ONDANSETRON VERSUS PLACEBO TO PREVENT POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING THYROIDECTOMY

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SUMMARY

Purpose : *One of the most common symptoms following anaesthesia is postoperative nausea and vomiting (PONV). The aim of this double blind study is to compare the antiemetic efficacy of ondansetron with placebo in the prevention of PONV in patients undergoing thyroidectomy.* ***Methods :*** *Following approval of the hospital ethic committee, 60 unpremedicated patients were randomly allocated into three groups to receive ondansetron 4 mg in 8 ml saline (Group I), placebo as 8 ml saline (Group II), or nothing (Group III). Patients received ondansetron or placebo infusion over 30 seconds prior to induction of anasthesia. Induction of anaesthesia was performed with thiopentone sodium 5mg kg-1, fentanyl citrate1μg/kg-1 and endotracheal intubation was facilitated with vecuronium bromide 0.08 mg kg-1. The number of nausea and vomiting episodes were recorded for the first 24 hours, postoperatively.* ***Results :*** *Ondansetron was significantly more effective than placebo or control in preventing emesis for 24 hours postoperatively ($p<0.05$ for both comparisons). Placebo was not shown to be statistically different from control.* ***Conclusion :*** *Consequently, 4 mg single dose of ondansetron was found to be effective when compared with placebo or control in the prevention of PONV.*

Key Words : *Ondansetron, Postoperative Nausea and Vomiting.*

INTRODUCTION

The most common and distressing symptoms following anaesthesia and surgery are postoperative nausea and vomiting (PONV). Despite significant advances in the delivery of general anaesthesia, PONV continue to be "the big 'little problem' for surgical patients" (1). PONV not only cause patient discomfort in the hospital and at home but also prolong recovery room stays and even the hospital stay (2, 3).

An effective antiemetic that could be used to treat PONV without extending recovery time and which would remain effective for at least 24 hours following treatment would be a significant asset to the anaesthesiologists (3).

Although 5-hydroxytryptamine subtype 3 (5HT3) receptor antagonists (ondansetron) are potent inhibitors of emesis induced by cytotoxic drugs and radiation, such compounds should be tested for their antiemetic activity against a wide spectrum of emetic challenges (4).

This study aims at comparison of antiemetic efficacy of low dose ondansetron versus placebo in the prevention of PONV in patients undergoing

thyroidectomy.

MATERIALS AND METHODS

60 patients (ASA I-II) undergoing elective thyroidectomy due to nodular goitre were included in the study. Patients who had a history of central or peripheral emetic stimulations and laboratory results (full blood count, blood chemistry, renal and liver function tests) which were out of normal range were excluded from the study.

After obtaining approval of the hospital ethic committee, unpremedicated patients were randomly allocated into 3 equal groups. Group I (ondansetron group) received 4 mg ondansetron hydrochloride dihydrate (Glaxo Operations, London, UK) in 8 ml saline, Group II (placebo group) received pure 8 ml saline, and Group III (control group) received nothing over 30 seconds immediately prior to the induction of anaesthesia. Neither the patients nor the anaesthesiologists who were responsible for the follow-up of the patients were aware of which patients belonged to which groups.

All of the patients received thiopentone sodium (İ.E. Ulgay İlaç San. A.Ş., İstanbul, Türkiye) 5 mg kg-1, fentanyl citrate (Abbott Lab. North Chicago, USA) 1 µg/kg-1, and vecuronium bromide (Organon Teknika, A.Ş., İstanbul, Türkiye) 0.08 mg kg-1 for the induction of anaesthesia. Then, anaesthesia was maintained with 50% nitrous oxide-oxygen mixture in 0.8-1 % isoflurane.

The number of nausea and vomiting episodes were recorded for the first 24 hours postoperatively. Postoperative follow up of vital signs and adverse effects (headache, dizziness, and or sedation) were recorded meticulously throughout the study.

Statistical data were analyzed with Chi square and ANOVA. $p<0.05$ was considered as significant.

RESULTS

Demograhic data of all the three groups are listed in Table 1. There were not any significant differences with respect to age, weight, height and duration of anaesthesia among the three groups (ANOVA).

The incidence of adverse effects such as; headache, dizziness, or sedation did not show any statistically significant difference among the groups (Table 2- ANOVA).

During the 24 hours of postoperative follow up, the incidences of nausea and vomiting episodes in the ondansetron group were significantly less than those of the placebo and control groups ($p<0.05$) (Fig. 1). Placebo was not shown to be statistically different from the control group (Fig. 1).

Data / Group	Ondansetron	Placebo	Control	p
n	20	20	20	
Age (year)	47.00 ± 8.19	45.00 ± 10.81	49.00 ± 9.75	ns
Weight (kg)	62.41 ± 8.12	65.50 ± 9.03	67.34 ± 7.25	ns
Height (cm)	169.06 ± 2.77	170.76 ± 3.82	172.25 ± 2.44	ns
Duration of anaesthesia (min)	110.4 ± 10.5	120.4 ± 15.3	115.6 ± 12.8	ns

ns : not significant

Table 1 : Demographic data and duration of anaesthesia (Mean ± Sd)

	Ondansetron	Placebo	Control	p
n	20	20	20	
Headache	4 (20 %)	3 (15 %)	3 (15 %)	ns
Dizziness	5 (25 %)	7 (35 %)	6 (30 %)	ns
Sedation	7 (35 %)	6 (30 %)	5 (25 %)	ns

ns : not significant

Table 2 : The distribution of adverse effects among the groups.

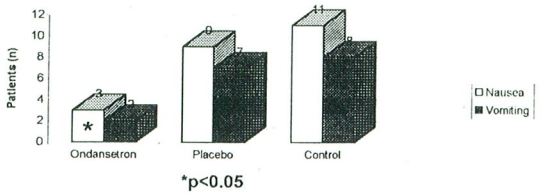

Fig. 1 : The distribution of incidence of postoperative nausea and vomiting among the groups. * : p<0.05 compared with control or placebo.

DISCUSSION

Although there is an extensive accumulation of knowledge which touches upon or incorporates data on PONV, these data are frequently difficult to interpret or compare because of the methodology used or the wide variety of variables (5).

Certain patient-related factors, such as gender, obesity,history of motion sickness, body habitus, anxiety, anaesthetic history, etc. may affect the incidence of PONV (1). PONV may also be induced by the anaesthetics or by the trauma or pertubations associated with surgery (6). Indeed, it is unlikely that PONV is caused by only pathophysiological input, but is multifactorial in origin. These pertubations may be peripheral, central or both, and involve direct effects on the vomiting system together with afferent inputs in the vagal, splanchnic, or trigeminal nerves (1).

Certain surgical sites are also proved to be associated with a greater frequency and in many instances, severity of PONV; i.e. intraabdominal surgery with an incidence of 70%, ear surgery 47% and laparascopic surgery 40-70% (7, 8). We have chosen thyroidectomy operations with the lowest expectancy of PONV in order to standardize and control surgery-related parameters.

Available antiemetic agents including antihistamines, butyrophenons and dopamine antagonists are considered effective to prevent PONV, but only a few have been proven potent as single-drug therapy (4, 9). These drugs also have undesirable side effects, such asexcessive sedation, hypotension, dry mouth, dysphoria, hallucinations, or extrapyramidal reactions, all of which may compound patient morbidity of the antiemetic agents currently used to treat PONV (3).

Of the antiemetic drugs currently used to treat PONV, droperidol would appear to be one of the most efficacious, but despite prophylactic use before the end of general anaesthesia, more than 30 % of the patients still complain of PONV (10). Metoclopramide is also effective, but the most important side effects are extrapyramidal reactions (10).

5HT3 antagonists-mainly ondansetron- are unique among antiemetics in that they have no effects at histaminergic, dopaminergic or cholinergic receptors and can therefore be expected to be devoid of troublesome side effects. Ondansetron as a 5HT3 receptor antagonists act by highly selective and potent antagonism of 5HT3 receptors in the brain, with a high density of 5 HT3 receptors occuring in the area postrema and the nucleus tractus solitarius equating with the chemoreceptive trigger zone. Ondansetron may be administered either orally or i.v. Oral bioavailability is approximately 60% with the peak plasma concentration occuring at about 1.5 hours after oral administration. Ondansetron is bound to plasma proteins to a moderate extent (70-76%). Its terminal plasma half life is approximately 3 hours with only 5% being excreted unchanged by kidneys. The major route of excretion is by glucuronide or sulphate conjugation in the liver. However, rare side effects such as hypersensitivity reactions may be seen (11).

Unfortunately, studies to illuminate the mechanism of PONV are also very hard to perform because the problem is complex in aetiology, there is inadequate quantification of the phenomenon and there are limited physiological or pharmacological studies due to the lack of a suitable animal model (12).

Dosing of the antiemetics is also controversial. Pilot studies have shown that 8 mg iv ondansetron is more effective than placebo in preventing PONV (4). Following these studies, Russell and Kenny studied 995 ASA I-II patients undergoing major gynecological surgery and compared the efficacy of 1, 8 and 16 mg ondansetron. They demonstrated

that a single dose of 4 mg ondansetron may be given by slow iv injection at the induction of anaesthesia for prophylaxis and for the treatment of established PONV (11). The results of three large multicentre, randomized, double blind, placebo-controlled trials, examining the safety and efficacy of single dose iv prophylactic ondansetron, showed that 8 mg of ondansetron was not statistically different from 4 mg in preventing PONV (1). For that reason, we used a single dose of 4 mg ondansetron in our study.

On the basis of the literature, a single 4 mg iv dose of ondansetron appeared to be the lowest acceptable dose in the prevention of PONV (1). In our study, we obtained similar results with Mc Kenzie et al. and Pearman by using 4 mg ondansetron. The incidence of nausea and vomiting in the postoperative 24 hours of the ondansetron group in the present study decreased with respect to the placebo and control groups. Although ondansetron appears to be a safe antiemetic, we observed headache, dizziness and sedation as a statistically insignificant percent when compared with the other groups.

In conclusion, we have showed the efficacy of the lowest dose of this antiemetic agent versus placebo or control.

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