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Effect of preemptive ibuprofen and dexketoprofen on postoperative pain after septorhinoplasty

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Abstract

In septorhinoplasty patients, postoperative comfort is as important as postoperative results. Intravenous non-steroidal anti-inflammatory drugs are playing an increasingly large role in analgesia, antiinflammation, and antipyresis in the hospitalized setting. The aim of this study is to assess the preemptive analgesic effects of intravenous ibuprofen and dexketoprofen on postoperative pain in patients undergoing septorhinoplasty. This study was performed with 76 patients who underwent open septorhinoplasty between 2016 and 2017. The patients were separated into two groups; Group D (n=46) received preemptive intravenous dexketoprofen (50 mg), and Group I (n=30) received preemptive intravenous ibuprofen (800 mg). A visual analogue scale (VAS) was used to assess pain at the 30 th minute, as well as the first, second, sixth, twelfth, and twenty-fourth hours after surgery. There was no statistically significant difference between the groups for sex, age, weight, height, ASA class, anesthesia, and surgery duration. VAS scores gradually decreased between 30 minutes and 24 hours in both groups and this decrease was statistically significant in both groups (Group D; $p < 0.001$, Group I; $p < 0.001$). The mean VAS scores in the same periods were lower in Group I at all times, but the difference was not statistically significant ($p > 0.05$). This study indicated that both ibuprofen and dexketoprofen had similar analgesic efficacy. Clinicians can use these two drugs interchangeably by comparing their side effects and costs.

Keywords: Analgesia, dexketoprofen, ibuprofen, pain, rhinoplasty

1. Introduction

Postoperative pain depends on the premedication applied, the type of operation and general anesthesia used, and the personal sensitivity of the patient (1). Poorly controlled pain has a negative effect on the quality of life, functions, and functional recovery and causes postoperative morbidity, complications and persistent pain and increases hospitalization and medical costs (2). 'Preemptive analgesia' means preventing or reducing pain that is likely to develop by administering analgesia before a painful stimulus. The purpose of preemptive analgesia is to prevent the occurrence of pain memory, thereby reducing the need for analgesics (3).

The postoperative pain management guideline recommendations for head and neck surgeries are not specific for surgical types, such as septorhinoplasty (4). Surgeons generally evaluate the success of septorhinoplasty based on late functional and cosmetic results (5). However, patients care about their early comfort as much as the late results. Pain, edema and bruising are factors that determine patient satisfaction and comfort in the early postoperative period.

Metamizole, paracetamol, dexketoprofen trometamol, ibuprofen, lornoxicam and opioids are used to control the pain after septorhinoplasty. Dexketoprofen and ibuprofen are non-steroidal anti-inflammatory drugs (NSAIDs) with few side effects (3, 6). The oral form of ibuprofen is one of the most commonly used NSAID for many years (5, 6). Intravenous (IV) ibuprofen has been approved in the USA since 2009 for the treatment of pain.

Limited studies have been reported about the IV ibuprofen used in postoperative pain management. The aim of this study was to evaluate and compare the pre-emptive analgesic efficacy of ibuprofen and dexketoprofen for postoperative pain control in patients who underwent septorhinoplasty.

2. Material and Methods

This study was performed with 76 patients who underwent open septorhinoplasty between January 2016 and December 2017 in a tertiary referral hospital. The patients included were those aged over 18 years with ASA score I–II, without a known systemic disease, with no history of peptic ulcer, allergy, chronic pain, routine analgesic use or analgesic use in the last 24 hours, and without sensitivity to NSAID agents. Written consent was obtained from all patients included in the study. The approval for all procedures in the study was granted by the Ondokuz Mayıs University Ethics Committee for Clinical Studies (2016/230).

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The patients were randomly separated into two groups: Dexketoprofen Group (Group D) and Ibuprofen Group (Group I).

Group D (n=46) received 200 ml saline containing 50 mg dexketoprofen trometamol (Arveles 50 mg/2 mL, Menarini International, Florence, Italy) as an infusion 1 hour preoperatively. Then, 50 mg IV dexketoprofen trometamol was administered two more times at 12-hour intervals at the 12th and 24th hours. In the 6th and 18th hours, 200 ml saline was administered.

Group I (n=30) received 200 ml saline containing 800 mg ibuprofen (Intrafen 800 mg/4 mL, Gen Ilaç, Istanbul, Turkey), as an infusion for approximately 30 minutes, 1 hour before the anesthesia induction. Then, 800 mg IV ibuprofen was administered four times at 6-hour intervals in the post-operative period.

The standard general anesthesia method was applied to all cases and all surgeries were performed by the same surgeon using the open technique. The times of medication, duration of anesthesia, duration of surgery and application of nasal packing were recorded. Extubation time was accepted as postoperative 0 minute. Patients were asked to score postoperative pain using a Visual Analogue Scale (VAS) (0: no pain and 10: worst pain). All patients were informed about VAS preoperatively. In the postoperative period, the patients were asked to note the pain level they felt at the 30th min, 1, 2, 6, 12 and 24th hours. 5 mgr/kg tramadol, an atypical opioid analgesic, was applied to patients with a VAS score greater than 4 as an additional analgesic. The additional analgesic requirements of patients were recorded during the first 24 h postoperatively. The postoperative follow-up and evaluation of the cases was performed by a researcher blinded to the groups.

2.1. Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn. 22 for Windows software (SPSS Inc, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) values, and frequency data as number (n) and percentage (%). The Shapiro-Wilk test was used to determine whether variables conformed to a normal distribution. Since the data did not show normal distribution, the Mann Whitney U-test was used in the comparison of two groups, and Variance Analysis-Friedman Test was used in the comparison of repeated measurements in the group. Fisher' s Exact Test was used to compare the data obtained by counting. A value of $p<0.05$ was accepted as statistically significant.

3. Results

As shown in Table 1, there was no statistically significant difference between the groups in terms of demographic characteristics such as age, gender and body mass index (BMI) ($p>0.05$). The comparisons of the groups according to VAS values and additional analgesic requirements are shown in Table 2. When the groups were evaluated within themselves, it was determined that mean VAS values gradually decreased between 30 minutes and 24 hours in both groups and this decrease was statistically significant in both groups (Group D; $p <0.001$ and Group I; $p <0.001$). In comparisons between the groups, the mean VAS values in the same periods were lower in Group I at all times, but there was no statistically significant difference ($p >0.05$). There was no significant difference between the groups in terms of additional analgesic requirement ($p>0.05$).

There was no significant difference in the rates of patients with and without nasal packing in Group D and Group I ($p>0.05$) (Table 1). It was observed that the VAS values decreased gradually from 30 minutes to 24 hours in both patients without nasal packing and patients with nasal packing in Group D and Group I, and this decrease was statistically significant in both groups (Group D; $p<0.001$ and Group I; $p<0.001$) (Table 3 and 4).

The pain scores in the same periods were lower in patients without nasal packing in Group I than Group D at all times and the difference was statistically significant in the 2nd hour ($p = 0.04$) and the 6th hour ($p = 0.03$) (Table 3).

In patients with nasal packing, although the mean VAS values in the same periods were lower in Group I at all times, there was no statistically significant difference (Table 4).

4. Discussion

As a result of this study, it was observed that both ibuprofen and dexketoprofen caused a significant decrease in VAS scores over time (Group D; $p<0.001$ and Group I; $p<0.001$), and ibuprofen caused a significant decrease in VAS at the 2nd and 6th hours compared to dexketoprofen in patients without nasal packing ($p = 0,04$, $p = 0,03$).

The International Association for the Study of Pain has defined pain as ‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage'. Surgical tissue trauma leads to nociceptor activation and sensitization, increased inflammatory cytokines, decreased tissue pH and oxygen tension. Inadequate analgesia decreases quality of life, increases the length of hospitalization and healthcare costs (7).

In a study, higher VAS pain scores have been reported in patients undergoing septorhinoplasty and open septoplasty than in other otolaryngological procedures (8).

Different doses of IV ibuprofen have been used to assess the analgesic efficacy in previous studies. In one study, a single dose of 800 mg ibuprofen given intravenously 15 minutes before thyroidectomy resulted in lower opioid consumption and less postoperative pain (9). Analgesic effect of preemptive single dose iv 800 mg ibuprofen on

Table 1. Demographic Characteristics of the Patients

	Group D (n:46)	Group I (n:30)	p
Gender, N (%) Female	28 (65.1%)	15 (34.9%)	0.48*
Male	18 (54.5%)	15 (45.5%)	
Age, (Mean±SD (min-max))	27,8±9,4 (18-52)	27.7±10.3(18-51)	0.92#
BMI (kg/m2), (Mean±SD (min-max))	22,7 ±3,9 (16,6-35,6)	22.9 ±3.5 (18.0-34.9)	0.62#
Nasal packing, N (%)	25 (65.8%)	13 (34.2%)	0.48*

* Continuity Correction, # Mann Whitney U-test

Abbreviations: BMI, Body Mass Index; Group D, Dexketoprofen Group; Group I, Ibuprofen Group; N, number; SD, Standart Deviation.

Table 2. VAS Score, Analgesic Requirement of Patients

		Group D (n:46) Mean±SD (min-max)	Group I (n:30) Mean±SD (min-max)	p#
VAS (cm) (Mean±SD)	30 min	5.4 ±2.8(0-10)	5.4 ±2.6(2-10)	0.86
	1h	4.8 ±2.2(1-10)	4.4 ±2.1 (1-9)	0.46
	2 h	4.0 ±2.2(0-10)	3.4 ±2.0(1-8)	0.20
	6 h	3.3 ±2.4(0-9)	2.6 ±2.0(0-8)	0.19
	12 h	3.1 ±2.6 (0-10)	2.6 ±2.0(0-8)	0.10
	24 h	2.3 ±2.5 (0-10)	1.6±2.0 (0-8)	0.20
		*p:<0.001	*p:<0.001	
Additional analgesia n(%)		3 (6.5%)	2 (6.7%)	1.00

* Variance Analysis-Friedman Test in repeated measurements # Mann Whitney U-test

Abbreviations: Group D, Dexketoprofen Group; Group I, Ibuprofen Group; N, number; SD, Standard Deviation; VAS, Visual Analog Scale

Table 3. VAS Scores of Patient Without Nasal Packing

		Group D (n:21) Mean±SD (min-max)	Group I (n:17) Mean±SD (min-max)	p#
VAS(cm) (Mean.±SD)	30 min	4.19 ±2.97	3.97 ±3.59	0.70
	1 h	3.71 ±2.36	2.82 ±2.94	0.20
	2 h	3.62 ±2.59	2.24 ±2.53	0.04
	6 h	2.90 ±2.80	1.06±1.67	0.03
	12 h	2.10 ±2.44	1.00 ±1.36	0.20
	24 h	1.95 ±2.57	0.59 ±1.17	0.07
	p*	*p:□0.001	*p:□0.001	

* Variance Analysis-Friedman Test in repeated measurements #Mann Whitney U-test

Abbreviations: Group D, Dexketoprofen Group; Group I, Ibuprofen Group; N, number; SD, Standard Deviation; VAS, Visual Analog Scale

Table 4. VAS Scores of Patient with Nasal Packing

		Group D (n:25) Mean±SD (min-max)	Group I (n:13) Mean±SD (min-max)	p#
VAS(cm) (Mean±SD)	30 mins	5.52 ±3.41	6.31 ±3.25	0.46
	1 hr	5.04 ±2.73	5.62 ±2.98	0.64
	2 hrs	3.84 ±2.98	4.15 ±2.70	0.83
	6 hrs	3.20 ±2.53	4.15 ±2.91	0.36
	12 hrs	3.56 ±3.02	3.62 ±2.56	0.85
	24 hrs	2.48 ±2.63	3.38 ±3.09	0.34
	p*	*p:<0.001	*p:<0.001	

* Variance Analysis-Friedman Test in repeated measurements #Mann Whitney U-test

Abbreviations: Group D, Dexketoprofen Group; Group I, Ibuprofen Group; N, number; SD, Standard Deviation; VAS, Visual Analog Scale

septorhinoplasty was investigated in a study and they reported that pain scores and total fentanyl consumption were lower in patients using ibuprofen (5). In another study, it was reported that postoperative VAS values and morphine consumption were lower after hysterectomy in patients who were administered 50 mg IV dexketoprofen one hour before and 8 and 16 hours after surgery than in the placebo group (10). In a study, it was reported that the use of dexketoprofen decreased the pain after septorhinoplasty regardless of the administration timing (preoperative or intraoperative) (11). Supporting these studies, in the current study, only 6.7 % of the patients in Group I and Group D needed additional analgesics and the decrease in VAS scores over time was significant (Group I: p□0.001, Group D: p□0.001). However,

in contrast to these studies, we preferred to compare ibuprofen and dexketoprofen, two different analgesic drugs, rather than comparing any one of them, whose analgesic efficacy is already known, to the placebo group.

As in our study, there are also several studies that compare the effects of two different analgesic drugs. In a study, comparing the analgesic efficacy of IV ibuprofen and ketorolac, it was reported that a preemptive and a second dose of IV 800 mg ibuprofen decreases postoperative pain and opioid consumption (12). It was reported that ibuprofen had a more potent analgesic effect compared to intravenous paracetamol after septorhinoplasty (3). In a study comparing the pain and tramadol consumption in patients who underwent septorhinoplasty, it was found that the analgesic efficacy of preemptive dexketoprofen trometamol was more potent than acetaminophen (13). Although there are a few studies comparing the analgesic effects of oral forms of ibuprofen and dexketoprofen, a study comparing the effectiveness of IV forms has not been found in accessible literature. When we examine the studies comparing oral forms of ibuprofen and dexketoprofen, some reported that ibuprofen was more effective, while others reported that dexketoprofen was more effective (14, 15).

When the literature is reviewed, it seems that the use of ibuprofen and dexketoprofen alone or in combination with opioids is very effective in postoperative pain management. In the current study, when the two groups were compared, there was no difference between the ibuprofen and dexketoprofen groups in terms of pain control. Moreover, when the groups were evaluated within themselves, it was determined that mean VAS values gradually decreased between 30 minutes and 24 hours in both groups and this decrease was statistically significant in both groups (Group D; $p < 0.001$ and Group I; $p < 0.001$). Incision, intervention to the nasal roof and skeleton, nasal roof osteotomies, and nasal packing were reported to be the most common causes of postoperative pain after septoplasty and septorhinoplasty (5, 16). When comparing only patients with or without nasal packing in both groups, although the mean VAS values in the same periods were lower in Group I at all times, there was no statistically significant difference between Group D and I in patients with nasal packing. Whereas, the pain scores in the 2nd hour and 6th hour were lower in Group I than Group D in patients without nasal packing. This indicates that the ibuprofen has more potent early analgesic efficacy than dexketoprofen and further studies are needed with larger study groups.

The absence of a placebo group was one of the limitations of the present study. Although both ibuprofen and dexketoprofen were observed to cause a significant decrease in pain scores over time, this could not be compared with a control group. However, it would not have been ethically acceptable to perform the painful procedure of septorhinoplasty without medication. Furthermore, side effects of drugs, postoperative hemorrhage, medical costs and length of hospital stay were not recorded in the present study. We think that evaluating these variables in the next studies can help us choose one of these two agents with similar analgesic efficiency by making a profit-loss ratio.

Our study indicated that both ibuprofen and dexketoprofen had similar analgesic efficacy. In conclusion, we demonstrated that ibuprofen and dexketoprofen had strong and similar analgesic efficacy. Clinicians can use two drugs interchangeably in their studies by analyzing of side effects and medical costs.

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