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The effects of dexamethasone vs low doses of propofol infusion on postoperative nausea and vomiting in tympanoplasty surgery: A randomized, placebo-controlled, double-blinded study

Timpanoplasti cerrahisinde postoperatif bulantı ve kusmaya deksametazon ile düşük doz propofol infüzyonunun etkilerinin karşılaştırılması: Randomize, plasebo-kontrollü, çift kör çalışma

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ABSTRACT

This prospective study investigated the effects of dexamethasone and low-dose propofol infusion on postoperative nausea and vomiting in 90 patients undergoing tympanoplasty. The dexamethasone group (Group D) received 8 mg dexamethasone and the control group (Group C) 2 ml saline 15 min before the end of surgery, while the propofol group (Group P) received ıntravenous propofol infusion at a dose of 20 mcg/kg/min throughout surgery following induction of anaesthesia. Incidence rates and severity of nausea-vomiting and antiemetic requirements were recorded throughout the first postoperative 24 hours. Between hours 0 and 2, any incidence of postoperative nausea and vomiting was not observed in 23 (76.7%) patients in Group P, 17 (56.7%) in Group D and 8 (26.7%) in Group C. Differences were observed between the groups in hours 0-2 and 2-8 in terms of verbal descriptive scale values for postoperative nausea and vomiting (p<0.01 and p=0.004, respectively). Total incidence rates of postoperative nausea and vomiting at hours 2-8 h were 10.0% (n=3) in Group P, 36.7% (n=11) in Group D and 53.3% (n=16) in Group C, the difference being statistically significant in favour of Group P (p=0.032). At 0-24. hrs, the number of patients vomiting, despite treatment, were lower in Groups P and D (n=4, 13.3% and n=5, 16.7%, respectively) compared to Group C (n=14, 46.7%) (p=0.005). Antiemetic use was higher in Group C than in Groups D and P (p=0.001). Intraoperative low-dose propofol infusion is as effective as dexamethasone in reducing the incidence and severity of postoperative nausea and vomiting, as well as reducing post-tympanoplasty antiemetic requirements.

Keywords: *Postoperative nausea and vomiting, tympanoplasty, dexamethasone, propofol*

ÖZ

Bu prospektif çalışmayla, timpanoplasti uygulanan 90 hastada postoperatif bulantı ve kusma üzerine deksametazon ve düşük doz propofol infüzyonunun etkileri araştırıldı. Ameliyat bitiminden 15 dk. önce deksametazon grubuna (Grup D) 8 mg deksametazon ve kontrol grubuna (Grup C) 2 ml salin yapılırken, propofol grubuna (Grup P), anestezi indüksiyonu sonrasında ameliyat boyunca 20 mcg/kg/dk. propofol intravenöz infüzyonu yapılmıştır. Postoperatif ilk 24 saat boyunca bulantı-kusma ve antiemetik gereksinimlerinin insidans ve şiddeti kaydedildi. Sıfır-iki saatlik periyotta, Grup P'de 23 (%76,7) hastada, Grup D'de 17 (%56,7) ve Grup C'de 8 hastada (%26,7) postoperatif bulantı ve kusma görülmedi. Gruplar arasında postoperatif bulantı ve kusma için sözel tanımlayıcı ölçek değerleri açısından 0-2 ve 2-8 saatlik süreler arasında farklar gözlemlendi (sırasıyla p<0,01 ve p=0,004). 2-8 saatlik postoperatif bulantı ve kusma sıklığı Grup P'de %10,0 (n=3), Grup D'de %36,7 (n=11) ve Grup C'de %53,3 (n=16) idi, bu fark Grup P lehine istatistiksel olarak anlamlıydı (p=0,032). Sıfır-yirmi dört saatte tedaviye rağmen, kusma sayısı grup C'ye kıyasla Grup P ve Grup D'de (sırasıyla n=4, %13,3 ve n=5, %16,7) daha düşüktü (n=14, %46,7) (P=0,005). Antiemetik kullanımı, Grup C'de Grup D ve P'ye göre daha yüksekti (p=0,001). İntraoperatif düşük doz propofol infüzyonu, postoperatif bulantı ve kusma sıklığını ve şiddetini azaltmada aynı zamanda timpanoplastiden sonra bir antiemetik kullanım gereksinimini azaltmada deksametazon kadar etkilidir.

Anahtar kelimeler: *Postoperatif bulantı ve kusma, timpanoplasti, deksametazon, propofol*

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INTRODUCTION

Nausea is an uncomfortable sensation that may occur alone or in association with vomiting in the postoperative period[1,2]. Postoperative nausea and vomiting (PONV), the most common anaesthesia and surgical procedure-related complication, generally occurs within the first 24 h after surgery and has an adverse impact on patient satisfaction and the healing process. While there has been a general decrease in the incidence and severity of PONV for reasons such as the use of anaesthetic agents with low emetic properties, advances in operative techniques and precautionary measures based on identification of risk group patients in advance, it still remains as a problem[3]. Inner ear surgery is one of the factors that increase the incidence of PONV[4]. Tympanoplasty is associated with a high incidence of PONV, which occurs in up to 80% of such operations[5]. This complication also poses a significant threat to surgical restructuring and anatomical adjustments, particularly after tympanoplasty[6-8]. Various drugs and types of general anaesthesia (including balanced and total intravenous anaesthesia) have been tested in order to prevent this complication following tympanoplasty[6-9]. The intraoperative use of dexamethasone and low-dose propofol infusion has been reported to be effective against PONV in the postoperative period in several studies[6,9-11]. Propofol, an anaesthetic agent particularly effective in preventing PONV, is used by many anaesthetists[10,12]. This study compared the antiemetic efficacies of dexamethasone and low-dose propofol infusion administered during the intraoperative period in preventing potential nausea and vomiting in the postoperative period following elective tympanoplasty performed under general anaesthesia.

MATERIALS and METHODS

This study was conducted as a prospective, randomized double-blinded trial following receipt of approval from the local ethical committee (Decision no. KAEK 2015/7-47). Ninety ASA (American Society of Anaesthesiologists) class I-II patients aged between 18 and 47 years who underwent tympanoplasty under general anaesthesia between 15 April 2015 and 30 March 2016 were enrolled in the study Patients were informed concerning PONV and signed informed consent forms were obtained from all subjects. Patients were randomly assigned to one of three groups using computer-generated random numbers: dexamethasone group (Group D, n=30), propofol group (Group P, n=30), and a control group (Group C, n=30). Exclusion criteria included pregnancy, use of any opioid, steroid or antiemetic drug 24 hours before tympanoplasty, history of nausea and vomiting during previous operations, emergency surgery and uncontrolled diabetes mellitus, susceptibility to nausea and vomiting (motion sickness etc.), menstruation at the time of surgery. Patients with bleeding exceeding 50 ml and with unstable hemodynamic status during the intraoperative period, and those who refused antiemetic prophylaxis were also excluded from the study. Power analysis results indicated by Celik et al. before the start of the study assumed overall incidence rates of PONV as 70% and 35% in the placebo and treatment groups, respectively. Based on an alpha error of 0.05 and a beta error of 0.2, group sizes of approximately 30 patients were determined to be adequate. Patients were taken to the operating room with no premedication. Venous access was opened in the left forearm with an 18 G branula. Noninvasive monitoring was established for systolic, and diastolic blood pressures, heart rates, capnometry and pulse oximetry measurements which was maintained throughout surgery. Intravenous (iv) fluid loading was provided with 5 ml/kg/h Ringer lactate solution throughout surgery. Following preoxygenation with mask (5 L/min), anaesthesia was induced in all patients with iv thiopental sodium 5 mg/kg, rocuronium 0.6 mg/kg, and fentanyl 1 mcg/kg. Following manual ventilation with 100% oxygen for 2 min, the trachea was intubated, and the patients were attached to an anaesthesia device providing mechanical ventilation. Maintenance anaesthesia was established with 5% desflurane in 40% oxygen with air. When intraoperative blood pressure and/or heart rate increased by 20% or more, 0.5 mcg/kg fentanyl was administered iv as an additional analgesic, and 10 mg rocuronium was given at half-hourly intervals. In Group D, 8 mg

dexamethasone (8 mg/2 ml) was administered iv 15 min before the end of surgery. In Group P, propofol (2% propofol, 1 g/50 ml ampoule) at an IV infusion dose of 20 mcg/kg/min was provided immediately after anaesthesia induction and intubation and throughout surgery. This was stopped together with anaesthetic gases at the end of surgery. In Group C, isotonic saline solution in a 2 mL syringe was administered 15 min before the end of surgery. Finally, neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and atropine sulphate (0.01 mg/kg) at the end of surgery. Once patients had awaken, they were monitored for the first 2 h in the post-anaesthesia care unit (PACU). All patients were monitored for the first 24 h postoperatively in terms of nausea, vomiting and antiemetic requirements by an otolaryngologist blinded to the anaesthetic technique employed, and antiemetics administered were recorded. Nausea and vomiting were assessed in three different periods after recovery from anaesthesia (0-2 h, 2-8 h and 8-24 h) using a verbal descriptive scale (VDS). Patients with VDS scores of 2, 3 or 4 received metoclopramide HCl 10 mg iv. VDS scores were recorded as follows; no nausea: 0, mild nausea: 1 (once in 15 min), moderate nausea: 2 (2 or 3 times in 15 min), severe nausea: 3 (4 or more times in 15 min), and vomiting despite treatment (TDS): 4. Paracetamol was used iv as an analgesic during the postoperative period. Statistical analyses were performed on SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). Data were expressed as mean±standard deviation for continuous variables and percentage (number) for nominal data. One-way ANOVA analysis of variance or Post Hoc tests with Bonferroni correction were used to evaluate differences between the three groups for continuous variables. The chi-square test was used to evaluate differences between the three groups for categorical variables. p values less than 0.05 were considered statistically significant.

RESULTS

Surgical procedures were completed in all 90 cases. No statistically significant difference was determined between the groups in terms of such parameters as age, sex, height, weight, body mass index (BMI), operative time, duration of anaesthesia, intraoperative fentanyl consumption, smoking status or ASA status (Table 1). No PONV was observed in 23 patients (76.7%) in Group P, 17 (56.7%) in Group D and 8 (26.7%) in Group C within the first 2 h postoperatively. Statistically significant variation was observed between the groups in terms of VDS values for PONV at 0-2 h and 2-8 h, postoperatively ($p<0.01$, $p=0.004$, respectively). However, there was no significant difference between the groups within the 8-24 h period ($p=0.168$). Total incidence of PONV at 2-8 h was 10.0% (n=3) in Group P, 36.7% (n=11) in Group D and 53.3% (n=16) in Group C, the difference being significant in favour of Group P ($p=0.032$). The number of patients vomiting despite treatment between 0-24 hs were significantly lower in Groups P and D

Table 1. Groups demographic and operative characteristics.

	Group P (n=30)	Group D (n=30)	Group C (n=30)	P values
Age (years)	28.47±7.95	28.43±7.93	28.53±6.99	0.999**
Sex/female n (%)	13 (43.3)	14 (46.7)	12 (40.0)	0.873*
Height (cm)	168.77±8.20	169.03±7.92	170.90±8.41	0.548**
Weight (kg)	67.23±7.43	66.33±7.56	66.37±7.12	0.866**
BMI	23.66±2.59	23.21±2.09	22.75±2.10	0.304**
ASA I/II	30/0	30/0	30/0	1.000
Anaesthesia time (min)	81.50±9.35	82.50±8.57	81.17±7.06	0.814**
Op. time (min)	71.83±9.14	72.33±8.35	70.80±7.77	0.774**
Fentanyl consumption	167.23±7.43	166.33±7.12	166.37±7.12	0.866**
Smoking n (%)	8 (26.7)	8 (26.7)	9 (27.8)	0.946*

*Group P: Propofol group, Group D: Dexamethasone group, Group C: Control group. ASA: American Society of Anesthesiologists, BMI: Body Mass Index, Op. time: Operation time. Mean±SD: mean±standard deviation. Values are expressed as means±SD except for BMI, age, fentanyl consumption, Anaesthesia and Op.time, Weight and Height data. *The chi-square test. **One-way ANOVA*

Table 2. Comparison of the groups in terms of incidence of postoperative nausea-vomiting and antiemetic consumption.

VDS n (%)	Group P (n=30)	Group D (n=30)	Group C (n=30)	P values
0-2. h: None	23 (76.7)	17 (56.7)	8 (26.7)	
Mild	3 (10.0)	4 (13.3)	4 (13.3)	
Moderate	0 (0.0)	3 (10.0)	3 (10.0)	<0.01**
Severe	2 (6.7)	2 (6.7)	6 (20.0)	
TDS	2 (6.7)	4 (13.3)	9 (30.0)	0.115*
Total PONV	7 (23.3)	13 (43.3)	22 (73.3)	0.063*
2-8. h: None	27 (90.0)	19 (63.3)	14 (46.7)	
Mild	1 (3.3)	7 (23.3)	7 (23.3)	
Moderate	0 (0.0)	3 (10.0)	4 (13.3)	0.004**
Severe	0 (0.0)	0 (0.0)	2 (6.7)	
TDS	2 (6.7)	1 (3.3)	3 (10.0)	0.625*
Total PONV	3 (10.0)	11 (36.7)	16 (53.3)	0.032*
8-24.h: None	28 (93.3)	23 (76.7)	21 (70.0)	
Mild	2 (6.7)	6 (20.0)	5 (16.7)	
Moderate	0 (0.0)	0 (0.0)	2 (6.7)	0.168**
Severe	0 (0.0)	1 (3.3)	0 (0.0)	
TDS	0 (0.0)	0 (0.0)	2 (6.7)	0.147*
Total PONV	2 (6.7)	7 (23.3)	9 (30.0)	0.150*
Total vomiting (0-24h)	4 (13.3)	5 (16.7)	14 (46.7)	0.005*
Antiemetic use	2 (6.7)	9 (30.0)	15 (50.0)	0.001*

*Group P: Propofol group, Group D: Dexamethasone group, Group C: Control group. VDS: Verbal Descriptive Scale, PONV: Postoperative nausea and vomiting. TDS: Vomiting despite treatment. * The chi-square test. **Post Hoc tests with Bonferroni.*

(n=4, 13.3% and n=5, 16.7%, respectively) compared to Group C (n=14, 46.7%) (p=0.005). Antiemetic consumption was higher in Groups C and D than in Group P (p=0.001) (Table 2).

DISCUSSION

Vomiting following surgical procedures is distressing for patients[8]. Several strategies have been described for preventing PONV following middle ear surgery. Two of these involve the use of dexamethasone and propofol[5,13-15]. In this double-blinded, placebo-controlled study, we compared the effects of dexamethasone and intraoperative low-dose propofol infusion, which have not been investigated previously in the literature on the prevention of PONV after tympanoplasty. Other risk factors raising the incidence of PONV in addition to otolaryngology surgery include female gender, non-smoking status, laparoscopy, laparotomy, eye, head, and neck surgery, gynaecological, urological and intra-abdominal procedures, operative time, history of motion sickness and/or PONV, and inhalation anaesthetics and opioids use[2,16,17]. Several publications have reported a high level of association between PONV and tympanoplasty among ENT surgical procedures[7]. Fujii et al.[14] reported incidence rates of PONV following middle ear surgery as 60% in the first 0-3 h and 53% at 3-24 h. In another publication they reported an incidence of PONV of 70% in a placebo group following mastoidectomy. The incidence of PONV after tympanoplasty was 73.3% in the present study. This is comparable with previous studies. Numerous drugs have been tested for the purpose of preventing this high incidence of PONV following middle ear surgery, including traditional (scopolamine, promethazine, droperidol, metoclopramide etc.), and non-traditional antiemetics (glucocorticoids-dexamethasone, propofol, midazolam etc.), antiserotonins (ondansetron, granisetron and ramosetron). However, no traditional antiemetics have been shown to be completely effective in preventing PONV, and non-traditional antiemetics have been reported to be more effective[6,18]. Although the mechanism of action of glucocorticoids has not yet been fully explained, they exhibit analgesic, anti-inflammatory, immune-modulating and antiemetic effects[19]. Dexamethasone is a glucocorticoid used as an antiemetic drug in patients receiving

chemotherapy and against PONV[10,11,20]. Çelik et al.[10] administered 8 mg IV dexamethasone immediately prior to induction of anaesthesia in order to prevent PONV in patients undergoing laparoscopic cholecystectomy. The incidence of PONV within the first 0-24 h postoperatively was 72.5% in the control group compared to 37.5% in the dexamethasone group. The authors concluded that this was as effective as low-dose propofol infusion. Another study used 8 mg dexamethasone toward the end of tympanoplasty. A significant decrease in the incidence of dizziness and nausea was observed compared to the placebo group within the first 24 h postoperatively[13]. Makhdoom et al.[14] administered 8 mg dexamethasone immediately before induction of anaesthesia in middle ear surgery and reported an incidence of PONV as 35%, compared to 70% in the control group. In our study, we administered 8 mg dexamethasone 15 min before the end of surgery and achieved a 59.1% decrease in PONV compared to the placebo group. Another non-traditional antiemetic drug used to prevent PONV in several studies is propofol. Çelik et al.[10] investigated the effect of PONV of propofol infusion at a low dose (1 mg/kg/h) throughout laparoscopic cholecystectomy. They reported an incidence of PONV as 72.5% in the placebo group within the first 0-24 h postoperatively, compared to 40% in the propofol group. Dexamethasone combined with intraoperative IV propofol infusion at a rate of 20 µg/kg/min was administered in tonsillectomy surgery in one study. The authors concluded that combination provided greater effectiveness against PONV compared to dexamethasone alone[11]. Fujii et al.[5] administered droperidol and metoclopramide with a low dose of propofol (0.5 mg/kg IV) at the end of surgery in order to prevent PONV in adult patients undergoing middle ear surgery, and concluded that propofol was more effective. In our study, patients in Group P received propofol infusion at a rate of 20 µg/kg/min during the intraoperative period. No PONV was observed within postoperative 0-2 h, 2-8 h or 8-24 h in 76.7%, 90.0% and 93.3% of the patients, respectively. The corresponding percentages in the placebo group were 26.7%, 46.7% and 70%, respectively. However, there was no statistically significant difference between Groups P and D in terms of prevention of PONV after tympanoplasty, with 4 patients vomiting in Group P and 5 in Group D. Two patients (6.7%) in Group P required antiemetics, compared to 9 (30%) in Group D and 15 (50%) in the placebo group. In our study, both propofol and dexamethasone significantly reduced the incidence and severity of PONV as well as postoperative rescue antiemetic requirements following tympanoplasty, but failed to eliminate them entirely. A number of studies have reported that propofol and dexamethasone are more effective in preventing PONV in combination with each other or with other agents[11,14,21]. One study comparing TIVA (propofol-remifentanil) with balanced anaesthesia (sevoflurane-remifentanil) in mastoidectomy combined with tympanoplasty concluded that TIVA was more effective in preventing PONV[6]. There are a number of limitations to this study. First, we did not investigate whether or not patients experienced any dizziness. Second, we did not assess the postoperative analgesic effectiveness of dexamethasone. Third, the type and form of anaesthesia was kept fixed, and no combination was used.

CONCLUSION

The incidence of PONV following tympanoplasty surgery may be as high as 80 percent. We conclude that the use of intraoperative low-dose propofol infusion is at least as effective as dexamethasone in reducing the severity of PONV and antiemetic requirements.

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