ORIGINAL ARTICLE

PROPHYLAXIS OF POSTOPERATIVE NAUSEA AND VOMITING - A COMPARISON OF DROPERIDOL ALONE WITH DROPERIDOL PLUS DEXAMETHASONE COMBINATION

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ABSTRACT

Objective: Adequate control of postoperative nausea and vomiting (PONV) and early return to normal activity are important anesthetic goals. We compared the efficacy of droperidol alone with droperidol plus dexamethasone combination for preventing PONV.

Study: A prospective, randomized, double-blind study.

Period & Setting: June 2002 to November 2004, at Department of Anesthesiology, Namazee Hospital, Shiraz University of Medical Sciences, Shiraz (Iran).

Materials and Methods: Two hundred, ASA grade I-II, ambulatory gynecological surgical patients of ages 18-70 yrs received 2.5 mg of droperidol at the time of induction of general anaesthesia. At the end of the operation, group A (n = 100) received 2 ml of intravenous isotonic electrolyte solution (0.9% sodium chloride) and group B (n = 100) received 2 ml of intravenous dexamethasone (8 mg). A standard general anesthetic technique and post op analgesia were used throughout the operation. PONV were assessed 2, 4 and 12 hours after the operation.

Results: The incidence of postoperative nausea decreased significantly in group B as compared to group A (23% vs. 49%), as was the incidence of vomiting (12% vs. 39%) ($p = 0.014$). Mean duration of nausea was 34 minutes in group A and 23 minutes in group B ($p < 0.001$).

Conclusion: We conclude that addition of 8 mg of dexamethasone to droperidol prophylaxis is more effective than droperidol prophylaxis alone for successful control of PONV.

Key words: Postoperative nausea; vomiting; droperidol; dexamethasone; antiemetic

INTRODUCTION

Nausea and vomiting are the most common and distressing symptoms associated with surgery and one of the most common reasons for poor patient satisfaction rating in the post op period [1, 2]. Currently, the overall incidence of PONV for all surgeries and patients is estimated to be 25-30%.[3] PONV may be associated with serious complications such as dehydration, electrolyte disturbances, wound dehiscence, pulmonary aspiration and esophageal rupture; leading to a delay in post anesthesia recovery room discharge, thereby increasing medical costs [4]. In a study more than half of 121 patients undergoing day case gynaecological procedures reported nausea and vomiting at home, and 54% considered PONV to be more debilitating than the effects of the surgery itself.[5]

Droperidol is a major tranquilizer that also exhibits antiemetic properties as the result of its antagonistic action on dopamine receptors. Droperidol has been studied alone and in

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combination with other antiemetic drugs, with varying results [6]. Droperidol has been shown to significantly prevent PONV, better than Ondansetron (12.5% *v* 32.5%) during the immediate postoperative period [6].

Dexamethasone, a corticosteroid is also used as a PONV prophylactic drug [7]. Therefore, it seems that when combined with droperidol its efficiency would increase. The aim of this study was to investigate the efficacy of droperidol in preventing PONV and compare its effect with a combination of droperidol and dexamethasone.

MATERIALS AND METHODS

In a prospective randomized double-blind clinical trial, from June 2002 to November 2003, two hundred ASA grade I-II ambulatory gynecologic patients who had referred for operation to educational hospitals of Shiraz University of Medical Sciences were studied. A written informed consent was obtained from each patient and Shiraz University of Medical Sciences Research Committee had approved the study. The patients' age ranged from 18 to 70 years and they were scheduled for elective gynecologic operations.

Patients who gave positive history of cardiovascular disease, diabetes, or complained of pre-operative nausea / vomiting or dizziness and motion sickness, those who had received any antiemetic medication within 24 hrs before surgery, and those who were pregnant, lactating or with a body mass index of greater than 35 were excluded. Demographic characteristics, type of operation and drug consumption history were recorded.

The patients were randomly allocated to receive one of two treatment regimens: droperidol 2 mg and droperidol 2 mg with dexamethasone 8 mg. Droperidol 2 mg was administered by slow intravenous injection immediately after induction of anesthesia. At the end of the operation, group A received 2 ml of intravenous 0.9% sodium chloride (sodium chloride, 154 mEq/L). The second group (group B) received 2 ml of dexamethasone containing 8 mg of the drug. Personnel not involved in the study prepared identical syringes containing the study drugs. A standard general anesthetic technique and post op analgesia were used throughout the operations. Induction was done with diazepam (0.1 mg/kg) and morphine (0.15 mg/kg). Endotracheal intubation was accomplished with 4 mg/kg pentothal and 1.5 mg/kg of succinylcholine. Anesthesia was maintained with a mixture of oxygen and nitrous oxide (50% each) in halothane (0.5% end tidal) in a semi-closed circle system. Atracurium (0.3 mg/kg IV) was used for muscle relaxation. Neuromuscular block

Table 1: Demographic characteristic, duration of operation and ASA grades

	Droperidol alone (n = 100)	Droperidol with dexamethasone (n = 100)	*p* value
Age (years)	39.4 ± 12	40.1 ± 10.1	
Age Range (years)	18-65	18-70	
Weight (kg)	66.52 ± 6.9	68.2 ± 7.1	
Duration of operation (min)	63.55 ± 19	64 ± 18.29	
ASA grade I/II	80/20	76/24	

NS: not significant; $p > 0.05$

was reversed with neostigmine (50 μg/kg) and atropine (25 μg/kg). All patients received a maintenance IV fluid therapy of isotonic saline 1 ml/kg/hour throughout the operation and during the post op period. Blood pressure, heart rate, oxygen saturation, electrocardiogram, tidal volume, end-tidal CO_2, end-tidal concentration of the inhaled anesthetic, airway pressure, and minute volume were monitored.

Patients were interviewed by blinded nursing staff. They were asked if retching or vomiting had occurred, whether rescue antiemetics had been used and if they had felt nauseated in three time-periods: 0-2, 2-4 hours and at 12 hours post operatively, with only two possible answers (yes/no). Nausea was defined as the unpleasant sensation associated with awareness of the urge to vomit; retching was defined as labored, spasmodic, rhythmic contraction of the respiratory muscles without expulsion of gastric contents and vomiting was defined as the forceful expulsion of gastric contents from the mouth [1]. Failure of prophylaxis was defined as any episode of nausea, retching, vomiting or use of rescue antiemetic. The nursing staff and investigators recorded details of adverse events using an open

questioning technique.

A sample-size of 200 patients (100 in each group) was required to detect a difference in response rates of 0.25 from a baseline prevalence of 0.5, with 80% power at a two-sided significance level of 5%.

All data were analyzed and computed by SPSS® (Chicago, IL) software, version 10.0, and Microsoft EXCEL® (Microsoft®, Redmond, WA) software. Data are expressed as mean ± standard deviation (SD) and 95% confidence interval (CI) are also given when essential. The association between variables was assessed with Student's *t*-test; Fisher's exact, χ^2 test and Mann Whitney U-test. *P*-values less than 0.05 were considered statistically significant.

RESULTS

Patient demographic characteristics and types of operations were similar in each group (Table 1). There was no statistically significant difference between the two groups in demographic characteristics (age and weight), type of operation, or ASA classification (Table 1; $p > 0.05$). Additionally, there was no significant difference between them in the amount of anesthesia given and the duration of anesthesia (Table 1).

Failure to prophylaxis against nausea during the first 2 hours (0-2 hrs) after surgery was 13 and 8% of patients who had received droperidol alone, and droperidol-dexamethasone combination respectively. The incidence of the same during the next 2 hours (2-4 hrs) was 34 and 15% respectively, whereas it was 38 and 19% respectively during the 12 hour post operation (Table 2). The overall incidence of nausea for the 12 hours post surgery was 49% and 23% respectively. The overall incidence of vomiting for the 12 hours post operation was 39 and 12%, respectively (Table 2). Thus, the incidence of PONV was significantly less at 0-2, 4 and 12 hours post operation in those who had received droperidol-dexamethasone compared to droperidol alone ($p = 0.009$; Table 2). The incidence of PONV is shown in Table 2.

Mean duration of nausea in group A was 34 minutes (range of 10-180 minutes). The mean duration of nausea in group B was significantly shorter as compared to group A (23 minutes (range of 5-120 minutes; $p < 0.05$)

Table 2: Incidence of nausea and vomiting in the two studied groups. Values are numbers (proportions)

Time		Droperidol	Droperidol/ dexamethasone	*p* value
0-2 hours	Nausea	13%	8%	<0.05
	Vomiting	9%	5%	<0.05
2-4 hours	Nausea	34%	15%	<0.05
	Vomiting	21%	6%	<0.05
12 hours	Nausea	38%	19%	<0.05
	Vomiting	29%	9%	<0.05
Overall	Nausea	49%	23%	<0.05
	Vomiting	39%	12%	<0.05

DISCUSSION

The etiology of PONV after gynecological operations performed under general anesthesia remains unclear. Age, positive history of previous PONV and/or motion sickness, smoking, length of operation, type of operation, and use of post op opioids are important factors in predicting PONV [1-4]. Fortunately, there were no statistically significant differences in these factors between our study groups and, therefore, differences between groups may be attributed to differences in the antiemetic drugs utilized. In order to increase the ability to generalize our findings, a heterogeneous group of operations was included in the study. Dilatation and curettage were excluded from the study due to the lower incidence of PONV observed in this group of patients [8].

In published comparative studies of antiemetic efficacy, droperidol has been considered to be the 'gold standard' against which other agents are measured. The recent withdrawal of droperidol due to reports of cardiac arrhythmias and a potential for sudden death has left a vacancy for a safe and effective antiemetic [9]. In our study, the overall incidence of post-op nausea and vomiting in the droperidol group was 49 and 39%, respectively. Previous studies on PONV after gynecological operations have reported a mean prevalence of 50% [10, 11]. Therefore, it seems that in our study droperidol had been only effective in decreasing the incidence of post op vomiting. We do not know the reason for the high rate of post op nausea observed in our patients in spite of receiving

droperidol.

Our study demonstrated a significant difference between droperidol-dexamethasone combination and droperidol alone in all 3 periods of studied post op hours (0-2 hrs period, 2-4 hrs and 12 hrs). Reduction in PONV was also statistically significant. Overall incidence of post-op nausea and vomiting in droperidol-dexamethasone combination group was 23% and 12% respectively. This rate is similar to other antiemetic drugs being used. In a randomized, double-blind, parallel group, placebo-controlled, dose-ranging study, performed by Wilson and his colleagues, efficacy of a 5-HT_3 receptor antagonist, granisetron (Kytril®) as prophylactic therapy for the prevention of postoperative nausea and vomiting in three doses (0.1 mg, 1.0 mg and 3.0 mg) were compared [12]. They observed that two higher doses of granisetron (1.0 mg and 3.0 mg) provided effective prophylaxis against vomiting, with 78% and 77% of patients respectively being free from vomiting in the first 6 hrs after surgery, and 63% and 62% in the first 24 hrs. These figures are very much similar to what we have observed in the patients receiving the combination of droperidol-dexamethasone [12]. We, however, should note here that increased drowsiness, delayed discharge, and post-discharge restlessness may occur with droperidol; and granisetron and ondansetron are costly. Tang *et al* performed a prospective, randomized, double-blind, placebo-controlled study involving 161 women, in order to compare the efficacy, safety, and cost-effectiveness of ondansetron (4 mg IV) with droperidol (0.65 mg or 1.25 mg IV) in the prevention of PONV after outpatient gynecologic surgery [11]. They concluded that droperidol 0.625 mg IV provides antiemetic prophylaxis comparable to that of ondansetron 4 mg IV without increasing the side effects or delaying discharge and is most cost-effective [11]. We also, considering the price of drugs like granisetron and ondansetron, conclude that the combination of droperidol-dexamethasone is much more cost-effective, and it can obtain comparable results. In another randomized, double-blind, placebo-controlled study, 2061 adult surgical outpatients at high risk of PONV were enrolled to compare ondansetron 4 mg IV with droperidol 0.625 mg and droperidol 1.25 mg. Nausea, emetic episodes, adverse events, and patient satisfaction were analyzed for the 0 to 2 h and 0 to 24 h postoperative periods [13]. After surgery, the incidence of nausea, vomiting, medication side effects, and patient satisfaction were evaluated for 24 h. They reported that Droperidol 0.625 or 1.25 mg IV compared favorably with ondansetron 4 mg IV for the prevention of postoperative nausea and vomiting after ambulatory surgery [13].

Dexamethasone has been used in combination with other antiemetic drugs and has been reported to be beneficial. Thomas R and Jones N performed a double-blind randomized study on 177 gynecological patients. Three different treatments were given: dexamethasone 8 mg, Ondansetron 4 mg and dexamethasone 8 mg plus Ondansetron 4 mg [8]. They concluded that dexamethasone alone or in combination, may be particularly efficacious in preventing late or delayed PONV [8]. Gan TJ *et al* also used the combination of Dexamethasone with Ondansetron and granisetron [10]. They observed that the combination of small-dose granisetron administered just before tracheal extubation plus dexamethasone given at induction of anesthesia is an effective alternative to ondansetron plus dexamethasone in preventing vomiting during the 0 to 2-hrs interval after tracheal extubation [10].

We conclude that addition of 8 mg of dexamethasone to droperidol prophylaxis is more effective than droperidol prophylaxis alone for successful control of PONV.

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