Naproxen Versus Ibuprofen in Pain Control after Periodontal Surgery: a Randomized Crossover Double-blind Clinical Trial

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Abstract: Objective: The purpose of this study was to compare analgesic efficacy of two none-steroidal anti-inflammatory drugs( NSAIDS), ibuprofen and naproxen in the management of post operative pain and swelling after periodontal surgery. Design: this study used a double-blind cross-over design with the patients acting as their own controls. Methods: Thirty patients (18 females and 12 males) underwent two periodontal surgeries in bilateral mandibular quadrants one month apart. They did not need bone correction or tooth extraction or any other surgical manipulation. In 15 patients ibuprofen was administered after their first surgery and in 15 patients naproxen was given in the first 24 hour after surgery. The drugs were cross changed in the second schedule. The perceived pain was recorded using a visual analogue scale by a self reported pain diary. VAS value after 1st, 2nd, 6th and 24th hours after surgery was recorded. T-test was used for statistical analysis. Results: Mean age of patients was 32.1 ±5.83 [M:34.5± 6.23,F:30.5±5.12,range 19 to 54 years old]. After one hour, mean VAS(MVS) was less in ibuprofen regimen. (MVS =3.63 vs 3.83) After two hours both groups experienced almost similar pain values(MVS =2.85 vs 2.83), After 6 hours VAS was significantly lower in naproxen group(p=0.013)( MVS = 1.23 vs 2.69). The same result was acquired in 24th post operative hour. Patients in naproxen group(VAS=0.40) experienced less pain than ibuprofen group(VAS=1.48)(p=0.008). Conclusion: naproxen is more efficient in long term pain control(24 hours after periodontal surgery)(P<0.05) although ibuprofen was more effective in first hour after surgery due to short acting nature of this drug, this difference was not significant.(P>0.05)

Key words: clinical trial, cross-over studies, double-blind, ibuprofen, postoperative, pain control, naproxen

INTRODUCTION

Post operative pain management (POP) after surgery is one of the important factors in patient satisfaction and adherence to ongoing treatment phases. (Coulthard, 2008) Different drugs can be used in POP management. According to one study 70% of patients perceive some degree of pain following periodontal surgery (Curtis et al., 1985). The peak of pain experience is within first twenty-four hours after surgery and will decrease in subsequent days. (Seymour, 1983) Acetaminophen ,none-steroid anti-inflammatory drugs(NSAIDS) and mild opioids such as codeine are used alone or in combination to avoid POP. Ibuprofen is one of accepted NSAIDS used for POP management after most oral surgical procedures. (Pearlman et al., 1997) it is a propionic acid derivative with a peak plasma level 1 to 2 hours after an oral dose with a halflife of 1.6 to 2.5 hours. (Vogel

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et al., 1992) It acts through interference with the release of prostaglandins at the site of tissue injury. (Vogel et al., 1992) Naproxen is another member of this family with a longer halflife and may be effective in management of pain with origin other than inflammation. (Solomon, 2007) This study was designed to compare analgesic efficacy of these drugs in POP management after periodontal surgery.

Methods:
This study used a double-blind cross-over design with the patients acting as their own controls. Thirty patients, referred to Rafsanjan dental school from OCT2007 to Oct 2009, underwent two periodontal surgeries in bilateral mandibular sextants-from canine to molars- one month apart. Inclusion criteria were:1. Indication for bilateral mandibular surgery. 2. Agreement for participation in this study. Exclusion criteria were:1. Any contraindication for oral surgical procedures or NSAIDs administration. 2. Age>60 years old. All the patients were asked to assign an informed consent. The study proposal was approved by the committee of ethics of Rafsanjan University of Medical Sciences.

These patients were randomly categorized to two groups, 15 patients in each group. In group 1 ibuprofen was administered following first periodontal surgery and naproxen after second periodontal surgery. In group 2 the reverse regimen was advised.

Medical history was not contributory and no contraindication existed for aggressive surgery or administration of NSAIDs. During surgery a standardized amount of local anesthetic (maximum 3 cartridges) and similar extent (from canine to second molar, fullthickness flap) and duration for each side (maximum 30 minutes) was required. In group 1, 400 mg ibuprofen (Hakim, Iran) TID was administered. First dose was taken immediately after surgery. All the drugs were packed out of the original package and were placed in a home drug box, so the patient was blind about drug type. only the first author (EA) was informed about drug type. In group 2 naproxen 250mg TID (Pars daru, Iran) was administered after first surgery. The patients did not need bone correction or tooth extraction or any other surgical manipulation or antibiotic administration. They were asked not to use any herbal or over the contour drugs for pain relief in first day after surgery (study course) a self-completing pain dairy was delivered to each patient. Every patient was asked to record the pain value using a painted visual analogue scale (VAS) in 1st, 2nd, 6th and 24th hours after surgery.

All the patients were visited 24 hours after surgery and the checklists were gathered. The surgical site was examined by the clinician and pain control was performed on demand in following days. After 30 days, after the second surgery schedule, naproxen TID was administered to group 1 and Ibuprofen TID to group 2. Next stages were followed similarly. All the data were analyzed using SPSS 13.5 soft ware by T-test (SPSS Chicago, IL).

RESULTS AND DISCUSSION
Thirty patients, (18 females, 12 males) who needed bilateral mandibular periodontal surgery were enrolled in this study. Mean age of patients was 32.1 ±5.83[M:34.5±6.23,F:30.5±5.12, range 19 to 54 years old]. VAS value after 1st, 2nd, 6th and 24th hrs after surgery was recorded. table 1 demonstrates mean VAS in time intervals.

As table 1 shows, after one hour, mean VAS was less in ibuprofen regimen. After two hours both groups experienced almost similar pain values, but in naproxen group the range of VAS was narrower (0 to 8 compared with 0 to 10). After 6 hours VAS was significantly lower in naproxen group (p=0.013). The same result was acquired in 24th post operative hour. Since patients in naproxen group (VAS=0.40) experienced less pain than ibuprofen group (VAS=1.48) (p=0.008).

T-test showed a significant difference in 6th and 24th hours post operation, in other words naproxen was more effective in long term pain control than ibuprofen. (Chart 1) In addition the patients had a contracted range of pain perception in naproxen group in comparison to ibuprofen in three intervals. None of patients reported any adverse drug reaction.

Discussion:
Pain perception may be influenced by age, sex, smoking and location of surgery (Garcia et al., 2008). NSAIDS are peripherally acting analgesic drugs with anti-inflammatory properties. In this study two drugs of this family were compared in early POP management (first 24 hours after surgery). Our results show that although relatively equal pain control in first two hours after surgery, naproxen is significantly more effective in 6th and 24th hour after periodontal surgery. The most frequently reported side effects are gastrointestinal discomfort such as dyspepsia, abdominal pain, nausea or vomiting (Cooper et al., 1965; Cooper et al., 1980; Winter et al., 1978) Skin rashes, fatigue, headache, depression or euphoria, tinnitus and dizziness are also
reported (Voger et al., 1992). None of these side effects were reported by subjects in this study.

On the best of our knowledge comparison of these drugs in early POP management has not been performed. There are similar studies about different analgesics, with various regimens.

In one study effect of single dose of naproxen, ibuprofen and acetaminophen on pain after periodontal surgery, were compared. Although both drugs were significantly more effective than placebo but significant difference was found between them (Gallardo and Rossi, 1980). We can not compare our study with this survey because we have used multiple doses and we expect later response from naproxen due to relatively longer half-life than ibuprofen. In one study Rashman showed that acetaminophen-caffeine (500+300mg) was more effective than ibuprofen in 1st and 2nd hours after periodontal surgery but in 6th, 7th and 8th hours after surgery ibuprofen was more effective. (Rashwan, 2009) This study observed patients only 8 hours after surgery. (Rashwan, 2009) Gallardo and Rossi compared flubiprofen with acetaminophen and placebo with a QID regimen. They suggested flubiprofen as an alternative for POP management (Gallardo and Rossi, 1992) because of better pain control after periodontal surgery. Sodium melofenamate (100mg) was compared with aspirin (500mg) and placebo by these researchers. (Gallardo and Rossi, 1992) It was concluded that aspirin was not superior to placebo during the three hour period of POP evaluation, while melofenamate had analgesic effect specially two hours after periodontal surgery. (Gallardo and Rossi, 1992) Seymour showed that if 100 mg paracetamol be used better results will be obtained than 500mg dosing specially in moderate pain management. (Seymour, 1983) Betancourt et al revealed that combination of ibuprofen with hydrocodone was more effective than ibuprofen alone for treatment of POP (Betancourt et al., 2004). In a study on POP in foot surgery, naproxen 550mg BID was more effective than naproxen 275 BID and the side effects were not different in two groups. (Coli et al., 1992).

**Conclusion:**

Due to this cross-over doubleblind clinical trial, naproxen is more efficient in long term swelling and pain control (24 hours after periodontal surgery) and patients on naproxen regimen experienced a narrower range of VAS in comparison to ibuprofen. Although ibuprofen was more effective in first hour after surgery due to short acting nature of this drug, this difference was not significant.

![Chart 1: Mean VAS values in time intervals in Ibuprofen and Naproxen groups](image)

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Group</th>
<th>Freq.</th>
<th>Mean VAS</th>
<th>Sd</th>
<th>Range</th>
<th>difference</th>
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<td>Ibuprofen</td>
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<td>3.19</td>
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<td></td>
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<td>3.07</td>
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<tr>
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<td>Ibuprofen</td>
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<td>2.83</td>
<td>2.07</td>
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<td>0.4</td>
<td>0-8</td>
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323
Table 1: Continue

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<th></th>
<th>Ibuprofen</th>
<th>Naproxen</th>
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<td></td>
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<td></td>
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<tr>
<td>24th hr PO</td>
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PO=post operative; Freq= Frequency; Sd= standard deviation

*Significant difference, p<0.05

REFERENCES


