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Impact of Pre-Emptive Intravenous Ibuprofen on Perioperative Analgesia in Patients Undergoing Third Molar Extraction: A Randomised Controlled Study

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Abstract

Objective: The aim of the present study was to evaluate the analgesic efficacy of pre-emptive intravenous (iv) ibuprofen on pain during and after the mandibular third molar surgery.

Methods: A total of 60 patients were included in the study. They were allocated as ibuprofen 800 mg iv+dexketoprofen 50 mg (group 1), ibuprofen 800 mg iv alone (group 2) or placebo (group 3). A local anaesthetic infiltration was administered to all patients. In all patients, haemodynamic values (mean arterial pressure (MAP) and heart rate (HR)) were recorded preoperatively, and infusions were started. State-Trait Anxiety Inventory (STAI) scale was used to assess anxiety states. Surgery started 15 min after the infusion. Haemodynamic values and pain scores with visual analogue scale (VAS) were recorded. Pain scores were recorded postoperatively at rest (VASR) and swallowing (VASS).

Results: There was no significant difference in the preoperative STAI values between the groups ($p>0.05$). HR, MAP and VAS pain scores were significantly higher in group 3 than in groups 1 and 2 ($p<0.05$). VASR and VASS scores were significantly higher in group 3 than in group 1 in the first 4 h postoperatively ($p<0.05$). VASS scores were significantly higher in group 3 than in group 2 at 1-4 h postoperatively ($p<0.05$), but there was no difference in VASR and VASS scores at 48 h after surgery.

Conclusion: Ibuprofen alone or in combination with dexketoprofen provided similar analgesia in the perioperative period when administered pre-emptively.

Keywords: Analgesic efficacy, intravenous ibuprofen, pain, pre-emptive analgesia, third molar surgery

Introduction

There are many prophylactic and therapeutic indications for extraction of impacted teeth. Impacted third molar surgery is one of the most commonly performed dental procedures (1). Painful stimuli during surgical intervention or in the perioperative period may cause changes in the nervous system and affect postoperative pain levels. The pain that develops after impacted third molar surgery starts when the effect of local anaesthesia decreases and reaches a peak in the first 12 h postoperatively. Good analgesic coverage in the postoperative period not only reduces complications but also encourages rapid healing of the surgical wound (2).

The concept of pre-emptive analgesia, i.e., administration of analgesia before the initiation of a painful stimulus, such as a surgical incision, has been widely studied in recent years. Many researchers have reported positive results from the administration of prophylactic analgesia before pain can develop (3-5). Therefore, pre-emptive analgesia

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is now used extensively in dentistry and medicine to prevent postoperative pain.

Preoperative anxiety is associated with increased postoperative pain and, therefore, increased analgesic requirement and prolonged hospital stay. In the preoperative anxiety measurement, the State-Trait Anxiety Inventory (STAI) scale developed by Spielberger et al. (6) is shown as the gold standard in the literature.

The primary objective of the present study was to evaluate the intraoperative analgesic efficacy of intravenous (iv) ibuprofen when administered pre-emptively in patients undergoing third molar extraction. The secondary objectives of the present study were to investigate the relationship between preoperative anxiety and pain and to investigate the contribution of pre-emptively administered iv ibuprofen to postoperative analgesia.

Methods

The study protocol was approved by the Erzincan Binali Yıldırım University Clinical Trials Ethics Committee (09/05/2017, approval no. 06/04). Written consent was obtained from all patients who participated in the study. The study is registered at ClinicalTrials.gov as NCT03170726.

A total of 60 symptomatic patients undergoing elective extraction of an angular or horizontal third molar tooth were enrolled into the study. The age of the patients ranged from 20 to 35 years. Exclusion criteria included patients aged <20 years or >35 years, patients with known allergy to nonsteroidal anti-inflammatory drugs (NSAIDs), pregnancy, patients with severe renal or liver failure and patient's unwillingness to participate in the study.

STAI scale was applied to all patients by using the one-to-one interview method to measure preoperative anxiety level in the operating room on the day of surgery. No premedication was applied to the patients in the operating room, which could change their anxiety status.

The patients were allocated to receive a preoperative iv infusion containing ibuprofen (Intrafen; Gen Ilac, Ankara, Turkey) 800 mg+dexketoprofen (Deksalgin; Nobel Ilac, Istanbul, Turkey) 50 mg (group 1), a preoperative iv infusion containing ibuprofen 800 mg alone (group 2) or a preoperative iv infusion of placebo (normal saline) (7). The patients in all three study groups received the preoperative iv infusion in 150 ml of normal saline over 30 min. A postoperative infusion of dexketoprofen+methylprednisolone (Prednol-L; Mustafa Nevzat, Istanbul, Turkey) 40 mg+sultamicillin tosilate (Ampisid; Mustafa Nevzat) in 150 mL of normal saline was also administered in all three study groups.

To maintain double-blinding, the study treatments were prepared beforehand by an anaesthesia technician not involved in the study, and the researchers were unaware of the group allocation when treating patients. Inclusion of a control group was considered ethical, considering that a postoperative infusion of dexketoprofen+methylprednisolone 40 mg+sultamicillin tosilate infusion in 150 mL of normal saline is routinely used at our institution for pain relief after oral surgery.

Non-invasive blood pressure measurements, electrocardiography and peripheral oxygen saturation values were recorded in all patients according to the American Society of Anesthesiologists monitoring standards. All surgical procedures were performed by the same surgical team.

Haemodynamic values, including mean arterial pressure (MAP) and heart rate (HR), were recorded preoperatively in all patients, after which the infusion was started. Surgery was commenced 15 min after the start of the infusion. Buccal anaesthesia using 2 mL of lidocaine with adrenaline (Jetocain; Adeka, Samsun, Turkey) and inferior alveolar nerve block were performed by a maxillofacial surgeon. Haemodynamic values and visual analogue scale (VAS) pain scores were recorded at 5, 10, 15, 20 and 25 min intraoperatively and at the end of surgery. VAS pain scores were recorded at rest and during swallowing at 1, 2, 4 and 48 h postoperatively.

Statistical analysis

All data were analysed using IBM Statistical Package for the Social Sciences Statistics for Windows version 20.0 software (IBM SPSS Corp., Armonk, NY, USA). The power of the study was determined using the power analysis in the study performed by Tuzuner Oncul et al. (8), according to which a 30% reduction in VAS score was considered statistically significant and a total of 60 patients was required to have 80% power and α=0.05. Kolmogorov-Smirnov test, skewness-kurtosis and histogram were used to assess normal distribution and analysis of variance. Numerical data are presented as mean and standard deviation, and categorical data are presented as number. The chi-square test was used to compare categorical data between the groups. The Mann-Whitney U test was used to compare the mean values between the two groups, and the Kruskal-Wallis test was used to compare three or more groups. A p-value <0.05 was considered statistically significant.

Results

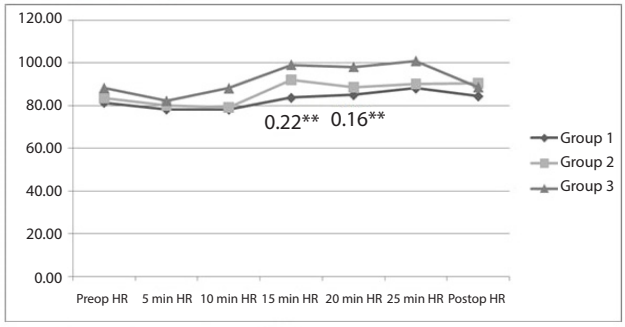
Demographic data

A total of 60 patients were included in the study. The study comprised 26 male and 34 female patients. The mean age of the patients was 25.9±4.6 years. There was no significant difference in sex, age or preoperative STAI values between the study groups (p>0.05, Table 1).

Table 1. Demographic data

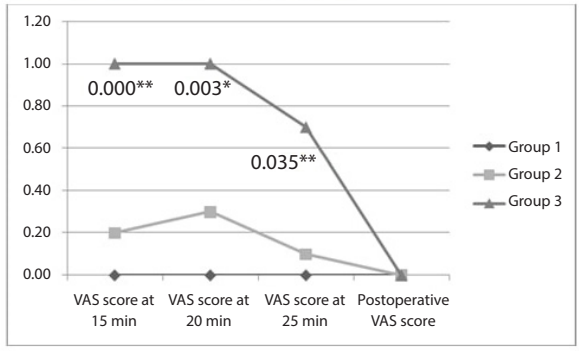
	Group 1	Group 2	Group 3	Total	p
Sex*					
Male	11	8	8	28	0.343
Female	9	12	12	32	
Age (years)*	25.8±4.3	24.9±5.2	26.9±4.4	25.9±4.6	0.408
Preop STAI*	47.5±7.8	48.4±7.4	45.7±7.3	47.7±7.3	0.318

*Chi-square test.



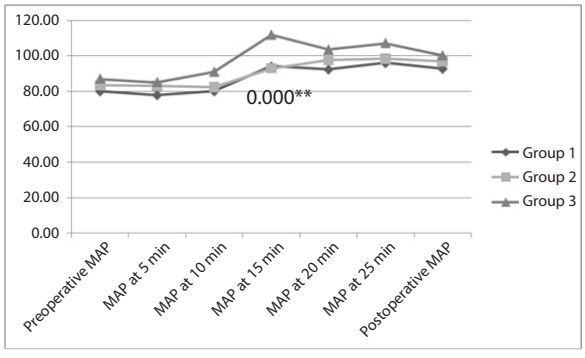
**The mean difference is significant at the 0.05 level

Figure 1. Intraoperative heart rate



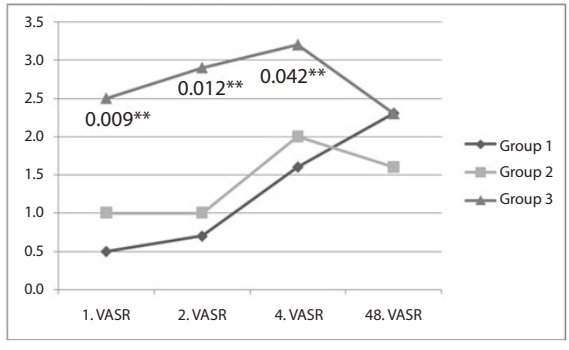
**The mean difference is significant at the 0.05 level

Figure 3. Intraoperative visual analogue scale



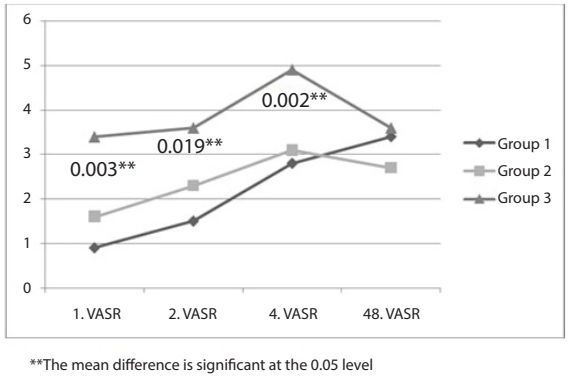
**The mean difference is significant at the 0.05 level

Figure 2. Intraoperative mean arterial pressure



**The mean difference is significant at the 0.05 level

Figure 4. Visual analogue scale at rest



**The mean difference is significant at the 0.05 level

Figure 5. Visual analogue scale score during swallowing

Intraoperative data

There was no significant difference in HR, MAP or VAS pain scores between the groups in the first 15 min of infusion of local anaesthesia (p>0.05). The HR, MAP and VAS scores were higher in group 3 than in the other groups at the end of surgery (p<0.05, Figures 1-3).Thereafter, there was no significant difference in the VAS pain score between groups 1 and 2; however, there was a significant difference between group 3 and the other two groups (p<0.05, Figure 3).

Postoperative data

There was a significant difference in the postoperative pain scores between the groups in the first 4 h, but not in the pain scores at rest or while swallowing at 48 h (Figures 4, 5). The pain scores were significantly higher in group 3 than in group 1 in the first 4 h postoperatively (p<0.05). However, the pain score while swallowing at 1-4 h was observed to be significant

(Figure 5). There was no significant difference in postoperative pain scores between groups 1 and 2.

Discussion

In the present study of the contribution of pre-emptively administered iv ibuprofen to perioperative analgesia, it was determined that ibuprofen provided effective analgesia in the perioperative period whether administered alone or with dexketoprofen. Extraction of an impacted mandibular third molar causes severe pain and swelling because of soft tissue and bone trauma and inflammation; thus, perioperative pain management is essential (9). Acute pain is often associated with physical signs originating from the sympathetic branch of the autonomic nervous system and manifests as tachycardia, hypertension, sweating, mydriasis and a sallow appearance (10). Therefore, in the present study, intraoperative analgesia was evaluated by HR, MAP and VAS scores recorded from 15 min after the start of the infusion of local anaesthesia.

Postoperative pain after third molar removal is often used as a model to test the efficacy of analgesics. The efficacy of ibuprofen, a propionic acid derivative, in patients with postoperative toothache has been well investigated (11-14). Jain et al. (12) reported that ibuprofen is more effective than aceclofenac in this indication, and that the analgesic effect lasts longer. In a systematic review (15), ibuprofen was found to be more effective at all doses than paracetamol. However, all of these studies used an oral formulation of ibuprofen and most investigated postoperative pain. In the present study, pre-emptive ibuprofen administered via the iv route was found to be as effective as combination therapy for postoperative analgesia, which is consistent with the literature. The originality of the present study is that an iv form of ibuprofen was used preoperatively.

Sensory nociception is disproportionally higher in the oral cavity than in other parts of the body (16). Impacted mandibular third molar surgery is known to cause more intense pain than any other oral surgical procedure (17). The prostaglandin concentration in the acutely injured tissue reaches its maximum level at 3-4 h after the injury, and this results in an increase in postoperative pain intensity (18). The pain after extraction of an impacted third molar is of short duration and is usually accompanied by cheek swelling and trismus. The pain reaches maximum intensity at 4-6 h after surgery (12, 19). In the present study, the group that received placebo had higher pain scores in the first 4 h postoperatively than the group that received ibuprofen and dexketoprofen ($p<0.05$). The pain scores were higher in the group that received placebo than in the group that received ibuprofen alone and were significantly higher during swallowing at 1-4 h postoperatively. In the present study, iv ibuprofen alone was found to be as effective as combination treatment with respect to postoperative analgesia.

The present study has some limitations. First, trismus and oedema were not evaluated, given that postoperative swelling that develops as a result of increased tension in the tissues may contribute to postoperative pain (7, 20). Second, we could not show the effect of preoperative anxiety on pain due to the small number of samples.

Conclusion

The present study investigated the contribution of pre-emptively administered iv ibuprofen to perioperative analgesia, and its results suggest that ibuprofen had the same perioperative analgesic efficacy whether administered alone or with dexketoprofen.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erzincan Binali Yıldırım Unıversıty (Date: 09/05/2017; Approval no. 06/04).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – İ.K., Y.G.; Design – İ.K., Y.G.; Supervision – İ.K.; Resources – Y.G., İ.K.; Materials – Y.G.; Data Collection and/or Processing – Y.G.; Analysis and/or Interpretation – İ.K., Y.G.; Literature Search – İ.K., Y.G.; Writing Manuscript – İ.K.; Critical Review – İ.K., Y.G.; Other – İ.K., Y.G.

Conflict of Interest: The authors have no conflicts of interest to declare.

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