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Research Article

Effectiveness of a Single Dose Intravenous Paracetamol and Rectal Indomethacin on Pain after Open Septorhinoplasty

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Abstract

Background: Effective analgesia after open septorhinoplasty is still a constant concern. However, the information about appropriate pain management after the surgery is not sufficient yet. Therefore, this single blind randomized controlled trial was planned to determine whether the analgesic efficacy of a single dose of intravenous paracetamol differs from a single dose of rectal indomethacin in patients undergoing open septorhinoplasty.

Methods: Seventy-five American Society of Anesthesiologists physical status I-II patients, undergoing elective primary cosmetic open septorhinoplasties with general anesthesia were randomly divided into 3 groups of 25 each. They received either intravenous paracetamol 1 g in 100 ml normal saline, indomethacin 100 mg rectally, or 100 mL of 0.9% normal saline infusion, thirty minutes before completion of surgery. Postoperative pain was assessed using a 0-10 visual analog scale at 30 minutes, and 1, 2,3,4,5, 6, 7 and 8 hours after anesthesia. Patients received intravenous morphine for supplemental analgesia if pain scores were 4 or greater.

Results: Patients' and surgery characteristics, and intraoperative fentanyl and remifentanil use were similar in 3 groups. No statistically significant difference in postoperative pain scores, and supplemental morphine usage was found between the groups. Conclusion: In patients having open septorhinoplasty, analgesic efficacy of a single dose of 1 g intravenous paracetamol was comparable to 100 mg rectal indomethacin given at the end of the surgery.

Keywords: Analgesia; Pain postoperative; Paracetamol; Non-steroidal anti-inflammatory agents; Rhinoplasty

Introduction

Cosmetic open septorhinoplasty is among the common procedures of plastic surgery in adults. Pain and discomfort in the immediate postoperative period after septorhinoplasty has been reported as an undesirable experience and patients stated dissatisfaction with pain therapy regimens. Although effective analgesia after septorhinoplasty is still a constant concern, the information about optimal postoperative pain management is not sufficient yet [1-3]. Postoperative analgesia is often provided with opioids alone or along with non-opioid analgesics [4]. Adverse effects associated with systemic opioids (such as nausea, vomiting, pruritus, urinary retention, and respiratory depression) may limit their administration after septorhinoplasty and the resulting inadequate pain relief. Either non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol (acetaminophen) as non-opioid analgesics with different mechanisms of action are widely used for postoperative pain management. They decrease the need for opioids and cause less opioid-related adverse effects. This is particularly important in day-case patients [5,6]. However, the efficacy of paracetamol for pain control after septorhinoplasty has not been fully described in literature. The effectiveness of rectal indomethacin for postoperative pain control has been reported by a number of studies [7,8]. However, a review of the literature revealed no studies evaluating its analgesic efficacy after septorhinoplasty. Considering the few studies available, this study was planned to determine whether the analgesic efficacy of a single dose of intravenous (IV) paracetamol differs from a single dose of rectal indomethacin in patients undergoing primary cosmetic open septorhinoplasty. The rationale explanation for administering this dose of study medications was that, in clinical practice, they are common dosage of the drugs routinely used for relief of postsurgical moderate pain level.

Methods

This prospective, randomized, single-blind, controlled trial was approved by the Institutional Human Ethics Committee and written informed consent was obtained from the participating patients. Seventy-five patients with American Society of Anesthesiologists physical status I–II, undergoing primary elective cosmetic open septorhinoplasty under general anesthesia were enrolled in the study. Patients were randomly divided into 3 groups of 25 each.

They received either IV paracetamol 1 g in 100 ml of saline (0.9%) (Paracetamol group), or indomethacin suppository 100 mg + 100 ml infusion of saline (Indomethacin group), or 100 mL of saline (control group) 30 minutes prior to completion of surgery. Infusions were continued for 15 min. Patients with drug or alcohol abuse, allergy to study drugs, history of renal or hepatic disease, bleeding disorder, peptic ulcer, or asthma, were excluded from the study.

Those receiving a regular analgesic medication were also excluded. Randomization was done according to a computer-generated random numbers and by closed-envelope technique. An envelope was blindly drawn each time an eligible participant entered the trial by a staff not involved in the study. Oral clonidine 0.2 mg was given for premedication one hour before arrival in the operating room. Anesthesia was induced with midazolam, fentanyl, sodium thiopental and atracurium and was maintained with O_2 100%, atracurium, and continuous IV infusion of propofol and remifentanil. Electrocardiogram, arterial oxygenation using pulse oximetry (SpO_2) and blood pressure were continuously monitored throughout the

surgery. After induction of anesthesia, topical phenylephrine 0.25% was applied for nasal mucosal decongestion and local anesthesia performed with 10 mL solution of 1% lidocaine combined with 1:100,000 epinephrine injected into the operation area by the surgeon.

Another 4 ml solution of lidocaine + epinephrine combination was also injected before osteotomy. At the beginning of the surgery, a single dose of 8 mg dexamethasone and 500 mg tranexamic acid were administered intravenously in order to decrease perioperative blood loss, edema and ecchymosis. Systolic arterial pressure was kept between 80-90 mmHg for controlled hypotensive anesthesia by changing doses of anesthetics, altering the rate of intravenous fluid infusion, or giving intravenous nitroglycerin if necessary.

At the end of the surgery, muscle relaxation was reversed with neostigmine and atropine. All patients were extubated once fully awake and transferred to the recovery room. The length of time from the end of anesthesia until tracheal extubation was recorded. They were observed in the recovery room for 30 minutes after the anesthesia. All open septorhinoplasties were performed by one of the four senior otolaryngology residents who used similar surgical techniques.

Postoperative pain intensity was assessed by the patient 30 minutes after anesthesia in the recovery room, and 1, 2, 3, 4, 5, 6, 7 and 8 hours after anesthesia in the surgery ward. Patients were asked to evaluate the severity of postoperative pain using a 0-10 (0=no pain, 10=pain as bad as it could be) visual analog scale (VAS). Those who experienced a VAS pain score of 4 or greater or requested an analgesic were treated with supplemental boluses of 2 mg intravenous morphine until pain was relieved. Supplemental morphine consumptions, the number of patient required additional analgesia, and drug related side effects were also documented during study period.

The anesthesiologists conducted the anesthesia were aware of the study drugs given and did not involve in the assessment of the patients. The study drugs were administered by anesthetic technicians in charge of the patient in the operating room who did not participate in the postoperative assessment of the patients. A study observer blinded to the study protocol closely monitored and recorded postoperative pain scores and other study measures throughout the study period. The patients and staff nurses were blinded to the study groups.

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 21. A sample size of a minimum of 25 patients per group was required to detect a one point difference in VAS pain score between the 3 study groups, with a power of 80% and a significance level of 5% (two-tailed test adjusted for three comparisons).

Fisher's exact test and chi-square test were used to analyze categorical variables where appropriate. Analysis of variance test (ANOVA) or its non-parametric counterpart, the Kruskal–Wallis test were applied to continuous data when appropriate. The differences in VAS score between groups were evaluated using non-parametric Friedman test. Values (Data) are presented as mean (SD) or number (%). A P-value of less than 0.05 was considered statistically significant.

Results

From 75 enrolled patients, 45 were men and 30 women with a mean age of 33.3 ± 11.8 years (range: 18 to 40 years). Patients' characteristics, operative and anesthetic data, intraoperative fentanyl and remifentanil usage, and time to tracheal extubation were comparable between the three groups (Table 1).

No significant difference in postoperative pain scores, supplemental morphine usage, and the number of morphine doses required to obtain pain relief was found between the groups at each time point after surgery (Tables 2, 3 and 4).

There were also no differences in the number of patients who received intravenous morphine supplementation between the paracetamol, indomethacin, and placebo groups (12:10:11 respectively).

No intraoperative and postoperative complications were observed. Three cases of nausea in the paracetamol and one case in the control group were detected with no need for treatment.

Variables	Control (n=25)	Indomethacin (n=25)	Paracetamol (n=25)	P-value
Age (yr)	26.04 ± 5.18	26.88 ± 4.65	25.64 ± 6.18	0.708
Sex (male/female)	14/11	17/8	14/11	0.607
Weight (kg)	65.72 ± 11.47	68.50 ± 14.59	68.08 ± 2.10	0.711
Height (cm)	170 ± 10.03	172.04 ± 8.51	169.44 ± 8.88	0.757
ASA class (1/2)	23/2	25/0	24/1	0.769
Fentanyl dose (µg)	149.0 ± 179.19	127.0 ± 49.96	127.0 ± 39.48	0.745
Remifentanil dose (mg)	2.41 ± 1.33	2.48 ± 1.11	2.26 ± 0.82	0.846
Propofol dose (mg)	1812.5 ± 573.6	1898.0 ± 658.99	1918.0 ± 403.86	0.781
Anesthesia duration (min)	238.68 ± 71.91	234.2 ± 64.48	226.8 ± 55.75	0.805
Surgery duration (min)	213.68 ± 65.91	206.80 ± 66.61	201.0 ± 61.95	0.788
Extubation time (min)	20 ± 17.38	16 ± 12.58	15 ± 12.16	0.371

Table 1: Characteristics and operative data in three study groups Data are mean ± SD and number P>0.05: not significant.

Postoperative VAS	Paracetamol (n=25)	Indomethacin (n=25)	Control (n=25)	P value
VAS at 30 min	1.92 ± 1.68	2.16 ± 1.37	2.44 ± 1.96	0.481
VAS at 1hr	1.84 ± 1.11	1.96 ± 1.10	1.84 ± 1.25	0.921
VAS at 2hr	1.48 ± 0.92	1.80 ± 0.76	1.56 ± 0.87	0.382
VAS at 3hr	1.48 ± 0.96	1.68 ± 0.80	1.44 ± 0.82	0.704
VAS at 4hr	1.52 ± 0.92	1.64 ± 0.64	1.28 ± 0.74	0.348
VAS at 5hr	1.84 ± 1.40	1.56 ± 071	1.36 ± 0.86	0.466
VAS at 6hr	1.40 ± 0.87	1.68 ± 0.80	1.32 ± 0.69	0.437
VAS at 7hr	1.44 ± 0.92	1.52 ± 0.82	1.48 ± 1.00	0.959
VAS at 8hr	1.36 ± 0.70	1.40 ± 0.65	1.32 ± 0.9	0.891

Table 2: Comparison of mean postoperative VAS pain scores at each time point after surgery between IV paracetamol, rectal indomethacin and control groups. Data are mean ± SD. VAS: visual analogue scale, There was no significant differences between groups (P>0.05).

Postoperative IV morphine	Paracetamol (n=25)	Indomethacin (n=25)	Control (n=25)	P value
Total morphine (mg)	1.64 ± 2.36	1.16 ± 1.86	1.20 ± 1.66	0.738
No. of morphine doses	0.96 ± 1.33	0.60 ± 1	0.64 ± 0.86	0.655

Table 3: Comparison of postoperative mean total supplemental morphine usage, and the number of morphine doses administered, between IV paracetamol, rectal indomethacin and control groups. Data are mean ± SD. There were no significant differences between groups (P>0.05).

Postoperative time	Paracetamol (n=25)	Indomethacin (n=25)	Control (n=25)	P value
30 min	0.32 ± 0.75	0.24 ± 0.66	0.36 ± 0.76	0.774
1hr	0.24 ± 0.60	0.24 ± 0.66	0.20 ± 0.58	0.922
2hr	0.08 ± 0.40	0.08 ± 0.40	0.08 ± 0.40	>0.999
3hr	0.08 ± 0.40	0.08 ± 0.40	0.0 ± 0.0	0.602
4hr	0.12 ± 0.44	0.0 ± 0.0	0.0 ± 0.0	0.132
5hr	0.32 ± 0.69	0.0 ± 0.0	0.08 ± 0.40	0.025
6hr	0.08 ± 0.40	0.08 ± 0.40	0.0 ± 0.0	0.602
7hr	0.08 ± 0.40	0.08 ± 0.40	0.0 ± 0.0	>0.999
8hr	0.0 ± 0.0	0.0 ± 0.0	0.08 ± 0.40	0.368

Table 4: Comparison of mean postoperative supplemental morphine consumption (mg) at each time point after surgery between IV paracetamol, rectal indomethacin and control groups Data are mean ± SD. There were no significant differences between groups (P> 0.05)

Discussion

The results of the present study showed no significant difference in postoperative pain reduction after IV injection of paracetamol and rectal indomethacin before completion of open septorhinoplasty. Furthermore, their analgesic efficacy was not superior to that of the control group. Interestingly, VAS scores in the control group were low during observation time. Our findings are in agreement with the study of Sener et al. [3]. They reported no significant differences in postoperative pain scores during 24 h following septorhinoplasty between lornoxicam, a potent NSAID, dipyrone and placebo. Our present study is also in accord with negative findings of some previous clinical trials [9,10] and in contrast to the positive findings described in the literature [11-13].

The most likely explanation for the results of our study is the nature of the moderate baseline pain intensity after septorhinoplasy. As pointed out by Bjune et al. [14] the degree of initial pain experience without pain therapy must be high enough to distinguish two analgesics and also analgesics from placebo. Moreover, the required baseline pain intensity should be higher in a single dose study, than in repeated-dose studies. Therefore, our pain model may have insufficient sensitivity to differentiate analgesic effect of paracetamol and indomethacin from control [1,10]. It is shown that inadequate sensitivity of a trial may cause false negative findings [14]. However, including a control group, studying pain after a particular type of surgery in patients of the similar age improved the power and assay-sensitivity of our study [14]. Previous studies also failed to show any effect of paracetamol in patients with moderate baseline pain level [15]. Significant differences in pain scores between parenteral paracetamol and placebo was not shown after arthroscopy. In this study low pain scores in placebo group made it a poor model for evaluating the effectiveness of analgesics [10]. Our present study also confirms the negative findings on postoperative pain relief with rectal NSAIDs [11,16]. In contrast, Forse et al. [13] demonstrated that preoperative administration of intramuscular ketolorac and rectal indomethacin equally reduced early postoperative pain after laparscopic cholecystectomy. However, it has been suggested that the degree of difference in the analgesic efficiency of NSAIDs and paracetamol may depend on the type of surgery. The analgesic efficacy

of NSAIDS was similar to paracetamol in major abdominal and orthopedic operations and also in ear, nose and throat surgery, whereas in dental or gynecological minor surgery NSAIDS was superior to paracetamol [9].

Additional possible explanation for the results of our study may be the perioperative use of IV dexamethasone, oral clonidine, and local infiltration of lidocaine. The beneficial roles of these drugs in reducing early postoperative pain and opioid consumption have been demonstrated in systematic reviews. Dexamethasone commonly given preoperatively to reduce facial edema and ecchymosis after septorhinoplasty [17]. Administration of a single-dose of dexamethasone 60 min or more before surgical trauma was associated with reductions in postoperative pain and opioid consumption [18,19]. Furthermore, Goktas et al. [20] showed that lidocaine use in rhinoplasties decreased the analgesic need of the patients in the early postoperative period. Derkay and colleagues [21] also found that intraoperative administration of 4% lidocaine eardrops had the benefit of a good postoperative pain relief. Clonidine, an alpha-2 adrenoreceptor agonist has central sympatholytic effect with antihypertensive, anti-anxiety and analgesic properties. It has a half-life of 9-12 h. Oral premedication with clonidine decreased intra-operative anesthetic and narcotic doses, and diminished postoperative pain intensity and analgesic requirements [22,23].

It could be argued that the small sample size may be the reason for lack of a difference in our study. Therefore, more data are needed for strong conclusions about the effect of the analgesic drugs on pain after septorhinoplasty. However, according to Hein et al. [15] the influence of a small sample size may be questionable because the pain scores, the need for supplemental morphine, and the number of patient required additional analgesia were similar in three groups throughout the study. Another limitation of the present study was the short duration of observation time. This could prevent more conclusions on the additional time of postoperative pain assessment. However, it is not likely to have an important clinical influence.

In conclusion, postoperative analgesic efficacy of 1 g intravenous paracetamol and 100 mg rectal indomethacin given at the end of the open septorhinoplasty was comparable and was not superior to that of control group. Instead, premedication with oral clonidine, along with intraoperative infiltration of local anesthetics into the surgical field and intravenous dexamethasone may protect the patients from the postoperative pain.

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