	7	17-34	23.9

NTG^A: Naproxen treated group pre– and post–operatively.

NTG^{B}: Naproxen treated group post–operatively only.

Table (2): Sex distribution and mean age of ibuprofen treated group

Group Tested	Sex		Age Range	Mean Age
	Male	Female		
BTG^{A}	3	7	18-33	24.3
BTG^{B}	5	5	17-30	23.3

BTG^{A}: Ibuprofen treated group pre– and post–operatively.
BTG^{B}: Ibuprofen treated group post–operatively only.

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3- Details of operated cases, involves surgical trauma and operation time:

In NTG^{A} there were 2 cases mild, 8 moderate. The operation time range 9–46 minutes; the mean operation time 22.5 minutes. In NTG^{B} there were 4 cases mild and 6 cases moderate. The operation time range 10–30 minutes; the mean operation time 22.0 minutes. In BTG^{A} there were 3 cases mild, 6 cases moderate and 1 case severe. The operation time range 7–42 minutes; the mean operation time 19.2 minutes. In BTG^{B} there were 5 cases mild and 5 cases moderate. The operation time range 13–25 minutes; the mean operation time 18.1 minutes as shown in Table (3).

4-Comparison between NTG^{A} and NTG^{B}:

Statistical comparison between NTG^{A} and NTG^{B} using chi–square and t–test gives that there were significant differences of pain at day 3 and day 7, swelling at day 3 only and trismus at day 7 as revealed by Table (4).

5-Comparison between BTG^{A} and BTG^{B}:

Statistical comparison between BTG^{A} and BTG^{B} using chi–square and t–test gives that there were no significant differences of pain, swelling and trismus at day 3 and day 7 as revealed by Table (5).

Table (3): Details of operated cases, involves surgical trauma and operation time

Group Tested	Surgical Trauma			Operation Time Range (Minutes)	Mean Operation Time (Minutes)
	Mild	Moderate	Severe		
NTG^{A}	2	8	-----	9-46	22.5
NTG^{B}	4	6	-----	10-30	22.0
BTG^{A}	3	6	1	7-42	19.2
BTG^{B}	5	5	-----	13-25	18.1

NTG^{A}: Naproxen treated group pre– and post–operatively.
NTG^{B}: Naproxen treated group post–operatively only.
BTG^{A}: Ibuprofen treated group pre– and post–operatively.

BTG^B: Ibuprofen treated group post–operatively only.

Table (4): Comparison between NTG^A and NTG^B

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Group Tested	Pain +		Swelling +		Trismus++	
	Day3	Day7	Day3	Day7	Day3	Day7
	χ^2				t–test	
NTG^A NTG^B	7.9**	5 **	10.5**	5.6*	1.7**	2.9*

*Not significant $p>0.05$.
** Significant $p<0.05$
+ Analysis using χ^2 test.
++Analysis using t-test.
NTG^A: Naproxen treated group pre– and post–operatively.
NTG^B: Naproxen treated group post–operatively only.

Table (5): Comparison between BTG^A and BTG^B

Group Tested	Pain +		Swelling +		Trismus++	
	Day3	Day7	Day3	Day7	Day3	Day7
	χ^2				t–test	
BTG^A BTG^B	1.3 *	1.82 *	6.5*	1.83*	1.58*	0.49*

*Not significant $p>0.05$.
** Significant $p<0.05$
+ Analysis using χ^2 test.
++Analysis using t-test.
BTG^A: Ibuprofen treated group pre– and post–operatively.
BTG^B: Ibuprofen treated group post–operatively only.

6- Comparison between NTG and BTG at day 3 post–operatively:

Paired t–test showed significant differences of pain in naproxen treated groups at day 3 post–operatively, not significant in swelling and trismus compared to ibuprofen treated groups as revealed by Table (6).

7- Comparison between NTG and BTG at day 7 post–operatively:

Paired t–test showed no significant differences of pain in naproxen treated groups at day 7 post–operatively, but significant differences in swelling and trismus compared to ibuprofen treated groups as revealed by Table (7).

Table (6): Comparison between NTG and BTG at day 3 post–operatively

Group Tested	Pain		Swelling		Trismus	
	Mean	Paired t–test	Mean	Paired t–test	Mean	Paired t–test
NTG	7.9	0.0001*	10.5	0.025**	1.5	0.775**
BTG	1.3		6.5		1.58	

*Significant $p<0.0001$.
** Non significant $p>0.0001$.
NTG: Naproxen treated group.
BTG: Ibuprofen treated group

Table (7): Comparison between NTG and BTG at day 7 post–operatively

Group Tested	Pain		Swelling		Trismus	
	Mean	Paired t–test	Mean	Paired t–test	Mean	Paired t–test
NTG	5.0	0.043*	5.5	0.002**	2.5	0.0001**
BTG	1.82		1.83		0.49	

*Non significant $p>0.0001$.
** Significant $p<0.0001$
NTG: Naproxen treated group.
BTG: Ibuprofen treated group.

DISCUSSION

In the present study two drugs belong to similar groups of non–steroidal anti–inflammatory drugs namely naproxen as (sodium) and ibuprofen were assessed on fairly frequent post–operative complains to the patients.

There were no significant results on pain, swelling and trismus at day 3 and 7 between ibuprofen treated groups (post-operatively only or pre– and post– operatively). These findings agreed with Sisk *et al*.[20] They used ibuprofen following surgical removal of impacted M_3 in which the prostaglandin antagonists were administrated 30 minutes pre– operative and 30 minutes post– operative. They showed that post–operative administration is just as effective as pre–operative administration.

Significant differences were noticed in pain, swelling and trismus at day 3 between naproxen treated groups (post-operatively only or pre– and post– operatively), in addition to pain at day 7. These can be attributed to fact that the naproxen plasma half life is 12 hours which means that naproxen remain more in the blood. Accordingly, less amount of supplement analgesic tablets intake by the patients.[21] The non significant differences in swelling and trismus at day 7 between naproxen treated groups can be explained that after 7 days the chemical mediators will be cleaned from the area of inflammation, as the drug was prescribed for 5 days post-operatively.[22]

In the statistical comparison at day 3 between naproxen treated groups and ibuprofen treated groups, only significant differences in pain were noticed. These can be attributed to the great differences in the plasma half life between naproxen and ibuprofen as the naproxen half life is 12 hours, while ibuprofen half life is 2 hours.[21] While the non significant differ-

ences in swelling and trismus between naproxen treated groups and ibuprofen treated groups at day 3 were due to that chemical mediators other than prostaglandin ava-ilable in the surgical traumatized area act as neurotransmitters namely glutamate and aspartate are involved. Blocking agents of these neurotransmitters are not found yet.[23]

In the statistical comparison at day 7 between naproxen treated groups and ibuprofen treated groups, no significant differences in pain were noticed, while significant differences were found in both swelling and trismus. This can be exp-lained by the fact that the ibuprofen reduced the tissue level of immuno-reactive bradykinine (IBK), immuno-reactive PGE2 (IPGE2) and immuno-reactive substance P (OSP) more than naproxen.[24]

CONCLUSION

It is concluded that using naproxen one hour before operation will play an important role in lowering post–operative pain, swelling and trismus compared to ibuprofen.

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