SINGLE DOSE INTRAVENOUS ONDANSETRON IN THE PROPHYLAXIS OF POSTOPERATIVE NAUSEA AND VOMITING

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SUMMARY

The purpose of the present randomized, double blind placebo controlled study was to compare the effect of ondansetron, a 5 HT 3 subtype of serotonin receptor antagonist, with placebo, in preventing postoperative nausea and vomiting. A total of forty-nine patients undergoing total abdominal hysterectomy were assigned to the study. The patients received either 4 mg intravenous ondansetron or a matching placebo, prior to induction of anesthesia. The number of episodes of emesis and nausea were recorded at 1 hour, 4 hour and 8 hour after recovery from anesthesia. The nausea and womiting scores at 1h 4h and 8h in the ondansetron group were significantly lower than the placebo group ($p<0.05$). The incidence of the most frequently occuring side effects in the ondansetron group were headache in 15.38 % and dizziness in 7.7 % of the patients. In conclusion, ondansetron appears to be an effective agent in the prophylaxis of postoperative nausea and vomiting in gynecologic operations.

Key Words: Prophylaxis emesis, ondansetron

INTRODUCTION

Nausea and vomiting are among the most common and troublesome adverse events after operative procedures requiring general anesthesia, with an incidence of 75% after gynecological surgery (1).

Ondansetron (Zofran, Glaxo, United Kingdom) is a serotonin antagonist that selectively inhibits 5 HT3 subtype of serotonin receptors with little or no activity on dopamine or other receptors (2). Both animal and human studies have shown ondansetron to be effective in preventing nausea and vomiting associated with cancer chemotherapy and radiation therapy (3-5).

The purpose of this douple blind, randomized, placebo controlled study was to compare the efficacy of 4 mg. ondansetron with placebo in the prevention of postoperative nausea and vomiting in patients undergoing gynecologic operations.

METHODS

Forty-nine patients, aged 26-69 scheduled to have total abdominal hysterectomy for benign reasons under general anesthesia were included in the study. Patients gave informed consent. Patients who had clinical or laboratory evidence of renal, hepatic, cardiovascular, metabolic or endocrine dysfunction were excluded. Patients were asked not to receive antiemetic medication for 24hr before entering the study. Patients were randomly allocated to receive either 4 mg ondansetron diluted in 20 ml saline or 20 ml physiologic saline as placebo in a double blind fashion. The study drug or saline was infused intravenously (iv) over 2-5 minutes prior to induction of anesthesia.

All patients were premedicated with 5 mg diazepam orally, 0.5 mg atrophine sulphate, and 50 mg meperidin intramuscularly (im.). Anesthesia was induced with 5 mg/kg thiopental sodium, and 1.5 mg/kg succinylcholine. Anesthesia was maintained using 2 1/min oxygen, 4 1/min nitrous oxide and 1 MAC enflurane or izoflurane. Pancuronium bromide was used as muscle relaxant. Reversal of muscle relaxation was achieved with 1.5 mg prostigmine. Postoperative analgesia was provided by 4 x 100 mg (im) mephedrine hydrochloride for all patients.

Nausea and vomiting were assessed at 1h, 4h, and 8h after recovery by an investigator who was totally blind to randomization. Any vomiting productive of liquid was recorded as an emetic episode and the number of episodes of emesis was recorded for each patient. In addition, one to five retches (vomiting not productive of liquid) within any 5- minute period were counted as a single emetic episode (6). Nausea was scored as none (0), mild (+1), moderate (+2) and severe (+3) (7).

After the nausea and vomiting assessment at 1.4 and 8 hours, antiemetic treatment with intramuscular metoclopramide was administered as indicated. The number of doses of this rescue antiemetic was recorded. The duration of anethesia and the time to

Table I: Demographic data

	ONDANSETRON GROUP n = 26	PLACEBO GROUP n = 23	P VALUE
AGE (year)	48.61 (SD, 7.70)	47.0 (SD, 8.85)	NS*
WEIGHT (Kg)	68.69 (SD, 9.35)	70.17 (SD, 10.18)	NS*
RECOVERY TIME (min)	8.69 (SD, 3.36)	8.43 (SD 3.07)	NS*
DURATION OF ANESTHESIA (min)	125.57 (SD, 26.95)	122.609 (SD, 25.31)	NS*

* P > 0.05

Table II: Nausea and vomiting scores

	ONDANSETRON GROUP n = 26	PLACEBO GROUP n = 23	P VALUE
VOMITING SCORE			
I. HOUR	0.11 (SD, 0.43)	0.43 (SD, 0.84)	<0.05
4. HOUR	0.23 (SD, 0.71)	0.69 (SD, 1.01)	<0.05
8. HOUR	0.38 (SD, 0.80)	1 (SD, 1.34)	<0.05
NAUSEA SCORE			
1. HOUR	0.42 (SD, 0.80)	0.91 (SD, 1.80)	<0.05
4. HOUR	0.69 (SD, 0.88)	1.21 (SD, 0.99)	<0.05
8. HOUR	1 (SD, 0.97)	1.65 (SD, 1.19)	<0.05
MEAN RESCUE ANTIEMETIC	0.46 (SD, 0.64)	1.34 (SD, 1.19)	<0.05

recovery from anesthesia were assessed. The patients were questioned about any possible side effects of the study medication during hospitalization. All patients' weights were recorded prior to surgery.

The data were analyzed by Student's t test for parametric data. A Mann Whitney U test was used for comparison of the non parametric data. Results were expressed as means +/— standard deviation.

RESULTS

Forty-nine patients entered the study. Table I demonstrates that the mean age and weight of the patients and the duration and recovery from anesthesia were not significantly different between the treatment groups.

The mean scores for vomiting were 0.11 +/— 0.43, 0.23 +/— 0.71, 0.38 +/— 0.80 for ondansetron group and 0.43 +/— 0.84, 0.69 +/— 1.01, 1.00 +/— 1.34 for placebo patients at 1h,4h and 8h respectively. Similarly, the nausea scores were 0.42 +/— 0.80,0.69 +/— 0.88, 1.00 +/— 0.97 for ondansetron group and 0.91 +/— 1.08, 1.21 +/— 0.99, 1.65 +/— 1.19 for placebo patients at 1h, 4h, and 8h respectively (Table II).

Ondansetron treatment resulted in a significantly lower score of both nausea and vomiting during the study period ($p<0.05$). The mean rescue antiemetic required was significantly less in the ondansetron group than in the placebo group ($p<0.05$) (Table II).

A total of 12 doses of metoclopromide were administered to 10 patients in the ondansetron group, compared with 31 doses administered to 16 patients in the placebo group. The most frequently occuring side effects in the ondansetron group were headache and dizziness. The incidence of headache was 15.38 % and 7.7 % for ondansetron patients and 13.04 % and 4.4 % for placebo patients.

DISCUSSION

Antihistaminics, anticholinergics and dopamine receptor antagonists are the most commonly used antiemetic medications but they have side effects such as hypotension, sedation, restlessness, dysphoria and extrapyramidal symptoms, which frequently limit their use (8).

Antiemetics are occasionally given prophylactically at premedication or induction to prevent postoperative nausea and vomiting, but are more often given postoperatively for the treatment of nausea and vomiting. An acceptable prophylactic drug must be effective and especially without appreciable side effects.

Ondansetron is a selective antagonist of 5 HT receptors and appears to mediate physiologic responses both at the peripheral nervous system (9) and in the vomiting center of the central nervous system (10). Ondansetron has been already proved to be an effective treatment for the prevention of nausea and vomiting induced by cancer chemotherapy and radiotherapy (11).

Oral ondansetron has already been shown to be effective in the prophylaxis of postoperative nausea and vomiting in gynaecologic patients (12,13). Several studies have reported that 8 mg intravenous ondansetron is effective in the prevention of postoperative nausea and vomiting (14-18). Mc Kenzie et al (19) in a dose range preliminary study have demonstrated that the optimal dose of iv. ondansetron for the prevention of postoperative nausea and vomiting was 4 mg in patients undergoing laparoscopy.

The current study demonstrates that 4 mg iv prophylactic ondansetron is significantly more effective than placebo in prevention of postoperative nausea and vomiting, in women undergoing major gynecologic surgery. Several factors may influence the incidence of postoperative nausea and vomiting and there was no significant difference between our study groups with respect to age, weight, type of surgical procedures, duration of anesthesia, narcotic analgesic usage and recovery time. Ondansetron group required less antiemetic and yet significantly less nausea and vomiting was observed at 1,4 and 8hr postoperatively.

Our data show that ondansetron decreases the number of emetic episodes and nausea experienced by the subjects in the first 8 postoperative hours. As a conclusion ondansetron appears to be a safe and effective agent in the prohylaxis of postoperative nausea and vomiting in gynecologic operations.

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