KLİNİK ÇALIŞMA – ORIGINAL RESEARCH

COMPARISON OF INTRAVENOUS PARACETAMOL AND TRAMADOL FOR POSTOPERATIVE ANALGESIA IN PATIENTS WITH SEPTO-RHINOPLASTY

SEPTO-RİNOPLASTİ AMELİYATLARINDA POSTOPERATİF ANALJEZİ AMACIYLA İNTRAVENÖZ PARASETAMOL İLE TRAMADOL'ÜN KARŞILAŞTIRILMASI

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SUMMARY

Objective: *The aim of the study was to compare the efficacy of i.v. tramadol and i.v. paracetamol for postoperative analgesia after septo-rhinoplasty operation.*

Method: *Fifty American Society of Anesthesiology (ASA) physical status I-II patients, aged between 18-50, receiving septo-rhinoplasty operation are included in the study. The patients were randomly divided into two groups for postoperative analgesia. In Group I; i.v. paracetamol 1 gr was infused 30 minutes before the end of the operation. In Group II; i.v. tramadol 1 mg kg^{-1} was given 20 minutes before the end of the operation. A blinded observer recorded the pain intensity, analgesic need, patient satisfaction and side effects of drugs for postoperative at 1 h, 6 h and 24 h hours.*

Results: *The VAS values are similar in both groups at postoperative 1st hour, no statistically significant differences were found ($p> 0.05$). VAS values for group II were significantly lower than group I at 6 h and 24 h postoperatively ($p< 0.05$). No serious side-effects were recorded during the study. The most frequent adverse effect was nausea (25%) in group II. No significant difference was found between groups in terms of vomiting ($p>0.05$), whereas the rate of nausea was significantly lower in group I than group II. Cortisol levels significantly decreased in both groups at postoperative period.*

Conclusion: *Intravenous paracetamol administration provided adequate analgesia as opioids especially at early postoperative period for mild-moderate pain therapy in perioperative period.*

KEY WORDS: *Paracetamol; Tramadol; Postoperative Pain*

ÖZET

Amaç: *Bu çalışmada septo-rinoplasti ameliyatı sonrası postoperatif analjezi amacıyla intravenöz yoldan verilen parasetamol ile tramadolün etkilerinin karşılaştırılması amaçlandı.*

Yöntem: *Septorinoplasti ameliyatı olan ASA I-II risk grubuna giren yaşları 18 ile 50 arasında değişen 50 hasta çalışmaya dahil edildi. Hastalar postoperatif analjezi amacıyla rastgele iki gruba ayrıldı. Grup I'de operasyon bitimine 30 dk kala 1gr i.v. parasetamol infüzyon şeklinde uygulandı. Grup II'de ise operasyon bitimine 20 dk kala i.v. 1 mg kg^{-1} tramadol verildi. Kör bir çalışmacı ağrı düzeyi, analjezik ihtiyacı, hasta memnuniyeti ve ilaçların yan etkilerini postoperative 1., 6., ve 24. saatlerde kaydetti.*

Bulgular: *Postoperatif 1. saatte VAS değerleri her iki grupta benzerdi, istatistiksel olarak anlamlı bir fark bulunamadı (p> 0,05). Grup II deki VAS skoru postop 6. ve 24. saatlerde grup I den anlamlı olarak daha düşük bulundu (p< 0,05). Çalışma süresince ciddi bir yan etki gözlenmedi. Grup II de en sık görülen yan etki ilk 24 saatte bulantıydı (%25). Kusma açısından her iki grupta anlamlı bir fark görülmedi (p> 0,05), buna rağmen Grup I de Grup II ye göre anlamlı olarak bulantı daha azdı. Kortizol seviyesi postoperative dönemde her iki grupta anlamlı olarak düşüktü.*

Sonuç: *Perioperatif intravenöz olarak verilen parasetamol'ün özellikle erken postoperatif dönemdeki hafif-orta şiddetli ağrıların tedavisi için, opioidlerle eşit derecede analjezi sağladığı görüldü.*

ANAHTAR KELİMELER: *Parasetamol; Tramadol; Postoperatif Ağrı*

INTRODUCTION

Effective postoperative pain management can reduce postoperative pain-related complications and be cost effective and decrease the duration of hospitalization by enabling early mobilization (1-2). Opioid and non-opioid analgesics are widely used in the treatment of postoperative pain.

Clinical usage of opioids is limited or used in low doses due to their potential side effects such as nausea, vomiting, urinary retention, sedation, and respiratory depression etc. However, non-opioid analgesics have been used for postoperative pain management with an increasing incidence. Paracetamol is frequently used effectively for therapy of postoperative pain (3). Its mechanism of action is not fully understood, but it is generally accepted that paracetamol is centrally acting drug.

Tramadol, a synthetic analog of codeine, binds to opioid receptors and inhibits norepinephrine and serotonin reuptake (4). It is an effective postoperative analgesic drug.

In this prospective randomized double-blind study; we compared analgesic efficacy, side effects and biochemical parameters of intravenous tramadol and paracetamol in septo-rhinoplasty operations.

METHODS

After approval of The Ethical Committee of Harran University Medical Faculty and written informed consent, 50 patients assessed as ASA I or II, aged between 18-50 and undergoing septo-rhinoplasty surgery was included in the study. Exclusion criteria were alcoholism, drug dependence, psychiatric disease, pregnancy, lactation, allergy, hepatic, renal or cardiovascular disease.

All patients received nasal 0.1 mg kg^{-1} midazolam 40 minutes before the operation as premedication. For reestablishment of the fluid balance, 5 ml kg^{-1} h^{-1} Ringer's solution was infused during surgery. All of the patients were monitored with D II derivation ECG, heart rates, transdermal O_2 Saturation (SpO_2), systolic, diastolic and mean arterial blood pressure, end-tidal CO_2 ($etCO_2$) and esophageal temperature (Datex-Engström AS/3 monitor, Helsinki, Finland). Hemodynamic and respiratory data were recorded per 5 minutes during operation and same parameters were recorded per 10 minutes in postoperative one hour period.

All of the patients were preoxygenated 4 L min^{-1} O_2 for 3 minutes and then for the induction of anesthesia 1 µg kg^{-1} remifentanil, 2 mg kg^{-1} propofol and 0.8 mg kg^{-1} rocuronium bromide were intravenously given. After the endotracheal intubation, anesthesia was maintained with 1-2% isoflurane, 3 L min^{-1} air, 2 L min^{-1} O_2 and 0.25 µg $kg^{-1}.min^{-1}$ remifentanil infusion. In both groups, mechanical ventilation is set for $etCO_2$ to be between 30-40 mmHg (mode IPPV, rate 12-15 min^{-1}, Tidal volume 10 ml kg^{-1}, I/E:1/2). At the end of anesthesia, the neuromuscular block was reversed with 0.5 mg atropine and 1.5 mg neostigmine i.v. when necessary. No local anesthetics were used during septo-rhinoplasty.

The patients were randomly divided into two groups for postoperative analgesia. In Group I paracetamol (Perfalgan® infusion, Bristol MS) 1 gr and Group II tramadol (Contramal® ampul, Abdi Ibrahim) were infused 30 minutes before the end of the operation.

Pain intensity, analgesic need, patient satisfaction and side effects of drugs were recorded for 24 hours postoperatively.

Postoperative pain intensity was assessed by a 10 cm visual analog scale (VAS), a 10 cm horizontal line with end points marked 'no pain at all' and 'worst pain imaginable'. Patient satisfaction and side effects of drugs

were evaluated as 0= none, 1= present. In the postoperative period, the patients who required additional analgesia were dosed with oral paracetamol 500 mg tablet where total dose did not pass beyond 3 g per day. Tramadol 0.5 mg kg^{-1} was given i.v. bolus additionally to the patients who still had pain after this rescue analgesic implementation.

Blood samples were obtained preoperative and at the end of the surgery (postoperative) in order to measure biochemical parameters (Cortisol, ACTH, and AST/ALT levels) of the groups. Blood samples were separated by centrifugation at 3000 rpm for 10 min to separate plasma. The plasma samples were stored at -80°C until analysis of total oxidant status (TOS). Plasma TOS levels were determined by using a novel automated measurement method, developed by Erel (5).

Student's t test and Pearson's correlation analyses were performed by using the Statistical Package for Social Sciences (SPSS 11.5, SPSS Inc, Chicago, IL) and $p \leq 0.05$ was considered statistically significant.

RESULTS

Demographic data concerning the patient's age, sex, weight, duration of surgery and anesthesia were similar in the study groups (Table I).

Table I. Patient characteristics

	Group I	Group II	p
Weight (kg)	77±13.5	74±9	p> 0.05
ASA physical class (I/II)	21/4	20/5	p> 0.05
Gender (M/F)	16/9	16/9	p> 0.05
Anesthesia time (min)	48 (15)	49 (13)	p> 0.05
Age (year)	31.5±11	31.8±10	p> 0.05

The VAS values are similar in both groups at postoperative 1h, no statistically significant difference was found (p> 0.05). VAS values for group II were significantly lower than group I at 6 h and 24 h postoperatively (p< 0.05) (Table II).

The postoperative 24 hours; rescue analgesic was given to 16/25 patients (64%) in group I and 11/25 patients (44%) in group II (Table III).

Table II. Postoperative VAS scores

	Group I	Group II	p
VAS 1. h	0.4±0.8	0±0	p> 0.05
VAS 6. h	1.9±1.0*	1.6±0.6*	p< 0.05
VAS 24. h	3.0±0.7 *	2.5±0.7*	p< 0.05

VAS: Visual Analog Scale

Table III. Postoperative tramadol requirements

	Group I	Group II	p
AN 1. h	0±0	0±0	p> 0.05
AN 6. h	17±21*	14±12*	p< 0.05
AN 24. h	44±20*	30±12*	p<0.05

AN: (additional analgesic need)

No serious side-effects were recorded during the study. The most frequent adverse effect was nausea (25%) at the first 24 h in group II. No significant difference was found between groups in terms of vomiting (p> 0.05), whereas the rate of nausea was significantly lower in group I than group II.

Cortisol levels decreased significantly in both groups at postoperative period. Other biochemical parameters (ALT/AST, TOS) showed no significant difference between pre- postoperative periods (Table IV-V).

Table IV. Biochemical parameters for Group I

Group I (n=25)	Preoperative	Postoperative	p
ALT (IU L^{-1})	25±11	26±8	0.66
AST (IU L^{-1})	24±10	23±9	0.37
ACTH (pg ml^{-1})	6.5±3.9	6.1±2.6	0.59
Cortisol (µg dl^{-1})	12.4±6.2	7.8±6.0*	0.001
TOS (µmol H_2O_2 L^{-1})	11.1±1.3	10.7±1.5	0.30

ALT: Alanine transaminase, AST: Aspartate transaminase, ACTH: Adrenocorticotropic hormone, TOS: Total oxidant status

Table V. Biochemical parameters for Group II

Group II (n=25)	Preoperative	Postoperative	p
ALT (IU L^{-1})	20±10	21±7	0.13
AST (IU L^{-1})	27±14	22±11	0.12
ACTH (pg ml^{-1})	6.1±2.1	6.7±3.3	0.32
Cortisol (µg dl^{-1})	8.3±4.3	6.1±4.1*	0.005
TOS (µmol H_2O_2 L^{-1})	10.7±1.4	10.6±1.5	0.52

ALT: Alanine transaminase, AST: Aspartate transaminase, ACTH: Adrenocorticotropic hormone, TOS: Total oxidant status

DISCUSSION

Effective postoperative pain management is a main concern for the anesthesiologist and surgeon (6). Because continuous postoperative pain may result in clinical and psychological changes that increase morbidity and decrease quality of life (7-8).

In this study, we compared the analgesic efficacy, side effects and biochemical parameters of the parenteral formulation paracetamol, to tramadol for pain relief after septo-rhinoplasty operations.

The results of this study showed that administration of paracetamol and tramadol for acute postoperative pain management resulted in a significant decrease in VAS

values 1h after septorhinoplasty similarly. According to this result, paracetamol provided equal analgesic level as tramadol at postoperative 1 hour.

The visual analog scale (VAS) has been used to evaluate the efficacy of pain management for acute postoperative pain, because of its defining the pain intensity, easy usefulness, currency and reliability. Generally, the VAS has been used to measure pain in the immediate postoperative period to compare the effect of different analgesic regimens like this study (8).

Septo-rhinoplasty is reasonable for mild–moderate postoperative pain; however, routine use of local anesthetic infiltration is not sufficient for the treatment of postoperative pain after septo-rhinoplasty, requiring additional systemic analgesic (9). Postoperative pain after nasal surgery is generally maximal in the first postoperative hours. Opioids, NSAIDs and paracetamol are commonly used analgesics for symptomatic relief. When oral administration is not possible or rapid analgesia is needed, which is often the case following surgery, i.v. administration is the route of choice. Therefore we preferred parenteral analgesic agents in this study (8,10).

Opioid analgesics are commonly used drugs for controlling postoperative pain. Even though they provide effective pain relief, this effect is associated with adverse effects like nausea, vomiting, pruritus, urinary retention and respiratory depression (11). Tramadol causes less respiratory depression, but commonly causes postoperative nausea and vomiting (PONV) (12). This study showed no significant differences in side effects such as nausea, vomiting, could be found between the groups, but less patients in the paracetamol group suffered from nausea than in the tramadol group.

It is well known that all surgical procedures are followed by pain, elicits local as well as systemic neuro-endocrine, immune, and metabolic responses. Optimal treatment of postoperative pain is mandatory in order to improve recovery period and reduce morbidity (13). In this study, in respect of stress response, we evaluated pre-postoperative Cortisol levels. Postoperative Cortisol level was observed significantly decreased compared to preoperative levels in both groups. These results indicate that in both groups a successful pain treatment has implemented.

Oxidative stress increases during painful stimulation. TOS may provide a useful tool to aid in the assessment of the oxidative status (14). TOS levels were showed no significant difference between pre-postoperative periods. These results indicate that paracetamol and tramadol were equally effective in preventing pain stress response to surgery by providing dynamic analgesia.

Serum AST/ALT levels were similar in all groups at all times. In sensitive persons, large doses of paracetamol may possibly disturb the hepatocellular integrity. We do not suggest the use of i.v. doses of paracetamol higher than 1 g.

CONCLUSION

Intraoperative i.v. paracetamol administration provided adequate postoperative analgesia in patients undergoing septorhinoplasty. Based on these findings, intraoperative i.v. paracetamol appears to be a reasonable choice for postoperative analgesia in this patient population.

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