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Comparison of the effects of preoperative and intraoperative intravenous application of dexketoprofen on postoperative analgesia in septorhinoplasty patients: randomised double blind clinical trial

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Abstract. – BACKGROUND: Postoperative analgesia is important because it prevents the adverse effects of pain. To study the effect of preoperative or intraoperative application of dexketoprofen on postoperative analgesia and patient comfort in patients undergoing septorhinoplasty.

PATIENTS AND METHODS: A randomized, double-blind, placebo-controlled study. The study included 100 patients randomly assigned to four groups. Patients from group 50/0 got 50 mg dexketoprofen 30 minutes prior to the operation; patients from group 0/50 got 50 mg dexketoprofen 30 minutes after the operation, and patients from group 25/25 got 25 mg dexketoprofen both 30 minutes prior and 30 minutes after the operation. Dexketoprofen was not applied to any of the patients from group C. Once in the recovery room, patient-controlled analgesia was received to all patients. The patients' visual analog scale (VAS), sedation, nausea and vomiting and dyspepsia complaints were recorded at 1, 2, 3, 4, 5, 6, 7, 8, 12 and 24 hours. In addition, patient satisfaction, intraoperative fentanyl and consumption of tramadol in the postoperative 24 hour period were recorded.

RESULTS: The VAS, nausea and vomiting, sedation and patient satisfaction scores were lower in patients from all groups that had received dexketoprofen compared to the controls. There was no difference in intraoperative fentanyl consumption between the groups. The consumption of tramadol was significantly higher in group C compared to all other groups.

CONCLUSIONS: Dexketoprofen provides good postoperative analgesia and patient satisfaction if applied intravenously to septorhinoplasty patients. However, there is no significant difference between preoperative and intraoperative applications of dexketoprofen.

Key Words:

Septorhinoplasty, Post-operative analgesia, Dex ketoprofen, Fentanyl, Tramadol.

Introduction

Postoperative pain is the acute pain that starts with surgical trauma and gradually decreases when the tissue starts healing. If not treated, postoperative pain might lead to thromboembolic and pulmonary complications, prolonged hospital stay, return to the hospital after discharge, reduction of the quality of life of the patients and development of the chronic pain[1].

One of the methods of postoperative analgesia is preemptive analgesia, which is antinociceptive treatment that intercepts with the formation of altered processing of afferent input that is known for amplifying postoperative pain[2].

Dexketoprofen is the propionic acid derivative and is a non-steroidal anti-inflammatory drug. It blocks prostaglandin synthesis by inhibiting cyclooxygenase and indirectly affects kinin, which is the inflammatory mediator. The efficacy of dexketoprofen was demonstrated for moderate and severe muscular and skeletal system pain, renal colic and surgical pain when administered orally, intravenously and intramuscularly[3-5].

In this study, we aimed to compare postoperative analgesic efficacy and side effects of different doses of dexketoprofen applied by the way of intravenous infusion in the preoperative or intraoperative period in patients undergoing septorhinoplasty.

Materials and Methods

Consent of the Ethics Council of Fırat University was obtained to perform this study (10/03/2011, number 05/05). A randomized, double-blind, placebo-controlled study included 100 patients with ASA status I-II scheduled for sep-

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torhinoplasty. Patients with known heart, kidney, liver and hematological diseases, peptic ulcer and gastrointestinal bleeding, with allergic reaction to non-steroid anti-inflammatory drugs (NSAIDs) and chronic pain history and those who received analgesics in the last 24 hours were not included into the study. During the preoperative evaluation, patients were instructed about pain scales such as Visual Analog Scale (VAS) and patient-controlled analgesia (PCA) and they signed a written consent form to participate in the study. As a premedication, 0.07 mg/kg midazolam and 0.01 mg/kg atropine was applied intramuscularly to all patients 30 minutes before the operation. Once the patient was in the operating room, vascular access was opened in the antecubital region and electrocardiography (ECG), peripheral oxygen saturation (SpO_2) and noninvasive blood pressures were monitored.

Patients were randomly divided into four groups:

Group C (n=25): patients who received 100 ml serum physiologic (SP) containing 0.9% NaCl as an infusion 30 minutes before and 30 minutes after the surgical procedure.

Group D 50/0 (n=25): patients who received 100 ml SP containing 50 mg dexketoprofen as an infusion 30 minutes before the surgical incision and received 100 ml SP 30 minutes before the end of the surgical procedure.

Group D 0/50 (n=25): patients who received 100 ml SP as an infusion 30 minutes before the surgical incision and received 100 ml SP containing 50 mg dexketoprofen 30 minutes before the end of the surgical procedure.

Group D 25/25 (n=25): patients who received 100 ml SP containing 25 mg dexketoprofen as an infusion 30 minutes before the surgical incision and 30 minutes before the end of the surgical procedure.

The infusions of dexketoprofen and SP were prepared by a practitioner who was not involved in either application of anesthesia or postoperative evaluation. The solution that was applied preoperatively was labeled as solution A, while the solution that was applied 30 minutes prior to the end of the surgery was labeled as solution B.

The induction of anesthesia in all patients was supplied by 2 mg/kg propofol, 0.1 mg/kg vecuronium and 2 μg/kg fentanyl. The anesthesia was continued by 5-6% concentrated desflurane in 50% O_2-50% N_2O after endotracheal intubation. Respiratory $ETCO_2$ was arranged to 30-40 mmHg and maintained mechanically. During the surgery as needed, additional doses of fentanyl was administered for analgesia and vecuronium for muscle relaxation. While recovery from the anesthesia, 0.04 mg/kg neostigmine and 0.01 mg/kg atropine was administered intravenously because needed to remove the residual effect of muscle relaxant. After the cessation of the anesthetic drugs time of spontaneous respiration, spontaneous eye opening, extubation, space and time orientation and response to verbal stimuli were recorded

After the patients were transferred to the recovery room their VAS score was evaluated and if it was above 3, intermittent intravenous administration of 10-20 mg tramadol was done until the VAS score was below 3. After basal analgesia was supplied, PCA was given at 20 mg bolus dose, 5 mg/h basal infusions with lockout time of 15 minutes and 4 hour limit arranged to 150 mg via PCA. According to the modified Aldrete scoring system[6], patients that had a score of nine or above were transferred from recovery room to service.

Postoperative nausea and vomiting was classified by using the following numerical scoring system, 0: no nausea or vomiting, 1: only nausea, 2: vomiting once in 30 minutes, 3: vomiting twice or more in 30 minutes[7]. Patients with a nausea and vomiting score of 3 or the ones that have persistent nausea for more than two hours were assessed as severe nausea and vomiting and were administered 150 μg/kg metoclopramide intravenously. Patients that had gastrointestinal side effects (gastric pain, reflux, bleeding) were administered 40 mg famotidin intravenously.

The degree of sedation was assessed according to the Ramsay Sedation Scale[8] as following; 1: irritable agitated, restless patient, 2: cooperative, oriented and calm patient, 3: the patient that only follows the orders, 4: patient that immediately responds to glabellar beats, 5: patient who slowly responds to glabellar beats, 6: no response to glabellar beats.

The patient satisfaction in 24 hours was evaluated according to the following 5 point scale; 1: very satisfied, 2: satisfied, 3: neither satisfied nor unsatisfied, 4: unsatisfied and 5: very unsatisfied.

Patients' mean arterial blood pressures (MAP) and heart rates (HR) were recorded in 10 minute intervals during the operation and in the post-anesthetic care unit. VAS, sedation score, nausea and vomiting score and dyspepsia complaints were recorded hourly in the first 8 hours then at 12^{th} and 24^{th} hour. In addition, length of stay in the recovery room, patient satisfaction, intraoper-

Table I. The VAS scores of all groups.

	Group C	Group 50/0	Group 0/50	Group 25/25
Age	27.16 ± 8.84	26.60 ± 7.57	30.24 ± 7.36	32.35 ± 10.29
Sex (female/male)	11/14	6/19	11/14	5/20
ASA	1.12 ± 0.33	1.08 ± 0.27	1.24 ± 0.43	1.08 ± 0.27
Duration of surgery	89.20 ± 21.19	96.80 ± 30.13	97.80 ± 20.00	94.80 ± 21.23
Recovery criteria (minute)				
Recovery time	18.60 ± 4.21	19.60 ± 3.20	20.00 ± 4.78	17.00 ± 4.08
Spont. breathing	1.16 ± 1.72	2.12 ± 2.86	2.04 ± 2.65	0.84 ± 1.57
Extubation	4.72 ± 2.09	5.68 ± 2.82	6.08 ± 2.08	4.52 ± 1.53
Spont. eye opening	6.32 ± 2.73	6.96 ± 3.10	8.04 ± 3.25	6.04 ± 1.79
Verbal response	7.36 ± 2.21	8.96 ± 3.38	9.16 ± 3.19	6.36 ± 1.82
Orientation	10.00 ± 4.08	11.32 ± 3.89	11.32 ± 4.64	9.32 ± 0.94

ative consumption of fentanyl and postoperative 24 hour consumption of tramadol were recorded.

Statistical Analysis

Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) 15.0 program was used for statistical evaluation. Obtained variables were taken as mean ± standard deviation. One-Way ANOVA, Tukey HSD, Kruskal Wallis and Mann-Whitney U tests were used for the comparison between groups. The p value < 0.05 was considered as statistically significant.

Results

There was no significant difference determined between groups in terms of demographic variables and recovery criteria (Table I).

The VAS score of all groups: Group 50/0 (except for the 2nd hour), Group 0/50 (except for the 4th hour) and Group 25/25 at all times were lower than the VAS score of Group C. There was no significant difference detected between other groups (Table II). There was also no significant difference between groups in terms of intraoperative fentanyl consumption. However, the total tramadol amount consumed in 24 hours to control the acute pain during the recovery was significantly higher in Group C than in all other groups (Table III).

When nausea and vomiting scores of all groups are compared, Group C had significantly higher scores at all times than Group 50/0 (recovery and 3rd hour, $p < 0.05$), Group 0/50 (recovery, $p < 0.01$) and Group 25/25 (recovery, $p < 0.05$) (Figure 1). However, none of the patients had extensive nausea and vomiting that required the application of metoclopramide. There was no significant difference between groups in terms of dyspeptic complaints and none of the patients needed administration of famotidine.

When the sedation levels were compared, it was detected that Group C's levels were significantly higher than Group 50/0's (recovery, 1st and 2nd hour, $p < 0.05$), Group 0/50's (recovery, $p <$

Table II. The VAS scores of all groups.

VAS	Group C	Group 50/0	Group 0/50	Group 25/25
Recovery	6.00 ± 0.91	4.16 ± 2.21‡	4.16 ± 1.24‡	3.64 ± 2.07‡
At 1. hour	3.64 ± 1.60	2.52 ± 1.82*	1.88 ± 1.30‡	2.12 ± 1.05‡
At 2. hour	3.48 ± 1.55	2.56 ± 2.06	2.00 ± 1.91‡	2.20 ± 0.86‡
At 3. hour	3.28 ± 1.74	2.24 ± 1.98*	1.68 ± 1.67‡	1.72 ± 1.10‡
At 4. hour	2.76 ± 1.73	1.56 ± 1.22*	1.96 ± 1.61	1.68 ± 2.07†
At 5. hour	2.64 ± 1.65	1.08 ± 0.86‡	1.28 ± 1.67†	1.04 ± 1.81‡
At 6. hour	2.72 ± 1.81	1.24 ± 1.33†	0.92 ± 0.99‡	0.72 ± 1.20‡
At 7. hour	2.40 ± 2.04	0.68 ± 1.18†	0.64 ± 0.70†	0.60 ± 1.11‡
At 8. hour	1.88 ± 1.39	0.47 ± 0.89‡	0.56 ± 0.65‡	0.32 ± 0.74‡
At 12. hour	1.48 ± 1.32	0.60 ± 1.19†	0.32 ± 0.69‡	0.32 ± 0.74‡
At 24. hour	1.08 ± 0.99	0.16 ± 0.55‡	0.36 ± 0.63†	0.32 ± 0.74†

*$p < 0.05$; †$p < 0.01$; ‡$p < 0.001$; when Group C was compared the other groups.

Table III. Intraoperative and postoperative consumption of analgesic of all groups.

	Group C	Group 50/0	Group 0/50	Group 25/25
Intraoperative fentanyl (μg)	224.00 ± 41.12	198.00 ± 36.74	208.00 ± 51.39	212.00 ± 41.53
Tramadol at recovery (mg)	50.80 ± 12.22	30.80 ± 21.58‡	37.60 ± 13.31*	28.00 ± 16.32‡
Total tramadol consumption (mg)	350.80 ± 70.05	256.40 ± 95.60‡	280.00 ± 81.03*	283.60 ± 68.36*

0.01) and Group 25/25's (recovery, 1st and 2nd hour, $p < 0.01$). Moreover, the sedation score of Group 0/50's 2nd hour was determined to be higher than the sedation scores of Group 50/0 and Group 25/25 ($p < 0.05$) (Figure 2).

Although, the patients satisfaction was determined to be positive in all groups, Group C's scores were significantly higher than those of Group 50/0 ($p < 0.01$), Group 0/50 ($p < 0.001$) and Group 25/25 ($p < 0.01$) (Figure 3).

Intraoperative and postoperative values of mean arterial pressure and heart rate did not differ significantly between the groups.

Discussion

When controlling the acute postoperative pain it is still a controversy whether to use the preemptive analgesic intervention or conventional regimens for more effective results[9]. Some studies have shown that values for pain intensity, need for supplemental analgesic and time of the first analgesic request were better in patients who were administered preemptive analgesia rather than in patients who were administered post-incisional analgesic[10,11]. Moreover, there are studies that show that there is no significant difference between pre-incisional and post-incisional nonsteroidal anti-inflammatory drug application[12,13]. For these reasons, in this study we evaluated dexketoprofen, which is efficient in moderate-to-severe pain and has few gastrointestinal side effects. We particularly focused on the effect of preoperative and intraoperative administration of dexketoprofen on postoperative analgesia.

In the study where dexketoprofen was administered orally before and/or after the operation, the group that had received the dexketoprofen had lower VAS scores and lower postoperative consumption of opioids than the control group[14,15]. Moreover, intramuscular administration of dexketoprofen as a postoperative analgesic was found to be more effective than diclofenac and ketoprofen[5,16]. There are a limited number of reports about the intravenous application of dexketoprofen as a postoperative analgesia. In the existing researches, preemptive analgesia had been supplied by dexketoprofen and compared with placebo[17,18]. In our work, unlike the existing studies we evaluated the effect of preoperative and intraoperative intravenous application of dexketoprofen on analgesia and side effects.

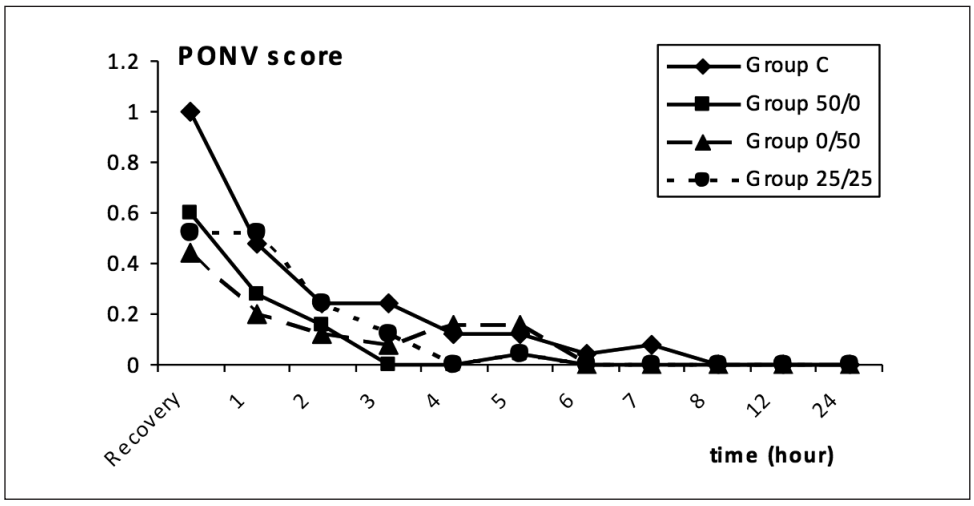

Figure 1. Patients' nausea and vomiting scores.

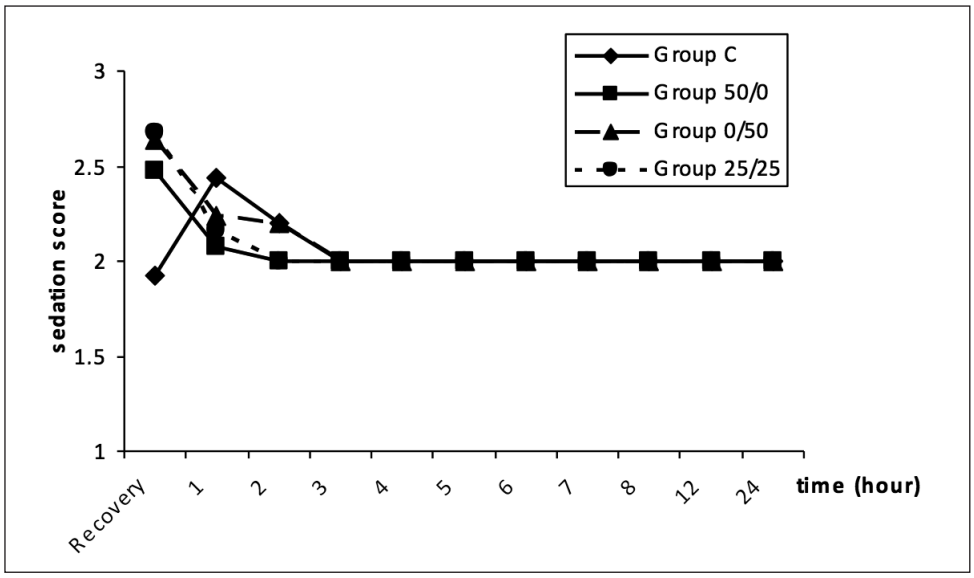

Figure 2. Patients' sedation scores.

In this study it was determined that all groups that had received dexketoprofen had significantly lower VAS scores along with significantly lower consumption of tramadol during both 24 hours post-operation and recovery room when compared to the control group. The difference in postoperative 24 hour consumption of tramadol between Group 50/0 and Group C was more pronounced than in other groups. However, there was no significant difference between preoperative or postoperative application of dexketoprofen. In a report where they compared 50 mg versus 25 mg intravenous application of dexketoprofen in acute renal colic patients, total pain relief (TOTPAR) was found to be more in patients that got 50 mg than in patients that got 25 mg dexketoprofen. However, this difference was not statistically significant[3]. In our study, Group 25/25 got preoperative and postoperative 25 mg dexketoprofen, making total of 50 mg. We did not detect any significant difference between groups that got either preoperative or postoperative 50 mg dexketoprofen and the group that got 25 mg dexketoprofen in both periods.

The nausea, vomiting and gastrointestinal problems are among the negative effects that develop due to the use of NSAIDs. Related studies show that patients that were administered with dexketoprofen had less nausea and vomiting than patients in the control group[14,15,17]. Similar to the literature, our patients that received dexketoprofen had lower scores of nausea and vomiting than patients from the control group. There was no significant difference detected between the all other groups that had received dexketoprofen.

Studies evaluating the sedation scores in postoperative analgesia show variability. Some reports show that sedation score is low in dexketoprofen group[14], some others that the score does not change[17,19], while some others studies show that it increases[5]. We have determined that the sedation scores were lower in dexketoprofen groups than in the control group. When compared between dexketoprofen groups, the sedation score in the second hour of Group 0/50 was

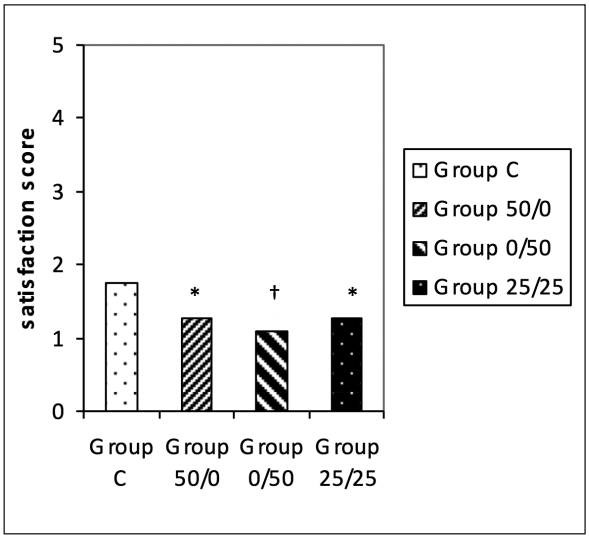

Figure 3. Patients' satisfaction scores.

higher than the other two groups. We suggest that this situation might be due to Group 0/50's heavy consumption of opioids during that period.

Likewise to the literature, we detected the satisfaction to be high in patients receiving dexketoprofen[15,16].

Conclusions

Patients undergoing septorhinoplasty showed that preoperative and/or intraoperative intravenous administration of dexketoprofen as a postoperative analgesia served as a good analgesic, had a low side effect profile and provided good patient satisfaction. However, there was no significant difference between preoperative and intraoperative application of predetermined doses of dexketoprofen.

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