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Original Article

Comparison of Naproxen and Gelofen for Pain Relief in Lower Third Molar Surgery: A Single-blinded Randomized Clinical Trial

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Abstract

Objectives: Third molar surgeries are a routine procedure in oral and maxillofacial surgery and its associated pain is bothersome to patients. The purpose of this study was to compare the analgesic effect of Gelofen and naproxen in lower third molar surgery. **Materials and Methods:** A single-blinded randomized clinical trial was designed, and patients were randomly allocated into four groups (n = 20 cases in each group): pre-Gelofen group: 400 mg Gelofen 30 min preoperative and continuing every 6 h, Gelofen group: 400 mg Gelofen immediately postoperative and continuing every 6 h, pre-naproxen group: 500 mg naproxen 30 min preoperative and every 8 h, and naproxen group: 500 mg naproxen immediately postoperative and every 8 h. The pain intensity was recorded using the visual analog scale at 2, 6, 12, and 24 h after surgery. **Results:** Pain intensity decreased in a linear pattern in all groups after 2, 6, 12, and 24 h. In pre-naproxen group, pain decreased suddenly between 2 and 6 h, but after 6 h, pain relief was slower than other groups. The mean pain intensity at 2 h postoperative for the pre-naproxen group was significantly lower than Gelofen group, and at 6 h, it was less than all other groups. At 12 and 24 h after surgery, pain intensity in all groups was similar except for the Gelofen group. **Conclusion:** Under limitation of the present study, preoperative intake of naproxen showed more effective pain relief than other groups.

Keywords: Naproxen, nonsteroidal anti-inflammatory drug, oral surgery, pain, third molar

Introduction

Surgical extraction of lower third molars is one of the routine procedures done by oral and maxillofacial surgeons. Pain, swelling, and transient loss of normal jaw function are usually associated with the removal of impacted third molar teeth. Managing these postoperative symptoms are frequently based on pharmacological interventions of local and systemic mediators of pain and inflammation.[1] Prostaglandin E2 mediates posttraumatic pain, fever, and inflammation.[1,2] Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX)-1 and COX-2 and therefore reduce the synthesis of prostaglandins. The blocking of nociceptive response to endogenous mediators of inflammation is greatest in injured tissues.[3] Gelofen is a new form of ibuprofen that was traditionally administrated by surgeons after lower third molar operations. It has a soft Gelatin capsule and can be easily attached to plasma proteins. It can then be absorbed in the gastric system up to approximately 80% with 4–6 h of halftime.[4] Naproxen is a long-effect NSAID that can be attached to plasma proteins up to 99%, and it can easily be removed from the gastrointestinal system about 10–12 h of halftime.[4] Studies have demonstrated the efficacy of naproxen and ibuprofen for postoperative pain after third molar surgery.[5,6] The adverse effects of wisdom tooth surgery on the quality of life have been reported to show a three-fold increase in patients who experience pain, swelling, or trismus alone or as a combination, compared to those who were asymptomatic.[7] Pain intensity after third molar surgery

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is a significant factor for evaluating of patient satisfaction.[8] There is little information regarding the preemptive analgesic effectiveness of naproxen and its comparison with Gelofen following the mandibular third molar surgery. This study compared the effectiveness of Gelofen and naproxen when administrated preemptively and postoperatively for pain relief after a lower third molar surgery.

Materials and Methods

The study was a single-blinded, randomized clinical trial to evaluate the effectiveness of Gelofen and naproxen for pain relief in impact third molar surgery. Research committee approved the study design before conducting the study (IRB number: IR.SUMS.REC.1396.122), and all of the patients signed informed consent before their participation in the study. Study has been registered in the Randomized Clinical Trials Registry (https://www.irct.ir/, Trial ID: 30329). All of the patients had an impact mandibular third molar and were in the American Society of Anesthesiologists 1 Category. All the impacted teeth were in the Level A and Class 1 according to the Pell and Gregory classification.[9] None of the patients received analgesic medication at least 12 h before the surgery. Exclusion criteria were any condition which contraindicated the use of NSAIDs, such as pregnancy, known allergy to NSAIDs, any drugs interaction, active ulceration or gastrointestinal bleeding, liver dysfunction, inflammatory intestinal disease, kidney dysfunction, or any psychological disorders. Block randomization, randomized patients into four groups ($n = 20$). In pre-Gelofen group, patients received 400 mg Gelofen 30 min before surgery and continued taking it every 6 h postoperatively. In Gelofen group: patients received 400 mg Gelofen immediately after the operation and continued taking it every 6 h postoperatively. In pre-naproxen group, patients received 500 mg naproxen 30 min before surgery and continued taking it every 8 h postoperatively. In naproxen group, patients received 500 mg naproxen immediately after the operation and continued it every 8 h postoperatively. An experienced surgeon operated for all of the patients. All surgeries were carried out under local anesthesia using 2% lidocaine with epinephrine 1:80000 (3.6–5.4 ml). Impacted mandibular third molars were removed following a standard technique. Bone removal was carried out with a surgical bur under copious saline irrigation. For each individual, the operating time (from the first incision to the completion of the last suture) was recorded. Patients were blinded to the names of medications used and were instructed to report any side effects to the examiner. The pain intensity according to the visual analog scale (VAS) was taught to patients. For all the participants, the pain intensity was recorded on a 10-cm graduated VAS, on which the criteria were as follows: 0 cm, no pain; 0.1–3 cm, light pain; 3.1–7 cm, moderate pain; and 7.1–10 cm, intense pain. VAS was documented in 2, 6, 12, and 24 h after surgery for each group.

Statistical analysis

The statistical analyses were performed using SPSS version 19 (IBM, Chicago, IL, USA). The repeated measures ANOVA was used to assess the mean of pain over time in four groups. The Kruskal–Wallis one-way analysis of variance was applied to find whether samples originate the same distribution or statistically significant differences. The Tukey–Kramer test was used to compare the mean of pain between groups at each time point.

Results

In this study, 80 patients were randomly selected and divided into four groups (53 females and 27 males). There were 16 females and 4 males in pre-Gelofen group, 10 males and 10 females in Gelofen group, 7 men and 13 women in the pre-naproxen group, and 6 males and 14 females in naproxen group. No significant differences were in sex, age, and operation time among the groups [Table 1]. Significant differences in the pain intensity among the four groups were at 2, 6, 12, and 24 h [Table 2]. In pre-Gelofen and pre-naproxen groups, the pain intensity was lower than Gelofen and naproxen groups. The intensity of pain was decreased in four groups in a linear pattern from 2, 6, 12, and 24 h. In pre-naproxen group, the pain decreased suddenly between 2 and 6 h, and afterward, relief of pain continued to be slower than other groups [Figure 1]. Table 2 shows the differences in pain intensity between pre-naproxen group and other groups at 2, 6, 12, and 24 h. At 2 h after surgery, the mean pain intensity for the pre-naproxen group was significantly lower than Gelofen group. At 6 h postoperatively, pre-naproxen group showed significantly lower pain intensity than other groups, and at

Table 1: Comparison of variable factors among four groups ($n = 20$)

	Groups			
	Pre-Gelofen	Gelofen	Pre-naproxen	Naproxen
Age (mean±SD)*	24.1±6.3	25.8±4.8	23.3±5.4	24.7±4.9
Sex*				
Male	4	10	13	14
Female	16	10	7	6
Operation time (min)*	38.8±7.8	40.4±6.7	42.4±5.1	39.5±7.7

*There was no significant differences between groups ($P>0.05$).
SD – Standard deviation

Table 2: Comparison of the pain intensity among four groups in various measurement times

Groups	Mean±SD of pain intensity at different postoperative times			
	2 h	6 h	12 h	24 h
Pre-Gelofen	5.10±2.90[a]	4.40±1.69[a]	2.95±1.39[a]	2.00±0.91[a]
Gelofen	6.75±3.05[b]	5.75±2.73[a]	4.30±2.20[b]	2.85±1.42[b]
Pre-naproxen	4.40±2.81[a]	2.20±1.57[b]	2.00±1.83[a]	1.65±1.04[a]
Naproxen	6.75±1.07[b]	4.65±1.34[a]	2.90±1.07[a]	1.60±0.75[a]
P	0.008*	0.001*	0.001*	0.001*

*Values with the same superscript letters were not statistically different at each postoperative times ($P<0$ 05). SD – Standard deviation

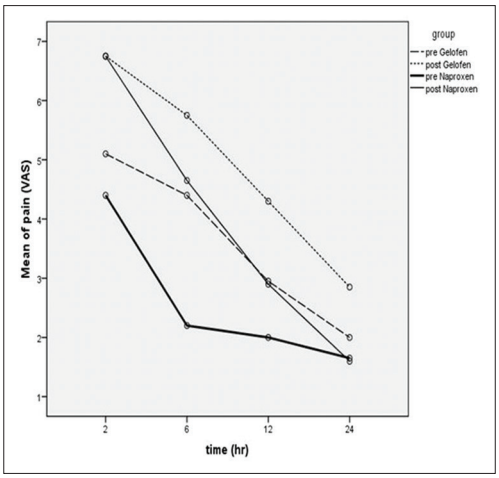

Figure 1: Mean pain scores (visual analog scale) over time in four group

12 and 24 h, the intensity of pain was similar to other groups except for the Gelofen group.

Discussion

The current study has demonstrated that patients have lower pain intensity when they use NSAIDs (naproxen or Gelofen) before the surgery rather than taking these medications after the surgery. Patients who received naproxen before or after the surgery had experienced lower pain intensity rather than Gelofen group. In comparison to the other groups, patients who consumed naproxen had a different pain relief after 2 h. Pain has suddenly decreased in the pre-naproxen group between 2 and 6 h, and afterward, it followed a slower pattern than groups. Previous studies demonstrated the beneficial effects of the preoperative administration of piroxicam, ketorolac, meloxicam, parecoxib, and dexamethasone with rofecoxib.[10] Saito *et al.* have assessed the efficacy and safety of an additional 200 mg dose of celecoxib which has been administered 5–12 h after an initial 400 mg dose of the drug following extraction of an impacted third mandibular molar. The results showed that an additional 200 mg dose of celecoxib was well tolerated and it was efficacious in reducing the pain associated with the surgery in their study population.[11] Others found lower consumption of rescue analgesics postoperatively and a delay in the onset of pain when the NSAIDs were administered before the surgical procedure.[12] Joshi *et al.* compared the effectiveness of three NSAIDS administered and concluded that preoperative analgesics are useful in relieving immediate postoperative pain. The side effects such as nausea, vomiting, and gastrointestinal discomfort occurred in all groups of analgesics with no significant difference between the analgesic groups.[13] New scientific evidence suggested that waiting for the patient to report severe pain before prescribing analgesic drug is not an acceptable concept and may reduce the efficacy of any subsequent treatment, but there are different ideas in the effectiveness of preemptive analgesia among clinicians.[14] Olmedo-Gaya *et al.* showed that the postoperative pain reaches its higher intensity during the first 8 h after surgery.[15] In our study, patients who started using analgesic drugs before surgery had lower pain in the first 8 h postoperatively than using them after the surgery. On the contrary, Sisk and Grover compared preoperative and postoperative effects of naproxen sodium in lower wisdom teeth surgery and showed no evidence of a preemptive effect.[16] They concluded that the administration of naproxen sodium in the immediate postoperative period may be as effective as 30 min preoperative intake of the drug and can be used for optimum postoperative analgesia for patients in whom preoperative oral intake is contraindicated.[16] In another study, Jung *et al.* compared analgesic effects of a NSAID for oral surgical pain according to three different administration times (1 h preoperatively, 1 h postoperatively, or no scheduled administration pre- or postsurgery). Whenever patients felt at least moderate pain (score ≥ 5 on a 10-point scale) after surgery, they were instructed to take the same drug. Pain intensities and times to the first and second onsets of postoperative pain from the end of the surgery were assessed for 24 h. The analgesic effects of NSAID administered preoperatively were no longer effective for postoperative pain. The results in this population implied that scheduled postoperative analgesics before pain development are adequate for postoperative analgesia without preoperative administration.[17] The efficacy and safety of single doses of naproxen sodium 440 mg and ibuprofen 400 mg were evaluated in a randomized, parallel, double-blind, placebo-controlled study conducted, and the results showed that both naproxen sodium and ibuprofen were well tolerated and provided pain relief superior to that of placebo. The duration of pain relief was longer with naproxen sodium than with ibuprofen.[18] Naproxen has a long-acting effect, >99% plasma proteins bound and completely absorbed in the gastrointestinal system.[19] It has 10–17 h halftime.[20] These pharmacologic properties may describe the effectiveness of naproxen in reducing pain more than Gelofen, especially when used before the operation. The preoperative oral intake of naproxen and Gelofen 30 min before surgery can significantly decrease pain more than postoperative usage in 2 and 8 h after surgery.

Conclusion

Preemptive use of both the NSAIDs can relief pain after third molar surgery. Under the condition of the present study, naproxen was more effective than Gelofen.

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Conflicts of interest

There are no conflicts of interest.

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