The Effect of Dexamethasone in Tramadol Induced Nausea and Vomiting

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Abstract

We aimed to investigate the efficacy of a single dose bolus of dexamethasone on tramadol induced nausea and vomiting in our study. After approval was taken from ethics committee and patients, a total of 60 ASA I-II patients who were planned to undergo total abdominal hysterectomy (TAH) under general anesthesia were included in this study. A patient-controlled analgesia device was explained for the patients with preoperative visit. After the non-premedicated patients were taken in the operation room, the routine monitorization was performed. Induction was provided with 1µg/kg of fentanyl, 2 mg/kg propofol and 0.1 mg/kg vecuronium. 6-8% concentration of desflurane in a mixture of 50% air and 50% O_2 was used for maintenance of anesthesia. When the incision was started to be closed, the patients were randomized into two groups by envelope method. 8 mg iv dexamethasone (2 mL) was given for Group D (n=30), iv Saline solution (2 mL) was given for Group K (n=30). After the incision was closed, a loading dose of intravenous tramadol 1 mg/kg was administered in both groups. The patients were taken in the postanesthesia care unit by extubating following the antagonism of muscle relaxant at the end of surgery. The patient-controlled analgesia device was scheduled to be as infusion: no, bolus: 12 mg, lock-out time: 10 min, 24 hour dosing limit: 400 mg. The pain and nausea and vomiting scores, additional analgesic and antiemetic requirements, the total amount of tramadol consumption were recorded at post-operative recovery and postoperative 2, 4, 6, 12 and 24 hours. Although the incidence of nausea and vomiting, and pain scores at 2 and 4 hours were not statistically significant, they were lower in Gorup D compared to Group K ($p>0.05$). 14 patients in Group K required additional antiemetics and 12 patients in Group D required additional antiemetics ($p>0.05$). Six patients in Group K required additional analgesics and 4 patients in Group D required additional analgesics. Although the total amount of tramadol consumption was not statistically significant, it was lower in Group D compared to Group K. It was concluded that a single bolus dose of dexamethasone 8 mg has not reduced tramadol induced nausea and vomiting in patients who were planned to undergo TAH.

Keywords: Tramadol, nausea, vomiting, dexamethasone

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Introduction

Insufficient postoperative pain control may increase morbidity, delay hospital discharge, reduce patient satisfaction [1]. Intravenous Patient-Controlled Analgesia (IV-PCA) was shown to be superior to conventional methods in the patients who could not undergo peripheral block or epidural block applications. There are publications reporting there was no difference between epidural PCA and IV-PCA for analgesia in the first 12 postoperative hours [2,3].

Tramadol shows analgesic efficacy by inhibiting serotonin and norepinephrine uptake besides it has a feature of weak μ-receptor agonist. It shows similar analgesic efficacy to morphine and pethidine in moderate pains. Unlike other opioids, tramadol has a minimal effect on the respiratory and cardiovascular systems [4,5]. However, it has been reported that the nausea and vomiting associated with the use of tramadol has high incidence [6,7]. The low dose naloxone infusion, transcutaneous electrical acupuncture point stimulation, ondansetron were preferred until today in the treatment of tramadol induced nausea and vomiting (TINV) [8-10]. However, there are publications suggest to that ondansetron may reduce the analgesic effect of tramadol. In recent years, dexamethasone has been shown to be an efficient on postoperative nausea and vomiting including nausea induced by opioids [11-13]. However, the efficacy of dexamethasone on TINV was not investigated sufficiently.

In our study, we aimed to investigate the efficacy of a single dose of intravenous dexamethasone administered before IV-PCA with tramadol on TINV.

Materials and Methods

After approval was taken from Local Ethic Committee of Faculty of Medicine of Inonu University, a total of 60 ASA I-II patients aged 18–65 years who were planned to undergo total abdominal hysterectomy operation were included in this study according to power analysis. The patients who had a history of drug allergy, opioid tolerance, diabetes mellitus, hypertension, motion sickness, nausea and vomiting were excluded from this study.

All patients were informed about PCA (Patient Controlled Analgesia) device which will be inserted in the postoperative period and Visual Analogue Scale (VAS). Premedication was not performed in the patients. A vascular access was placed before operation and 4mL/kg/hour Ringer Lactate solution infusion was started, standard monitorization was provided with electrocardiogram (ECG), noninvasive blood pressure (NIBP), peripheral oxygen saturation (SpO_2), heart rate (HR).

Anesthesia induction was performed with 1 µg/kg fentanyl, 2 mg/kg propofol ve 0.1 mg/kg vecuronium. 6-8% concentration of desflurane in a mixture of 50% air and 50% O_2 was used for maintenance of anesthesia. When the incision was started to be closed, the patients were randomized into two groups by envelope method. 8 mg iv dexamethasone (2 mL) was given for Group D (n=45), iv saline solution (2 mL) was given for Group K (n=45). After the incision was closed, a loading dose of intravenous tramadol 1 mg/kg was administered in both groups. The researcher who observed the patients during and after the operation was unaware of the study drug and the study. The patients were taken in the postanesthesia care unit (PACU) by extubating following the antagonism of muscle relaxant at the end of surgery. PCA device was scheduled to be as infusion: no, bolus: 12 mg, lock-out time: 10 min, 4 hour dosing limit: 150 mg, 24 hour dosing limit: 400 mg.

Pain scores were evaluated by VAS. If patient's VAS scores were 3 and above an hour after starting IV-PCA process, additional dose of 8 mg iv lornoxicam was administered in the patient.

Nausea and vomiting were evaluated on four-point scale. 0: No nausea and vomiting, 1: tolerable nausea or only one-time vomiting but no need for treatment, 2: intolerable nausea, there is a need for treatment in recurrent attacks of vomiting, 3: treatment-resistant nausea and vomiting. Additional dose of 10 mg metoclopramide was administered in patients with a score of 2, 4 mg iv ondansetron was administered in patients with a score of 3. Sedation was evaluated on four-point scale. 0: alert, 1: drowsy, 2: sleeping but arousable by tactile, 3: deep sleep. VAS, nausea, vomiting and sedation scores of the patient were recorded on 2, 4, 6, 12

and 24 hours in postoperative recovery room. Additional antiemetic requirement, additional analgesic requirement and the total amount of tramadol consumption were recorded.

SPSS 16.0 statistical software package was used in statistical evaluation of data. The data were evaluated as mean±standard deviation (mean±SD), % or number of cases (n). Independent Samples t test was used in the comparison of means in two groups. Yates corrected Chi-square test was used in the comparison of additional analgesic requirement and additional antiemetic requirement. In the assessments made, variables which were determined as $p > 0.05$ showed normal distribution. $p<0.05$ was considered to be statistically significant, $p< 0.01$ was considered to be highly significant.

Results

A total of 60 patients were included in our study. The demographic characteristics of the patients were similar ($p>0.05$) (Table 1).

Table 1. Demographic data for groups. Values are mean (SD) or (n)

	Group D (n=30)	**Group K (n=30)**
Weight (kg)	70.1±6.1	71.3±5.2
Age (year)	45.2±3.4	47.1±2.8
Height (cm)	162±2.8	161±9.7
ASA I/II (n)	18/12	17/13

Although the incidence of nausea and vomiting, and pain scores at 2 and 4 hours were not statistically significant, they were lower in Gorup D compared to Group K ($p>0.05$). The groups were similar in respect to nausea, vomiting and pain scores in another follow-up periods (Table 2 and Table 3). Nausea score was 2 in 14 (46%) patients in Group K and in 12 (40%) patients in Group D, they were treated with additional antiemetic (metoclopramide) ($p>0.05$). Ondansetron was not required because there was no patient with nausea score of 3 in both groups.

It was the need for additional analgesic in 6 (20%) patients in Group K and in 4 (13%) patients in Group D. Although the total amount of tramadol consumption was not statistically significant, it was lower in Group D (234±6.1 mg) than Group K (250±3.2 mg) (Table 4).

Table 2. Nausea and vomiting incidence of groups (n)

	Group D (n=30)	Group K (n=30)
PACU	6	7
2.h	8	10
4.h	10	12
6.h	4	5
12.h	2	3
24.h	1	1

Table 3. VAS Scores of the groups

	Group D (n=30)	Group K (n=30)
PACU	6 (7-5)	7 (8-6)
2.h	4 (5-3)	6 (7-5)
4.h	3 (4-2)	5 (6-4)
6.h	4 (5-3)	5 (6-4)
12.h	4 (5-3)	4 (5-3)
24.h	2 (3-1)	2 (3-1)

Table 4. Additional antiemetic and analgesic requirement, the total amount of tramadol of groups. Values are (n), percentage or mean (SD)

	Group D (n=30)	Group K (n=30)
Antiemetic requirement (n)	12 (40%)	14 (46%)
Analgesic requirement (n)	4	6
Total amount of tramadol (mg)	234±6.1	250±3.2

Sedation score was 1 in 10 patients in Group D and in 8 patients in Group K on recovery room and second postoperative hour, sedation score was 0 in all patients in other time periods.

Discussion

In our study, we found that a prophylactic single bolus dose of dexamethasone 8 mg did not change the incidence of nausea and vomiting, the need for additional antiemetic and the amount of tramadol consumption in patients undergoing IV-PCA with tramadol.

While it is stated that tramadol induced nausea and vomiting is due to serotonin reuptake inhibition, the incidence of tramadol induced nausea and vomiting varies between 25% and 49% [4,14]. Dexamethasone is a glucocorticoid and it also has a strong anti-inflammatory effect besides strong antiemetic effect. These features of dexamethasone increase patient satisfaction. Although the mechanism of action of dexamethasone is not known exactly, it was held responsible for central inhibition of prostaglandin synthesis, reduction of stimuli in operation site with the anti-inflammatory effect and reduction of serotonin release from the

gastrointestinal tract. Its direct inhibitory effect on 5-HT3 receptors is controversial. Moreover, the permeability changes in the central nervous system have been suggested to be responsible for the mechanism [15-17].

In study performed by Gurses et al [5], they have used tramadol in IV-PCA in postoperative analgesia and they have added metoclopramide, droperidol or ondansetron to tramadol in order to reduce tramadol induced nausea and vomiting. While the rate of vomiting was 6.4% in the tramadol group in that study, this rate has been as high as 46% in our study. The reason of this may be that the type of surgery performed in our patients is fixed TAH. In our study, we have not given dexamethasone in combination with tramadol. This may also be why we see less effective.

Liu et al. [18] have used tramadol or tramadol+droperidol combination in patients undergoing abdominal hysterectomy. Similar to our study, the rate of nausea and vomiting was found to be high in the tramadol group. There was no need for antiemetic in droperidol added group. In our study, administration of prophylactic dexamethasone and different mechanisms of action of drugs can explain the differences in our results.

Cekmen et al. [11] have administered 5 mg iv dexamethasone 10 minutes before extubation at the end of operation in patients undergoing laparoscopic cholecystectomy and they found that it reduced the incidence of nausea and vomiting in the first 24 hours compared to control group. Similarly, in our study, 8 mg dexamethasone was administered at the end of operation. However, metamizole was used instead of tramadol for postoperative analgesia in that study, this situation may be the reason of low nausea and vomiting score.

Similar to our study, Sekhavat et al. [12] administered 8 mg dexamethasone immediately after the operation in patients undergoing total abdominal hysterectomy and reported that prophylactic dexamethasone can reduce postoperative nausea and emesis. However, postoperative analgesic has not been used in that study. Tramadol that we have used for analgesia may be the reason of this.

Ko-lam W et al. [19] have combined dexamethasone with metpamid in patients undergoing laparoscopic cholecystectomy and they found that it is effective in preventing nausea and

vomiting. In our study, dexamethasone was only used, tramadol has also been used for analgesia.

In meta-analysis performed Bernardo WM et al. [20], they found that 8 mg dexamethasone which was given prophylactically reduced postoperative nausea and vomiting but also tramadol was not given in that study.

Consequently; we consider that a single bolus dose of dexamethasone 8 mg could not reduce tramadol induced nausea and vomiting in IV-PCA process for postoperative analgesia in patients who were planned to undergo TAH.

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