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The Effect of Paracetamol on Postoperative Nausea and Vomiting in Patients Undergoing Maxillofacial Surgery Under General Anesthesia

Genel Anestezi Altında Maksillofasiyal Cerrahi Geçiren Hastalardaki Postoperatif Bulantı ve Kusma Üzerine Parasetamolün Etkisi

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Abstract

Objective: The management of postoperative nausea and vomiting (PONV), a frequent issue, has included various medications. Maxillofacial surgeries are in the high-risk surgical group for PONV. This study evaluated the efficacy of paracetamol on PONV in adults undergoing maxillofacial surgery.

Materials and Methods: All patient files who underwent elective-maxillofacial-surgery under standard general anesthesia procedures between January 2016 and September 2021 were reviewed. The patients who received paracetamol infusion (i.v. paracetamol 1.5 mL/kg) as an additional analgesics in the recovery room were defined as the paracetamol group; patients who did not use additional analgesics were defined as the control group. The postoperative 0-4 and 4-24 h were defined as the early and late postoperative period, respectively. All episodes of PONV occurring within 24 h after general anesthesia were recorded in the patient files. Antiemetic drug use, postoperative pain and analgesic needs in the early and late postoperative periods were recorded in the first 24 h after surgery.

Results: The incidence of PONV during 0-4 h postoperatively was significantly higher in the control group compared with the paracetamol group (p=0.034 for nausea; p=0.030 for vomiting). The need for rescue antiemetic drug during 0-4 h postoperatively was significantly higher in the control group compared with the paracetamol group (p=0.013). There were no differences among the groups in terms of pain levels during the 24 h postoperatively.

Conclusion: Early period after maxillofacial surgery, the incidence of PONV is decreased by the use of intravenously paracetamol. Paracetamol may help prevent PONV.

Öz

Amaç: Sık görülen bir sorun olan postoperatif bulantı kusmanın (PONV) önlenmesinde hem yüksek etkili hem de yan etkisi düşük ilaçlar tercih edilmektedir. Maksillofasiyal cerrahiler PONV açısından yüksek riskli cerrahi grubundadır. Bu retrospektif çalışmayla, maksillofasiyal cerrahi geçiren erişkinlerde parasetamolün PONV üzerindeki etkinliğini değerlendirebilmek amaçlandı.

Gereç ve Yöntemler: Ocak 2016-Eylül 2021 tarihleri arasında standart genel anestezi altında elektif maksillofasiyal cerrahi uygulanan tüm hasta dosyaları incelendi. Derlenme odasında ek analjezik olarak parasetamol infüzyonu (i.v. parasetamol 1,5 mL/kg) alan hastalar parasetamol grubunu oluştururken, herhangi bir ek analjezik kullanmayan hastalar kontrol grubu olarak tanımlandı. Ameliyat sonrası 0-4 saat ve 4-24 saat sırasıyla erken ve geç postoperatif dönem olarak

belirlendi. Genel anestezi sonrası 24 saat içinde ortaya çıkan tüm bulantı kusma atakları hasta dosyalarından bakılarak kaydedildi. Ayrıca ameliyat sonrası ilk 24 saatte antiemetik ilaç kullanımı, postoperatif ağrı ve postoperatif erken ve geç dönemdeki analjezik ihtiyaçları kaydedildi.

Bulgular: Erken postoperatif dönem (0-4 saat) PONV insidansı, parasetamol grubu ile karşılaştırıldığında kontrol grubunda anlamlı olarak daha yüksekti (bulantı için p=0,034; kusma için p=0,030). Yine 0-4 saat arasındaki kurtarıcı antiemetik ilaç ihtiyacı kontrol grubunda parasetamol grubuna göre daha yüksek bulundu (p=0,013). Postoperatif 24 saat boyunca ağrı düzeyleri açısından gruplar arasında fark yoktu.

Sonuç: IV parasetamol kullanımı, maksillofasiyal cerrahi sonrası erken postoperatif dönemde PONV insidansını azaltır. Parasetamol PONV'yi önlemede yardımcı olabilir.

Introduction

General anesthesia patients frequently have postoperative nausea and vomiting (PONV) (1). The length of the patient's hospital stay is increased by PONV, which also causes oral intake to be delayed. It is also the leading cause for unanticipated hospital admissions (2). It may cause patient discomfort, electrolyte abnormalities due to dehydration, aspiration pneumonia, and intracranial pressure elevation (3). As a result, efforts have been made to use medications with an antiemetic effect to lower the frequency of PONV in patients following surgery (4).

Since more than a century ago, paracetamol has been used extensively as an efficient painkiller and as an antipyretic. In contrast to other analgesics, it has a favorable safety profile and well-established efficacy and tolerance (5). Single or repeated intravenous paracetamol doses generally provided efficient postoperative analgesia following a variety of surgical procedures in several large, well-designed trials including adult patients (6). Although paracetamol promotes descending serotonergic inhibitory pathways and inhibits the cyclooxygenase enzyme, the precise mechanism behind its analgesic actions is yet understood (5,6). According to certain research (7), paracetamol may also reduce the risk of PONV by affecting a few serotonergic pathways in the central nervous system.

We thought that intraoperative intravenously (IV) paracetamol, which is used as a pain reliever in adults in maxillofacial surgeries, may be useful in the prevention of PONV. Therefore, we aimed to retrospectively evaluate the risk of PONV in adult patients who underwent maxillofacial surgery with paracetamol used during the recovery period compared to those who did not use paracetamol.

Materials and Methods

This retrospective clinical study was approved by the Aydın Adnan Menderes University Institute of Health Sciences Clinical Research Ethics Committee (protocol no: 2021/038, date: 27.10.2021). In accordance with the Declaration of Helsinki, American Society of Anesthesiologists classification (ASA) physical status I-II eighty patients between the ages of 18-50, who underwent elective maxillofacial surgery (orthognathic surgery with maxillary and/or mandibular osteotomies) under general anesthesia between January 2016 and September 2021 were included in the study.

Patients with a history of opioid use, liver or kidney disease, coronary, psychotic and neurological diseases, those with a history of antiemetic, antihistamine, analgesic or corticosteroid use in the last 24 hours (h) before surgery, those who did not receive standard general anesthesia, those who were administered antiemetics at the end of surgery, those who received opioids in the postoperative period and those with missing information in their files was excluded.

A standard general anesthesia procedure was applied to all patients included in the study. As a standard general anesthesia procedure; after performing routine monitoring in the operating room, such as pulse oximetry, non-invasive arterial pressure monitoring, and electrocardiography, anesthesia was induced using propofol 2 mg/kg, remifentanil 1 g/kg, and rocuronium bromide 0.6 mg/kg. A nasotracheal tube was used to intubate all of the patients. 1.5-2% sevoflurane, 50% oxygen in the air, and an infusion of remifentanyl at 0.5-1 g/kg/min were used to maintain anesthesia. All patients received tenoxicam 0.3 mg/kg at the conclusion of surgery for analgesic and anti-inflammatory effects. The patients were extubated after the procedure, taken to the post-anesthesia care unit (PACU), and then released to the ward after being

under monitoring there. At the end of the follow-up in PACU, 50 mg IV dexketoprofen trometamol was used as rescue analgesia for postoperative pain control at visual analogue scale (VAS) 3 and above.

All patient files were reviewed. Patients who received paracetamol infusion as an additional analgesic in the recovery room were in the paracetamol group (i.v. paracetamol 1.5 mL/kg); Patients who did not use additional analgesics were divided into two groups as the control group.

Age, gender, weight, ASA, duration of anesthesia, recovery time data related to the patient and the surgical procedure were recorded from the patient files.

The primary goal of this study was to assess the effect of paracetamol on the incidence of nausea and vomiting in the first 24 h after surgery, while also investigating postoperative pain during the first 24 h. Early and late postoperative periods were defined as 0-4 h and 4-24 h, respectively. PONV was identified when there was a recording of vomiting or when actions suggestive of nausea, such as repeated gagging or spitting, were observed within 24 h of general anaesthesia. All episodes of nausea and vomiting occurring within 24 h of anesthesia were noted from the patient files. Antiemetic drug use in the early and late postoperative period was recorded in the first 24 h after surgery. In the event of two or more vomiting episodes, metoclopramide (0.2 mg/kg) was injected IV as a rescue antiemetic.

During the first 24 h after surgery, postoperative pain at rest was assessed using a standard 10 cm VAS (0 cm = no pain, 10 cm = worst pain imaginable). Hourly VAS values in patient files were recorded by taking the mean of the early and late postoperative period. The presence of analgesic need was recorded.

Statistical Analysis

The incidence of nausea and vomiting within the first 24 h postoperatively was the study's main finding. The IBM-SPSS Statistics program was used to conduct the statistical analyses. A 0.05 p-value was regarded as statistically significant. Depending on the parameter distribution, either parametric or non-parametric tests were used to assess the values of the two groups. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine whether the data were normal. For quantitative variables, the results are presented as mean standard deviation, and for categorical variables, as absolute frequency and %. Quantitative variables were compared using the independent sample t-test, while categorical variables were compared using the chi-square test or Fisher's Exact test.

Results

A total of 80 patients were analyzed (paracetamol group, n=40; control group, n=40) (Figure 1). The patients' characteristics including gender, age, weight, duration of anaesthesia and ASA status were similar in both groups (Table 1).

The total incidence of nausea and vomiting in all patients in the first 4 h after surgery was 35% and 20% respectively, and the total incidence of nausea and vomiting in postoperative 4-24 h was 21.3% and 6.3%, respectively.

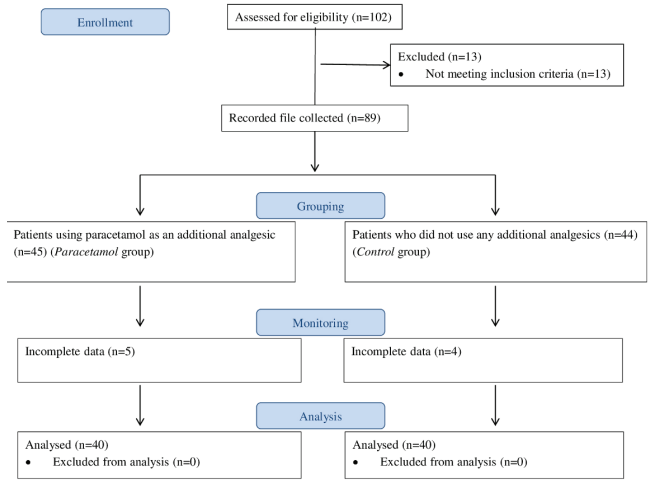

Figure 1. CONSORT flow diagram. The course of patients through this study was shown
CONSORT: Consolidated Standards of Reporting Trials

Table 1. General and clinical data of the patients

	Paracetamol group (n=40)	Control group (n=40)	p-value
Age (years)	32.62±10.66	36.85±11.43	0.091
Weight (kg)	70.97±12.06	69.72±10.34	0.620
Sex (M/F)	19/21	24/16	0.370
ASA (I/II)	27/13	22/18	0.359
Duration of anaesthesia (min)	195.87±84.00	185.12±75.23	0.548

Data are mean ± SD and numbers; F: Female, M: Male, p<0.05. ASA: American Society of Anesthesiologists classification, SD: Standard deviation

PONV was significantly more common in the control group than in the paracetamol group during the first 4 h postoperatively (p=0.034 for nausea; p=0.030 for vomiting). The frequency of nausea and vomiting was lower in the paracetamol group than in the control group during the first 4 h postoperatively (p=0.034 for nausea frequency; p=0.030 for vomiting frequency) (Table 2). The need for rescue antiemetic medication was significantly higher in the control group compared to the paracetamol group (p=0.013) (Table 3).

There are no differences in pain levels between groups during the first 24 h after surgery (Table 4). No patient in either group experienced a delay in receiving their hospital release, and no patient was ever readmitted because of PONV.

Discussion

In this retrospective study, the efficacy of IV paracetamol administrations for the prevention of PONV was investigated in patients undergoing maxillofacial surgery. Our study is the first to evaluate the effect of IV paracetamol on PONV in patients undergoing maxillofacial surgery. This study was demonstrated that IV paracetamol was effective in preventing PONV in the early postoperative period (0-4 h).

The reported incidence of PONV is generally reported to be around 20% to 30% for all surgical types. However, in high-risk surgeries for PONV, the incidence of PONV is reported to be up to 80% (8-11). Maxillofacial surgeries are among the predisposing surgeries to PONV. Oropharynx iritation, blood in the stomach, a changed diet, and hypotension throughout the recovery phase can all be used to explain this (8,11,12). However, only a small number of studies (8,12,13) have shown a greater prevalence of PONV following oral and maxillofacial surgery. The most frequent reason for postoperative complications in oral and maxillofacial operations, according to Perrott

Table 2. Postoperative nausea and vomiting during 24-h postoperatively

		Paracetamol group (n=40)	Control group (n=40)	p-value
0-4 h	Number of patients with nausea	9 (22.5)	19 (47.5)	0.034*
	Frequency of nausea	0.37±0.74	0.95±1.25	0.015*
	Number of patients with vomiting	5 (12.5)	11 (27.5)	0.030*
	Frequency of vomiting	0.17±0.54	0.52±0.87	0.036*
4-24 h	Number of patients with nausea	7 (17.5)	10 (25.0)	0.586
	Frequency of nausea	0.22±0.53	0.40±0.81	0.257
	Number of patients with vomiting	3 (7.5)	2 (5.0)	0.644
	Frequency of vomiting	0.07±0.26	0.07±0.34	0.952

Data are numbers (percentages); *p<0.05

Table 3. The need for rescue antiemetics during 24-h postoperatively

	Paracetamol group (n=40)		Control group (n=40)	p-value
Need for rescue antiemetics	0-4 h (+/-)	2 (5.0)	11 (27.5)	0.013*
	4-24 h (+/-)	3 (0)	4 (2.2)	0.692

Data are numbers (percentages); *p<0.05

Table 4. Postoperative pain during 24-h postoperatively

		Paracetamol group (n=40)	Control group (n=40)	p-value
Postoperative pain (VAS) score	0-4 h	2.47 (±1.75)	2.30 (±1.57)	0.640
	4-24 h	1.12 (±1.41)	1.27 (±1.43)	0.639
Need for rescue analgesics	0-4 h	17 (42.5)	17 (42.5)	1.000
	4-24 h	14 (35)	18 (45)	0.494

Data are mean ± SD; VAS: Visual analog scale, SD: Standard deviation, *p<0.05

et al., (12) was PONV. Dobbeleir et al. (8) found a PONV incidence as high as 46.1% after maxillofacial surgery in postoperative 3-day follow-up. Apipan et al. (11) reported that the overall incidence of PONV was 25.3% in patients of all ages who had undergone oral and maxillofacial surgery. Similarly, Alexander et al. (14) reported a PONV incidence of 11.3% in patients who have undergone maxillofacial surgery in all age groups during the postoperative 6 h, while Silva et al. (13) recounted a 40.08% incidence of PONV in patients over 14 years of age during the first 24 h postoperatively. We found the incidence of nausea and vomiting in all patients in the first 4 h postoperatively to be 35% and 20%, respectively, while the incidence of nausea and vomiting in postoperative 4-24 h was 21.3% and 6.3%, respectively. This high variability of PONV incidence may be due to differences in age and follow-up time.

It is generally known that paracetamol is a secure analgesic. It has been observed that paracetamol administered IV is efficient and secure for postoperative analgesia. Recently, paracetamol has been mentioned in its antiemetic activity as well as its analgesic effect (15). Many studies in head and neck surgeries such as thyroidectomy and tonsillectomy have reported preventive effects of paracetamol on nausea and vomiting (7,16). However, some studies have reported that paracetamol does not contribute to the prevention of PONV (17-19). It can be due to variations in treatment timing. Only when given prophylactically, either before surgery or while it is being performed, has intravenous acetaminophen been demonstrated to be beneficial for treating both nausea and vomiting. Studies have demonstrated that paracetamol inhibits the cyclooxygenase enzyme and affects various serotonergic pathways in the central nervous system, despite the fact that the analgesic activities of paracetamol have unknown mechanisms (7). According to Cok et al., (7) intraoperative IV paracetamol treatment reduces the likelihood of PONV in children for the first 24 h following strabismus surgery. The brainstem vomiting center contains serotonin. Anandamide reuptake is inhibited by AM404, a byproduct of paracetamol metabolism in the brain (20). In humans, it was discovered that decreased anandamide levels were linked to a high prevalence of nausea and vomiting (21). This may be yet additional explanation for paracetamol's antiemetic properties. Although paracetamol has not yet been shown to bind to receptors, recent research suggests that it indirectly modifies the serotonergic system (22). Paracetamol may interfere with the serotonergic system through the EP3 receptor, a crucial prostaglandin E2 receptor found in the majority of serotonergic cells in the medulla oblongata (23). Another putative mechanism of action is an increase in cannabinoid tone, which may assist in lowering vomiting brought on by the chemoreceptor trigger zone (22).

High dose antiemetics may cause minor side effects such as restlessness, dizziness, drowsiness, headache, constipation and diarrhoea. The therapeutic use of antiemetics in the prevention of PONV is, however, constrained by concern over extrapyramidal side effects. As an example, tardive dyskinesia and dystonic responses are uncommon side effects that are typically observed in individuals who are taking high doses of antiemetics (24). Analgesics are routinely used in all surgical procedures for postoperative patient comfort. When paracetamol was thought to demonstrate both analgesic and antiemetic activity, the use of paracetamol is of great importance, especially for surgical procedures with PONV risk, in avoiding side effects of antiemetic drugs, unnecessary drug use and cost effectiveness.

Previous research has shown that using intraoperative paracetamol reduces postoperative pain in a variety of surgeries (15,25). Some studies have also found that IV paracetamol administration after surgery has an antiemetic effect (7,15,25). This is the first study to look at the effect of IV paracetamol on PONV in patients undergoing maxillofacial surgery.

The antiemetic effect of non-steroidal anti-inflammatory drugs is widely thought to result from a dose-dependent reduction in opioid intake. However, Apfel et al. (15) associated the decrease in PONV with the reduction in pain intensity, regardless of the decrease in opioid consumption and showed that pain itself is a risk factor for PONV. We included patients who followed an opioid-free protocol for postoperative pain control. Thus, we were able to clearly evaluate the effectiveness of paracetamol by excluding the negative effect of opioid on PONV.

The pathophysiology of nausea and vomiting is extremely complicated and involves numerous central nervous system regions. Vomiting is a

brainstem reaction, whereas nausea is controlled in the cortex (9,10). According to several studies, postoperative analgesia that is effective may stop the stimulus for PONV from starting, and sufficient pain treatment eliminates 80% of these symptoms (7). Postoperative pain is a risk factor for PONV (15). However, according to our findings, while there was no difference between the groups in terms of pain in the early postoperative period, a significant difference was found in terms of PONV. Therefore, we think that the decrease in PONV incidence in the first 0-4 h after surgery in the paracetamol group may be due to the specific antiemetic effect of paracetamol rather than it's pain reduction.

We conducted a retrospective analysis on a modest sample size. Larger sample sizes are required for prospective studies to assess paracetamol's impact on the prevalence of PONV.

Conclusion

PONV is reduced in the early postoperative period after maxillofacial surgery under general anaesthesia when IV paracetamol is used. Furthermore, paracetamol significantly reduced the need for rescue antiemetic drugs. Paracetamol, a safe and effective analgesic, may be helpful in preventing PONV as well as postoperative pain. More research is needed to demonstrate the effectiveness of paracetamol in reducing the incidence of PONV in patients undergoing maxillofacial surgery.

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Ethics

Ethics Committee Approval: This retrospective clinical study was approved by the Aydın Adnan Menderes University Institute of Health Sciences Clinical Research Ethics Committee (protocol no: 2021/038, date: 27.10.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

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