Comparative Evaluation of Postoperative Pain Scores and Opioid Consumption in Septorhinoplasty After Administration of Single-Dose Preemptive Paracetamol and Ibuprofen: A Randomized Controlled Trial

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Abstract

Introduction Septorhinoplasty operates on the nose's bone and cartilage and is ensued by severe postoperative pain.

Objective The objective of this study is to evaluate the effects of preoperative administration of intravenous (IV) paracetamol and ibuprofen on postoperative pain scores in patients undergoing septorhinoplasty.

Methods A total of 150 patients undergoing septorhinoplasty were randomly assigned into 3 groups with 50 patients in each group. The control group (group A) was administered 100 ml saline solution; the paracetamol group (group B) was administered 1,000 mg of IV paracetamol in 100 ml of saline solution; and the ibuprofen group (group C) was administered 800 mg of IV ibuprofen in 100 ml of saline solution before surgery. Opioid analgesics were employed to achieve postoperative analgesia. Postoperative pain was evaluated using the visual analogue scale (VAS). Postoperative opioid consumption and adverse effects were also recorded for each patient.

Results In comparison with group A, the score in the VAS of groups B and C was statistically lower in all the time intervals ($p < 0.05$). In the 1st and 6th hours postoperatively, group C's score in the VAS in was lower than that of group B ($p < 0.05$). In the control group, total opioid consumption was highest in all time intervals ($p < 0.05$). In group C, total opioid consumption was significantly lower than in group B in the 0 to 6 and 6 to 12 hours intervals. ($p < 0.05$).

Conclusion The single-dose preemptive administration of ibuprofen has a more profound postoperative analgesic effect than paracetamol in the first 6 hours after septorhinoplasty. After the first 6 hours postsurgery, there is no difference between ibuprofen and paracetamol in terms of analgesic effect.

Keywords

- nasal septum/surgery
- rhinoplasty/methods
- analgesics
- visual analog scale
- pain
- postoperative/diagnosis
- treatment outcome

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Introduction

Pain is considered the fifth vital sign in modern medical practice. Hence, apart from other vital parameters, evaluation of pain has become a primary and necessary requirement for proper patient care and comfort. Septorhinoplasty is an elective and ambulatory surgical procedure which involves massive hard- and soft-tissue manipulation in the nasal region of the face. The postoperative pain is severe in septorhinoplasty since it involves the nasal cartilage and bone.[1] This postoperative pain is often upsetting, distressing and requires efficient pain control management.[2] Severe postoperative pain can lead to complications, such as delayed wound healing, ischemia, thromboembolism, pulmonary complications, immunological changes, and increased hospitalization and cost of treatment.[3,4] In this quest to provide effective postoperative pain control, patients are frequently prescribed opioids. Opioids act centrally on the nervous system and, thus, have strong analgesic potential.[5] Although providing relief in acute pain, they are associated with opioid-related adverse events (ORAEs), such as dependence, abuse, overdose, and deaths.[6] This situation is undesirable and, thus, has led to the need to develop regimens which involve the avoidance of opioid overmedication and at the same time provide adequate analgesia. Therefore, the American Society of Anesthesiologists (ASA) has recommended the use of multimodal analgesia techniques involving local anesthesia, regional anesthesia, and non-steroidal antiinflammatory drugs (NSAIDs) to potentiate pain relief and reduce adverse effects.[7]

Preemptive analgesia is one such modality to reduce the severity and duration of postoperative pain. Pioneered by George W Crile, it is an antinociceptive drug administration done before tissue trauma to prevent the peripheral and central sensitization as well as the hyperexcitability of the central nervous system.[8] This decreases the nerve sensitization and thereby reduces postoperative hyperalgesia and allodynia.[9] Administration of apt analgesia at the appropriate time, dose, and form before the surgical procedure has shown to reduce postoperative pain and need of analgesia. Preemptive analgesia also contributes to comfortable recovery, reduces the need of opioid consumption, improves patient's satisfaction, outcomes, and it reduces cost of care.[10]

Thus, the combination of multimodal and preemptive analgesia techniques in postoperative pain management have been researched and clinically experimented. Recently, preemptive intravenous (IV) administration of ibuprofen and paracetamol for postoperative pain management has been extensively researched. Ibuprofen is a common NSAID with antiinflammatory, analgesic, and anti-pyretic effect. It is a non-specific inhibitor of cyclooxygenase (COX) enzymes (COX-1 and COX-2 isoenzymes), which is associated with the analgesic effect.[11] Ibuprofen does not increase the risk of bleeding or gastrointestinal problems.[12] Paracetamol is another time-tested safe drug with analgesic and anti-pyretic effect but no antiinflammatory action. Paracetamol acts centrally, which affects both the peripheral and central antinociception processes.[13] Clinically, paracetamol is more advantageous and safer over other NSAIDs since it causes less gastric irritation, antiplatelet activity, and untoward drug interactions.[14]

The primary objective of the present study is to evaluate the effects of the preoperative administration of IV paracetamol and IV ibuprofen on postoperative pain scores in patients undergoing open septorhinoplasty. The study also aims to evaluate the postoperative opioid consumption in patients treated with the preemptive analgesia approach. The secondary objective of this study is to evaluate the incidence of adverse effects associated with the study drugs.

Method

Ethics

The study was conducted at our university hospital, and ethical approval was obtained from the institutional ethics committee. The study protocols were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki declaration of 1975, as revised in 2000.

Study Design

It was a prospective, randomized, and double-blinded study in which 150 patients between 18 and 60 years of age to be operated for open septorhinoplasty with ASA physical status I-II and planned hospitalization stay of minimum 24 hours were included. Written and informed consent form was obtained from each patient. Demographic data including age, gender, body mass index (BMI), ASA score, duration of surgery (minutes), and duration of anesthesia (minutes) were recorded. Patients graded ASA III and above, with history of renal, hepatic, cardiovascular or pulmonary disease, allergy to study drugs, long-term abuse of NSAIDs or opioids, history of angiotensin converting enzyme (ACE) inhibitors, furosemide or aspirin use, bleeding diathesis, platelet dysfunction, gastrointestinal disease, peptic ulcers, neuropathic diseases, pregnancy, those planning pregnancy in the near future, and breastfeeding mothers were excluded from this study.

On the day of the scheduled surgery, the study protocol was explained to the patients as well as the drugs used in the study and how the visual analogue scale (VAS) works. A computer software program was used to randomly assign patients to one of three groups (group A – control, $n = 50$; group B – paracetamol, $n = 50$; group C – ibuprofen, $n = 50$). Group A was given 100 ml of saline solution, group B was given 1,000 mg IV paracetamol in 100 ml of saline solution, and group C received 800 mg of ibuprofen in 100 ml of saline solution before the surgical procedure. General anesthesia was administered after a 30-minute waiting period to all the three groups. Propofol 2 to 3 mg/kg, rocuronium 0.6 mg/kg, and fentanyl 50 to 75 mcg were administered during induction. Anesthesia was maintained with sevoflurane 2% in 40 to 60% oxygen-air mixture and remifentanil 0.125 µg/kg/min intravenously. Standard electrocardiogram (ECG), peripheral oxygen saturation level (SpO_2), and non-invasive blood pressure were monitored and recorded in all the patients. All the surgical procedures were performed by the same surgical team using a similar technique. Fifty milligrams (50 mg) of tramadol were administered to all the patients $\sim$ 30 minutes

Table 1 Demographic characteristic of study patients of groups A, B, and C

	Group A ($n = 50$)	Group B ($n = 50$)	Group C ($n = 50$)	*P*-value
Age (years)	25.16 ± 4.67	26.56 ± 5.43	25.96 ± 5.17	0.095^{α}
Weight (kg)	68.39 ± 10.84	67.98 ± 9.87	68.25 ± 10.76	0.598^{α}
Height (cm)	166.40 ± 8.97	169.01 ± 8.01	167.03 ± 9.11	0.301^{α}
Gender (M/F)	28/22	23/27	25/25	0.297^{β}
ASA (I/II)	47/3	49/1	48/2	0.765^{β}
Duration of operation (min)	129.56 ± 15.44	132.54 ± 14.67	135.66 ± 15.02	0.189^{α}
Operative procedures				
Osteotomy (Y/N)	47/3	46/4	45/5	0.865^{β}
Turbinate reduction (Y/N)	40/10	42/8	42/8	0.832^{β}

Abbreviation: ASA, American Society of Anesthesiologists
Values are expressed in mean ± standard deviation or number
$^{\alpha}p > 0.05$ One-way ANOVA among groups
$^{\beta}p > 0.05$ chi-squared test among groups

before the end of surgery. Following surgery and extubation, all patients were taken to the postoperative care unit.

The patient, surgical team, and anesthesiologist were blinded to the study drugs. Postoperative pain intensity was self-assessed by the patient using the VAS (VAS 0 = no pain, VAS 10 = the most severe pain) in the presence of a nurse who was also blinded to the drugs and groups. Visual analogue scale was recorded at the 1st, 6th, 12th and 24th-hour intervals. Opioid consumption was measured at the 0 to 6, 6 to 12, and 12 to 24-hours intervals and total at 24 hours. Pethidine 0.25 mg/kg was given to patients with a VAS score of 4 and above for rescue analgesia. During postoperative care, all the patients received a single dose of 0.5 mg/kg methyl prednisolone to control inflammation and 40 mg of esomeprazole for gastric protection. During the 24-hour postoperative follow-up duration, the adverse effects of the drugs used in the study were recorded. Events of constipation, bleeding, nausea, vomiting, respiratory depression, sedation/confusion, urinary retention, pruritus, and dyspepsia were charted for each patient.

Statistics

The statistical analysis was performed using the IBM SPSS Statistics for Windows, Version 20.0 software (IBM Corp., Armonk, NY, USA). Power analysis was performed based on the total opioid (pethidine) consumption. It was found that the sample size was 95.42 in the 95% confidence interval, and the power was 0.99 in the significance level. This indicates that the sample size is sufficient. The descriptive statistics were explained as mean ± standard deviation (SD). The data distribution was analyzed using the Kolmogorov-Smirnov test. The Pearson chi-squared test was used to compare the categorial data between the three groups. The one-way analysis of variance (ANOVA) followed by the Tukey test was used to evaluate the differences among the groups at 5% significance level for normally distributed continuous variables.

Result

In this study, each group included 50 patients. Baseline demographic data, duration of operation, and type of operative procedure showed no statistical difference between the groups ($p < 0.05$) (►**Table 1**).

The postoperative VAS pain scores were significantly lower in groups B and C compared with group A at the 1st, 6th, 12th, and 24th-hour intervals ($p < 0.05$). Postoperative VAS pain scores were significantly lower in group C compared with group B at the 1st and 6th hour intervals (►**Table 2**).

Table 2 Comparison of postoperative visual analogue scale score among groups A, B, and C

	Group A ($n = 50$)	Group B ($n = 50$)	Group C ($n = 50$)	*P*-value
VAS recovery	7.07 ± 1.65	$3.98 \pm 1.29^{\alpha}$	$3.01 \pm 0.93^{\alpha,\beta}$	< 0.001
VAS 1st hour	5.76 ± 1.01	$3.19 \pm 1.09^{\alpha}$	$2.77 \pm 0.86^{\alpha,\beta}$	< 0.001
VAS 6th hour	5.02 ± 0.95	$2.84 \pm 1.13^{\alpha}$	$2.21 \pm 0.69^{\alpha,\beta}$	< 0.001
VAS 12th hour	4.25 ± 0.72	$2.06 \pm 0.94^{\alpha}$	$2.01 \pm 0.66^{\alpha,\gamma}$	< 0.001
VAS 24th hour	3.93 ± 0.83	$1.76 \pm 0.88^{\alpha}$	$1.71 \pm 0.58^{\alpha,\gamma}$	< 0.001

Abbreviation: VAS, visual analogue scale.
Values are expressed in mean ± standard deviation or number
$^{\alpha}p < 0.05$ One-way ANOVA compared with group A
$^{\beta}p < 0.05$ One-way ANOVA compared with group B
$^{\gamma}p > 0.05$ One-way ANOVA compared with group B

Table 3 Comparison of total postoperative opioid (pethidine) consumption and rescue analgesia among groups A, B, and C

	Group A ($n = 50$)	Group B ($n = 50$)	Group C ($n = 50$)	*P*-value
0–6 hours	180.20 ± 22.36	$158.20 \pm 38.28^{\alpha}$	$130.80 \pm 39.65^{\alpha,\beta}$	< 0.001
6–12 hours	159.40 ± 20.58	$126.60 \pm 30.25^{\alpha}$	$121.20 \pm 28.46^{\alpha,\gamma}$	0.015
12–24 hours	146.80 ± 21.62	$125.40 \pm 31.48^{\alpha}$	$120.80 \pm 30.32^{\alpha,\gamma}$	0.021
Total consumption	486.40 ± 40.84	$410.20 \pm 88.41^{\alpha}$	$372.80 \pm 90.45^{\alpha,\beta}$	< 0.001
Rescue analgesia (Y/N)	26/24	$11/39^{a}$	$4/46^{a,b}$	< 0.001

Values are expressed in mean ± standard deviation or number
$^{\alpha}p < 0.05$ One-way ANOVA compared with group A
$^{\beta}p < 0.05$ One-way ANOVA compared with group B
$^{\gamma}p > 0.05$ One-way ANOVA compared with group B
$^{a}p < 0.05$ chi-squared test compared with group A
$^{b}p < 0.05$ chi-squared test compared with group B

Table 4 Comparison of incidence of adverse effects between groups A, B, and C

	Group A ($n = 50$)	Group B ($n = 50$)	Group C ($n = 50$)	*P*-value*
Nausea	14	10	8	0.573
Vomiting	11	7	6	0.104
Itching	8	7	7	0.284
Bleeding	2	3	3	0.656
Breathing depression	0	0	0	1.000
Sedation	0	0	0	1.000
Urinary retention	0	0	0	1.000
Constipation	0	0	0	1.000
Dyspepsia	0	0	0	1.000

Values are expressed in mean ± standard deviation
*$p > 0.05$

The postoperative opioid (pethidine) consumption was significantly lower in groups B and C compared with group A ($p < 0.05$). In the 0 to 6-hours time interval, the total postoperative opioid consumption was significantly lower in group C compared with group B ($p < 0.05$). Groups B and C had statistically fewer occurrences of rescue analgesia than group A at all time intervals (►**Table 3**).

In terms of adverse effects, no differences were found in their incidence among the groups as a result of the medications used in the study (►**Table 4**).

Discussion

Rapid resumption of routine activities after surgical procedures is dependent on efficient postoperative pain management and minimum opioid consumption. This becomes more important in ambulatory and elective surgical procedure like septorhinoplasty or other facial plastic surgery which are routinely performed for cosmetic and functional purposes. In this study, it was found that the presurgical administration of intravenous ibuprofen or paracetamol significantly reduced the postoperative pain score and opioid consumption in the 24 hours postsurgical period in comparison with controls in patients treated for septorhinoplasty. Also, the utilization of rescue analgesia was significantly lower in the ibuprofen group followed by the paracetamol and control groups.

Compared with septoplasty, septorhinoplasty is associated with severe postsurgical pain as extensive hard-tissue incursion is involved.[15] Postoperative pain and discomfort can lead to increased hospital stay, extend healthcare cost, reduced readmission rates, and reduced patient satisfaction.[16,17] This can be controlled by effective and efficient postoperative pain management. Opioids have mostly remained the front-line drugs for the management of postoperative pain. Nevertheless, these opioids are associated with multifarious systemic adverse effects which hamper the postsurgical well-being of the patients.[6] Other drugs, such as GABA, local anesthesia, NSAIDS, and α-agonist, have also been experimented as analgesic regimen in patients treated for septorhinoplasty.[18] In the recent decade, clinicians and researchers have used alternative and combination analgesic strategies to reduce their over reliance on opioids and still provide adequate analgesia. Intravenous paracetamol and ibuprofen are two such drugs which have been studied actively considering their safety and analgesic profile.

In this study, 800 mg of IV ibuprofen provided better analgesic effect and reduced postoperative opioid consumption compared with 1 g of IV paracetamol in the first 6 hours after the surgery. This can be attributed to the superior antiinflammatory and COX inhibition capacity of ibuprofen. Cyclooxygenase-1-1 contributes to bleeding and gastrointestinal adverse effects. Cyclooxygenase-2is responsible for the ideal analgesic, antiinflammatory and anti-pyretic effect. The inhibition rate of COX-1 to COX-2 is 2.5:1 for ibuprofen, which is accountable for its lower risk of bleeding, constipation, and other undesirable gastrointestinal adverse effects. Other NSAIDs, such as ketorolac, have inhibition rate of 330:1, which increases the risk of bleeding.[19] A recent systematic review and meta-analysis has concluded that ibuprofen is not associated with an increased risk of postoperative bleeding in plastic surgery.[20] The other experimental drug in this study, paracetamol, is known to have less

contraindication, well established safety profile and lacks significant drug interactions.[14] Due to its lack of peripheral COX-1 inhibition, paracetamol does not amplify the risk of postoperative bleeding and is considered safe.[21] The concern with bleeding is compounded in septorhinoplasty due to the risk of epistaxis. Since the nose is a highly vascularized region, packing it leads to increased pressure and obstruction contributing to significant bleeding.[22] Hence, IV ibuprofen and paracetamol can be used safely in patients treated for septorhinoplasty without the risk of associated bleeding. The incidence of other adverse effects, such as nausea, vomiting, and itching was more frequent in the control group because of its higher opioid use. The requirement of rescue analgesia was less in ibuprofen and paracetamol groups, but no statistically significant difference was found in any of the three groups regarding adverse effects.

The contemporary literature hosts many studies regarding preemptive and multi-modal analgesia techniques to reduce postoperative pain and concurrent opioid consumption. Recently, Celik et al.[23] have reported more analgesic effect and less opioid consumption for 12 hours postoperatively with a preemptive dose of 800 mg of ibuprofen compared with 1 g of paracetamol in patients treated for septorhinoplasty. Gozeler et al.[24] suggested that a preemptive dose of 800 mg of IV ibuprofen, 30 minutes before septorhinoplasty is beneficial in reducing pain score and opioid consumption. In studies performed on other surgical procedures, Southworth et al.[25] found that 800 mg of IV ibuprofen was more efficient in reducing pain and opioid use than 400 mg of IV ibuprofen and placebo in patients treated for orthopedic and abdominal surgeries. In patients treated with elective orthopedic surgery, Singla et al.[26] reported a 31% reduction in opioid consumption and pain levels with the preemptive administration of IV ibuprofen. In the multi-centered placebo-controlled trial by Martinez et al.[27] for abdominal and orthopedic surgeries, they reported significant reduction in opioid use (52%) and reduced pain levels with 800 mg of IV ibuprofen. Moss[28] reported a reduction in the use of postoperative fentanyl with a preemptive dose of 800 mg of IV ibuprofen in pediatric tonsillectomy. In laparoscopic cholecystectomy, Ahiskalioglu et al.[29] found that a preemptive single dose of 400 mg of IV ibuprofen significantly reduced the postoperative pain and opioid consumption compared with placebo.

In studies comparing the preemptive effect of ibuprofen and paracetamol, Ekinci et al.[30] found that IV ibuprofen resulted in lower pain scores and opioid use in comparison with IV acetaminophen (paracetamol) in the first 24 hours postoperatively in patients treated with laparoscopic cholecystectomy surgery. Similar findings have been reported by Ciftci et al.[31] in patients after laparoscopic sleeve gastrectomy. In oral surgical procedures, Viswanath et al.[32] have found that preemptive analgesia with 800 mg of IV ibuprofen is more effective than 1 g acetaminophen in reducing postoperative pain and opioid use after third molar surgery. However, Kayhan et al.[33] reported that in comparison to IV acetaminophen, IV ibuprofen did not significantly reduce the postoperative opioid consumption but reduced the severity of pain in bariatric surgery.

The studies have employed ibuprofen and paracetamol separately for clinical evaluation. Since both drugs are efficacious and have established safety profile, they can be co-administered or used in combination. Gupta et al.[34] have reported that 800 mg of IV ibuprofen combined with 1 g of IV acetaminophen significantly decreased the pain level, opioid consumption, and ORAEs in patients undergoing knee or hip arthroplasty. In lower wisdom tooth extraction, a combination of 400 mg of ibuprofen and 1,000 g of paracetamol has shown to provide better analgesic effect than 200 mg of ibuprofen and 500 mg of paracetamol or 400 mg of ibuprofen or 1 g of paracetamol.[35]

There are a few limitations to this study. A fixed dose of 800 mg of ibuprofen and 1 g of paracetamol was used, irrespective of the weight and profile of the patient. Ibuprofen is available in 400 and 800-mg forms. Further studies can be planned with different dose combinations. Studies involving co-administration of IV ibuprofen and paracetamol in patients treated for septorhinoplasty can be done. The sample size was calculated based on opioid requirement, the primary aim. Studies with large sample size might be required to study the adverse effects of experimental drugs. The cost of postoperative care and length of hospital stay has not been evaluated in this study. Since all patients received 0.5 mg/kg of methyl prednisolone in the postoperative period, the analgesic efficiency of steroid was not considered or evaluated. Also, this study did not evaluate the reduction of swelling and bruising in patients postsurgically, which is an important factor for their early return to normal daily routine. Further research can be done considering the limitations of the present study.

Conclusion

In concluding this study, a single-dose preemptive IV administration of 800 mg of ibuprofen and 1 g of paracetamol before septorhinoplasty contributes significantly to postoperative pain reduction and opioid consumption in these patients. On comparing ibuprofen with paracetamol, postoperative VAS pain scores were lower with ibuprofen for the first 6 , after which the difference was not significant. In terms of postoperative rescue analgesia usage, the opioid consumption was lower in the ibuprofen group for the 0 to 6 hours interval after the surgery when compared with paracetamol. No serious adverse effects were observed with any of the study drugs. Thus, the author recommended the use of preemptive analgesia strategies involving IV ibuprofen or paracetamol to achieve adequate analgesia and reduce opioid requirement in patients being treated for septorhinoplasty.

Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later

amendments or comparable ethical standards. The study was approved by the research ethical committee of Najran University, Kingdom of Saudi Arabia (Reference No.: 442–42–52368-DS).

Consent to Participants

A written informed consent was obtained from each participant.

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Conflict of Interests

The author declares that he has no conflict of interests.

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