Comparison of Costs and Efficacy of Intravenous and Orally Disintegrating Ondansetron Tablet as a Prophylactic Antiemetic Therapy in Major Gynecologic Operations

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Abstract

Objective: The aim of the study is to compare the antiemetic efficacy and costs of oral rapid disintegrating ondansetron tablets and intravenously administered ondansetron in patients undergoing major gynecologic surgery.
Materials and Methods: Anesthesia was induced with thiopenthone, vecuronium and fentanyl. Nitrous oxide and sevoflurane were used to maintain anesthesia. Patients were prospectively randomized into three groups of 30 patients each, receiving either ondansetron 8 mg intravenously or saline infusion only or oral rapid disintegrating tablets of 8 mg ondansetron. The patients were evaluated for nausea and vomiting at 1st, 5th, 10th, 20th, 30th, 60th, and 120th minutes and 6th hours postoperatively.
Results: There were no significant differences in adverse effects between placebo group, intravenous ondansetron group and oral ondansetron group (P>0.05). The incidence rates of nausea, vomiting and the need of metoclopropamide were higher in placebo group than intravenous and oral ondansetron groups (P<0.05).
Conclusion: Postoperative nausea and vomiting are common during recovery from general anesthesia. Both oral and intravenous forms of ondansetron are efficacious in the prevention of this postoperative nausea and vomiting. Orally disintegrating tablets are inexpensive and may be administered more easily than the intravenous form of ondansetron. Therefore, oral ondansetron tablet may be an alternative to intravenous ondansetron infusion for postoperative nausea and vomiting after major gynecologic operations.

Keywords: anesthesia, gynecologic surgery, postoperative nausea and vomiting, ondansetron

Özet

Büyük Jinekolojik Operasyonlarda Profilaktik Antiemetik Tedavi Olarak İntravenöz Ondansetron İnfüzyonu ve Dil Üstü Hızlı Çözünen Ondansetron Tabletin Etkinlik ve Maliyet Açısından Karşılaştırılması

Amaç: Çalışmanın amacı, majör jinekolojik operasyon yapılan hastalarda, hızlı çözünen oral ondansetron tablet ile intravenöz ondansetron infüzyonunun antiemetik etkinliklerini ve maliyetlerini karşılaştırmaktır.
Materyal ve Metot: Anestezi indüksiyonu pentotal, vekuronyum ve fentanil ile yapıldı. Azot protoksit ve sevofloran idame olarak verildi. Hastalar prospektif olarak, yalnız 8 mg ondansetron infüzyonu alan veya yalnız izotonik infüzyonu alan ya da oral hızlı çözünen 8 mg ondansetron içeren tablet alan her biri 30'ar denek içeren üç gruba ayrıldılar. Ameliyattan sonraki 1., 5., 10., 20., 30., 60., 120. dakikalarda ve 6. saatte hastalar bulantı ve kusma şikâyetleri açısından değerlendirilirdi.
Sonuçlar: Plasebo, intravenöz ondansetron ve oral ondansetron grupları arasında yan etkiler açısından anlamlı fark bulunmadı. Bulantı, kusma ve metoklopropamid ihtiyacı plasebo grubunda oral ve intravenöz ondansetron gruplarına göre istatistiksel olarak daha yüksek orandaydı (P<0.05).

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Tartışma: Genel anestezi altındaki ameliyatlardan sonra, uyanma döneminde postoperatif bulantı ve kusma sık görülür. Hem oral hem de intravenöz ondansetron postoperatif bulantı ve kusmayı önlemede etkilidir. Hızlı çözünen dil üstü ondansetron tabletler daha ucuzdur ve kullanımı intravenöz ondansetrondan daha kolaydır. Bu nedenle majör jinekolojik operasyonlar sonrasında görülen postoperatif bulantı ve kusmalar için oral ondansetron tablet, intravenöz ondansetron infüzyonuna bir alternatif olabilir.

Anahtar sözcükler: anestezi, jinekolojik cerrahi, postoperatif bulantı ve kusma, ondansetron

Introduction

Postoperative nausea and vomiting are common complications occasioning significant discomfort to the patients in the early postoperative period. Many patients consider postoperative nausea and vomiting to be as debilitating as the pain associated with the surgery, and this may alter their attitude to otherwise successful surgery (1,2). Female patients are particularly susceptible, especially when undergoing gynecological surgery and other factors, including previous postoperative nausea and vomiting, is thought to influence the occurrence of these problems (3,4).

Ondansetron is a carbazalone derivative that is structurally related to serotonin and possesses specific 5-hydroxytryptamine (5-HT) subtype 3 receptor antagonism, without altering dopamine, histamine, and adrenergic or cholinergic receptor activity. Recent studies have evaluated the efficacy of ondansetron in the prevention (5,6) and treatment (7) of postoperative nausea and vomiting. The orally disintegrating tablet is a recently developed freeze-dried oral formulation that disperses rapidly when placed on the tongue. It does not require water to aid swallowing and therefore easily administered (8). In the present study, the antiemetic efficacy of the orally disintegrating tablet and intravenously administration of ondansetron were compared in patients undergoing major gynecologic surgery.

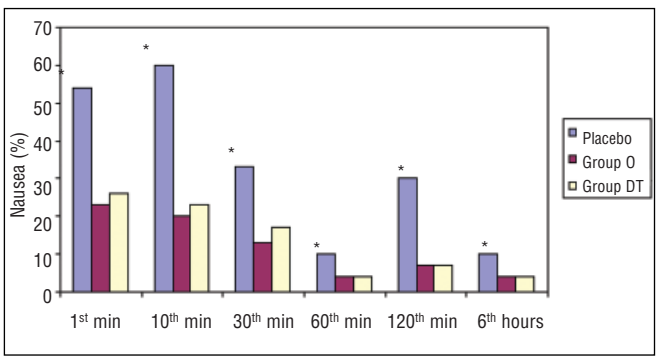

Figure 1. Incidence of nausea.
Group O: Intravenously ondansetron
Group DT: Orally disintegrating tablet
* Comparison of the groups (P<0.05).

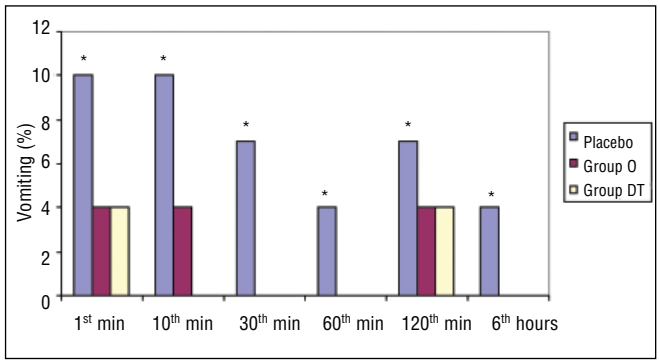

Figure 2. Incidence of vomiting.
* Comparison of the groups (P<0.05).

Materials and Methods

The study which was conducted between January 2003 and December 2004 was approved by the ethics committee of our university hospital. After obtaining the informed consent of all patients, we studied 94 consecutive female inpatients (ASA physical status I-III) scheduled to undergo gynecologic operations under general anesthesia (Table 1). Patients were interviewed during the routine preoperative medical and physical assessment and the details of previous postoperative nausea and vomiting, history of motion sickness, and migraine headaches were recorded. We excluded patients who had experienced nausea or vomiting 24 hours before the study or who were taking antiemetic medication.

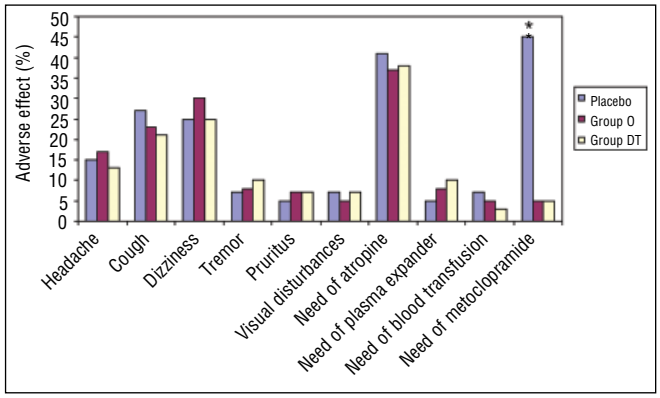

Figure 3. Overall incidence of adverse effects.
* Comparison of the groups (P<0.05).

Tablo 1. Types of the gynecologic operations under general anesthesia (n=90)

Procedures	No.
TAH/MPS	30
TAH/Burch colposuspension	15
VH/AC/PC	9
TAH/SCoP/Culdoplasty	6
TAH/ScoP/Culdoplasty/PC	12
VH/SSF/PC	6
VH/SSF/Culdoplasty/AC/PC	6
TAH/BSO/Pelvic para-aortic lymphadenectomy (ovarian cancer)	3
Type III hysterectomy/Pelvic para-aortic lymphadenectomy (cervical cancer)	3

TAH: Total abdominal hysterectomy and/or bilateral salpingo-oopherectomy; MPS: Midurethral polyproplyene sling; SCoP: Sacrocolpopexy; AC: Anterior colporraphy; PC: Posterior colporraphy; SCxP: Sacrocervicopexy; VH: Vaginal hysterectomy; SSF: Sacrospinous ligament fixation.

Tablo 2. Demographic data of the patients, duration of anesthesia, bleeding and cost-effectiveness

Variables	Placebo (n=30) Mean ± SD	Group O (n=30) Mean ± SD	Group DT (n=30) Mean ± SD
Age (years)	46 ± 16	49 ± 14	47 ± 17
Weight (kg)	68.4 ± 15.3	73.7± 15.0	71.6 ± 15.1
Height (cm)	157 ± 11	161 ± 13	159 ± 15
Duration of anesthesia (min)	149 ± 7	154 ± 8	145 ± 9
Bleeding (ml)	940 ± 60	980 ± 70	930 ± 40
Cost-effectiveness	2 Euro	30* Euro	10 Euro

Group O: Intravenously ondansetron

Group DT: Orally disintegrating tablet

* Comparison of the groups (P<0.05).

General anesthesia was induced with thiopental (7 mg/kg) and fentanyl (1 µg/kg). Muscle relaxation for tracheal intubation was achieved with vecuronium (0.1 mg/kg). Anesthesia was maintained with nitrous oxide (70%), oxygen (30%), and sevoflurane (1.5%-2.5%). Fentanyl (1 µg/kg) was given just before the incision and every 45 minutes thereafter. At the end of surgery, muscle relaxation was reversed with neostigmine (2.5 mg) and atropine (1 mg) intravenously. Bradycardia (heart rate <50 bpm) was treated with atropine (0.08 mg/kg) intravenously.

The patients were prospectively randomized to receive intravenous 100 mL saline (0.9% NaCl) containing either ondansetron 8 mg/4 mL enjectable (group O) (Zofran™-GlaxoSmithKline-Italy) or only saline (group placebo) within 15 minutes preoperative and 8 mg orally disintegrating ondansetron tablet (group DT) (Zofran™ Zydis-Glaxo SmithKline-Italy) were administered. The staff evaluating the patients during postoperative period was blinded for postoperative nausea and vomiting. We used tramadol (1 mg/kg IV) at the patient's request for postoperative analgesia.

The patients were evaluated for postoperative nausea and vomiting at 1st, 10th, 20th, 30th, 60th, and 120th minutes and 6th hours postoperatively. The rescue medication was metoclopramide 10 mg IV, which was prescribed for prolonged nausea (exceeding 10 minutes) or vomiting. The following adverse effects were recorded: headache, cough, dizziness, tremor, pruritus, disturbances in hearing and vision, low oxygen saturation (SpO_2 <90%), hypotension (systolic pressure <90 mm Hg), bradycardia (heart rate <50 bpm), and the need of blood or colloids.

Mann-Whitney U-test and χ^2 test were used for the incidence of postoperative nausea and vomiting and adverse effects. Demographic data was performed by Student's t test. A p value <0.05 was considered as statistically significant. Analyses were performed using commercially available software (SPSS 12.0 demo, SPSS Inc, Chicago, Illinois).

Results

Two patients in group O (because of missing data), one patient in group DT and one patient in the placebo group discontinued and all were excluded. Data from the remaining 90 patients included in the study were analyzed (30 patients in each group). There were no statistically significant differences between the group members in weight, height, age, bleeding and duration of general anesthesia (Table 2). Costs in group O was found to be higher than group DT.

The incidence rates of nausea and vomiting were higher in placebo group than other groups at 1st, 10th, 30th, 60th, and 120th minutes and 6th hours postoperatively (P<0.05) (Figures 1 and 2). Conversely, the incidence rates of nausea and vomiting in group O were similar to those in group DT.

There were no statistically significant differences in the incidence rates of headaches, cough, dizziness, tremor, pruritus, visual disturbances, need of atropine, need of plasma expander, and need of blood transfusion among all groups (Figure 3). Only, the need of metoclopramide in placebo group was higher than others (P<0.05). There were no statistically significant differences in the incidence of analgesic consumption among all groups (P>0.05).

Discussion

Postoperative nausea and vomiting is a common complication that is not easy to prevent. There are some medications such as cyclizine (antihistaminic), scopolamine (anticholinergic), and droperidol (antidopaminergic) in the prevention of the postoperative nausea and vomiting in practice. However, these medications have side effects such as sedation, disphoria, and extrapramidal symptoms with the limitation in using them (9).

Experimental studies showed that ondansetron, a selective seratonine receptor antagonist (5-HT3), has highly antiemetic effect with the lower side effects in the patients taking chemotherapy or radiotherapy (8,10,11). It was shown that ondansetron 8 mg orally disintegrating dissolving rapidly reduced the nausea and vomiting which were induced by radiotherapy (8). We have demonstrated that ondansetron intravenously and ondansetron orally disintegrating tablet decreased the incidence rates of nausea and vomiting and reduced the severity of nausea.

Postoperative nausea and vomiting was reported at 92% in gynecologic patients who underwent abdominal insufflation (12). In a placebo-controlled study, Leeser et al. (13) administrated 16 mg ondansetron one hour before anesthesia induction to the patients who underwent gynecologic operation. They found the incidence rates of nausea and vomiting 52% and 40% for the placebo group and 17% and 12% for the ondansetron group, respectively, in recovery room. Bilgin et al. (14) reported the incidence rates of nausea within first 10 minutes 75% in the placebo group, 40% in the ondansetron group, and 45% in the tropisetron group postoperatively and the incidence rates of vomiting 40%, 15%, and 20% in the same groups, respectively. In the present study, the incidence rates of nausea particularly during the first 10 minutes were 60%, 20%, 23% for placebo, group O and group DT, respectively. The incidence rates of vomiting were 15%, 4% and 0% in the same groups, respectively.

Bilgin et al. (14) found the incidence rates of vomiting in 60 minutes 25% for the placebo group, 5% for the ondansetron group, and 10% for the tropisetron group and no vomiting were observed in all groups. In our study, the incidence rates of vomiting in 60 minutes were found 10% for the placebo group, 4% group O, and 5% group DT. Vomiting in 60 minutes was determined in two patients in placebo group.

Bilgin et al. (14) reported no headache in the placebo and ondansetron group, whereas the incidence of headache was 10% in the tropisetron group. However, the incidence rates of headache reported by Du Pen et al. were 10% in the tropisetron group, 11-21% in the ondansetron group (15), and 11% in the ondansetron tablet group and the incidence reported by Davidson et al. was 9% in DT group (16). In the present study, the incidence rates of headache were 15% in placebo group, 17% group O, and 13% DT group. The incidence rates of the other side effects were similar to each other. Only the need of metoclopramide in placebo group was higher than the other groups (45% in the placebo group, 5% in group O, and 5% group DT).

Davidson et al. (16) observed that DT reduced perfectly the incidence rates of nausea and vomiting for cyclophosphamide-induced emesis in cancer patients. Lebourgeois et al. (8) showed that orally ondansetron disintegrating tablet subsided efficiently nausea and emesis in the treatment of fractioned radiotherapy-induced. In this study, we found that DT reduced greatly the incidence of nausea and vomiting after major gynecological procedures.

Postoperative nausea and vomiting is recognized to be a common complication of gynecological surgery performed under general anesthesia. The high incidence of postoperative nausea and vomiting in population may justify the use of prophylactic antiemetics. Using antiemetics in this way, however, does raise cost-effectiveness issues. At the drug dosages used, we found that ondansetron IV and DT performed similar antiemetic effects, despite an approximately 3-fold rised price for the IV form.

In conclusion, we found that ondansetron orally disintegrating tablets were as effective as the intravenous form in the prevention of postoperative nausea and vomiting after major gynecological procedures. Orally disintegrating tablets may be used instead of the intravenous form, as they are inexpensive and easier administrated.

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