The Efficacy of Different Antiemetics for Laparoscopic Gynecological Surgery

LAPAROSKOPİK JİNEKOLOJİK CERRAHİDE FARKLI ANTİEMETİKLERİN ETKİSİ

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Summary

Postoperative nausea and vomiting (PONV) remains one of the most unpleasant side-effects experienced by patients postoperatively. In the present study, we investigated the efficacy of droperidol, tropisetron, ondansetron, granisetron compared with metoclopramide for the prevention of PONV.

ASA I-II physical status between aged 20-45 years old, scheduled for laparoscopic gynecological procedures, 125 female patients were included in this study. Group I (control) received 10mg metoclopramide (M), group II received 2mg tropisetron (T), group III received 4mg ondansetron (O), group IV received 1mg droperidol (D) and group V received 3 mg granisetron (G) five minutes before induction of anaesthesia. With respect to nausea, vomiting and both nausea and vomiting, patients were observed at 30 min, 1, 2, 4 and 24 hours postoperatively.

$5HT_3$ receptor antagonists (T,O,G) and droperidol had much better effect than metoclopramide. However, droperidol group had the lowest requirement of postoperative analgesic and droperidol is also cheaper than $5HT_3$ receptor antagonists.

We can say, droperidol is an effective alternative to $5HT_3$ receptor antagonists and metoclopramide for prevention of PONV.

Key Words: Anti-emetics, Serotonin antagonists, Nausea and vomiting

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Özet

Postoperatif bulantı ve kusma, hastalar tarafından bu dönemde karşılaşılan yan etkilerden en hoş olmayanı olarak belirtilmektedir. Çalışmamızda postoperatif bulantı ve kusmayı önlemede droperidol, tropisetron, ondansetron ve granisetronun etkisini metoclopramide ile karşılaştırdık.

ASA I-II sınıfı, 20-45 yaş arası, laparaskopik jinekolojik girişim planlanan 125 bayan olgu çalışmaya dahil edildi. Olgular rasgele beş eşit gruba ayrılarak 1.grup (kontrol) 10 mg Metoclopramide, 2.grup 2 mg Tropisetron, 3.grup 4 mg Ondansetron ve 5.grup 3 mg Granisetron anestezi indüksiyonundan beş dakika önce aldı. Postoperatif dönemde 30.dk, 1.,2.,4. ve 24. saatlerde bulantı, kusma, bulantı+kusma ayrı ayrı değerlendirildi.

Çalışmamızda $5HT_3$ reseptör antagonistleri (T,O,G) ve droperidol grubu metoclopramid'den daha iyi bir anliemetik etkiye sahip idi. Ancak droperidol grubu en düşük postoperatif analjezik gereksinimine sahipti. Droperidol aynı zamanda 5HT3 reseptör antagonistlerinden daha ucuz bir ajandır. Sonuç olarak droperidolün postoperatif bulantı ve kusmayı önlemede metoclopramide ve $5HT_3$ reseptör antagonistlerine alternatif olabileceği düşüncesindeyiz.

Anahtar Kelimeler: Anti-emetikler, Seretonin antagonistleri, Bulantı ve kusma

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PONV is one of the most common complications following general anaesthesia and surgery. It predisposes patients to increased pain, bleeding, dehydratation, electrolyte imbalance and retardation in wound healing as well as being the principle source of prolonged discharge and unplanned postoperative hospital admission (1).

The aetiology and consequences of PONV are complex and multifactorial: gender, age, anxiety, anaesthetic and analgesic drugs, type and duration of the surgical procedure, previous history of motion sickness or PONV, obesity and pain (2,3). Currently, the overall incidence of PONV is estimated to be 25%-30% with severe, intractable PONV estimated to occur in approximately 0,18% of all patients undergoing surgery (4). One of the highest incidences of PONV occurs after gynecological laparoscopy, ranging from approximately ***40-11%*** (1).

A preferred anti-emetic would be the one which is effective while having minimal side effects that cause hospital admission (5). Commonly used antiemetics include anticholinergics (scopolamine), butyrophenones (droperidol), benzamides (metoclopramide), prochlorperazine, (phenothiazines) and promethazine. These antiemetics have varying effectiveness and have limitations due to side-effects such as sedation, hypotension, dysphoria, dry mouth or extrapyramidal reactions (4). The specific antagonist of the 5-hydroxy tryptamine (5-HT3) receptor have been progressively introduced in anaesthesiology to prevent or treat PONV (6). These antiemetics don't have the adverse effects of the older, traditional antiemetics. Headache and dizziness are the main adverse effects of the serotonin receptor antagonists in the dosages used for PONV (4).

The purpose of this study was to evaluate the effectiveness of droperidol, tropisetron, ondansetron and granisetron compared with metoclopramide for the prevention of PONV.

Material and Method

Following the Faculty Ethics Committee approval and having obtained written informed consent, we studied 125 female patients aged between 20-45 years old, ASA I-II physical status, scheduled for laparoscopic gynecological procedures. Exclusion criteria were laboratory or clinical evidence of cardiovascular, hematologic, pulmonary, renal, hepatic, neurological or endocrine abnormalities, morbid obesity, a history of substance abuse, antiemetic or psychoactive medication within 24 hr before surgery and the usage of nasogastric tube postoperatively.

Patients were randomly assigned to one of five intravenous treatment categories: Group I (control) received 1 Omg M, Group II received 2mg T, Group III received 4mg O, Group IV received lmg D, Group V received 3mg G. All of five medications were diluted to a final volume of 10ml with normal saline and were administered within 30 seconds, five minutes before induction of anaesthesia. Drugs were prepared in identical syringes by staff who were not involved in the study. The anaesthetist and investigator were unaware of the drug administered.

Vital signs, including heart rate, non-invasive arterial blood pressure and peripheric arterial oxygen saturation were recorded upon administration of the study medications, at 5^{1} min after administration of the antiemetics, after induction of anaesthesia and in every 15 min peroperatively.

None of the patients had premedication. All patients received a standardised anaesthetic technique. Anaesthesia was induced with 5mg.kg"' thiopentone, l,5mg.kg" Sch and maintaned with 70% $N_2$0-0_2, 0,7-1% isoflurane. Analgesia at induction and during maintenance of anaesthesia was provided by 0,05mg bolus doses of fentanyl. The muscle relaxation was achieved with 2mg bolus doses of vecuronium and where appropriate reversed with 0,5 mg atropine and lmg neostigmine. The duration of anaesthesia and surgery were recorded. The doses of used opioid intraoperatively were also noted. For postoperative analgesia, intramuscular (i.m) metamizol was administered. For the purpose of exploratory analysis, the observation period was divided into two assessment periods as early and late PONV. While early PONV was assessed at 30^{th}, 60^{th}min, 2^{nd} and 4%, late PONV was assessed at 4^{lh}-24^{lh} h during postoperative period. The occurrence of emetic episodes, the occurrence of nausea and the occurrence both nausea and vomiting were recorded separately for these two periods as present or absent. If the patients complained of nausea and vomiting, metoclopramide was administered in the postoperative period. Patients who received rescue medications were considered as treatment failures. Complete response was described as no ernes is and vomiting during the first 24 h after anaesthesia. The use of rescue antiemetics and the requirement of analgesic were also recorded. Assessments were continually made in the recovery room and during hospital stay by study nurse. Patients were questioned with regard to possible side-effects of study medications within 24 h postoperative period.

Continuous data were compared by analysis of variance using the Kruskal-Wallis test. Hemodynamic data were compared by analysis of variance

Table 1. The demographic datas (mean ± SD)

	Group I (n=25)	Group II (n=2S)	Group III (n=25)	Group IV (n=25)	Group V (n=25)
Age (year)	33,36±12,46	31,52+5,73	30,28+5,89	29,40+5,41	36,72±10,07
Duration of surgery (min)	51,24+50,54	52,28+20,26	58,84+31,86	57,08+30,88	67,40+34,97

for repeated measures within and between the study groups. The incidance of nausea and combined nausea and vomiting were compared by using the Chi-square test. Probability values under 0.05 were considered significant.

Results

No significant differences were found regarding age, weight and duration of surgery among the five study groups (p>0,05) (Table 1). Study groups were similar with respect to surgery type.

The percentage of nausea, vomiting, both nausea and vomiting are shown in Figure 1,2,3. The incidence of nausea at 30th min in Group D and O was significantly decreased than Group M (p<0,05). The incidence of nausea at 24th h was significantly decreased in all groups when compared with M. The vomiting at 30' min in Group D, O and T was statistically decreased than group M. The nausea at 60th min and 2nd h was similar among the groups. The incidence of vomiting at 30th min in Group D, O and T was significantly decreased compared with Group M (p<0,05). When both nausea and vomiting were considered, the differences at 30th min in Group T and D were significant compared with Group M.

When early PONV was assessed, complete response was reached at 2nd h and 4th h in Group O, D and G, at 60th min in group T. Regarding late PONV, group T, O, D and G had complete response. There were no significant differences among the groups regarding the haemodynamic parameters during the postoperative period (Figure 4,5,6).

The requirement of postoperatively antiemetic was significantly high in Group M (%40). The lowest antiemetic requirement was observed in

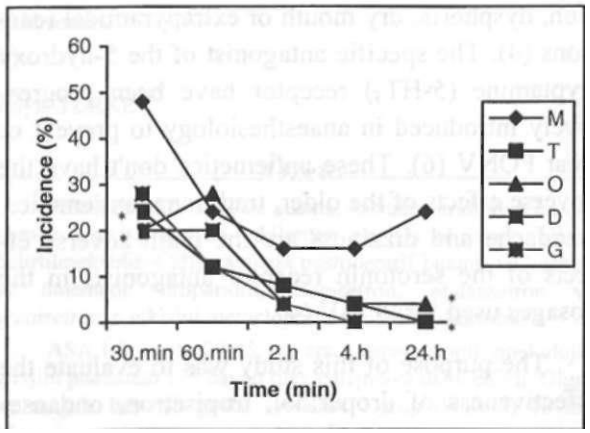


Figure 1. The percentage of nausea.
(*)p<0,05 when compared with metoclopramide group

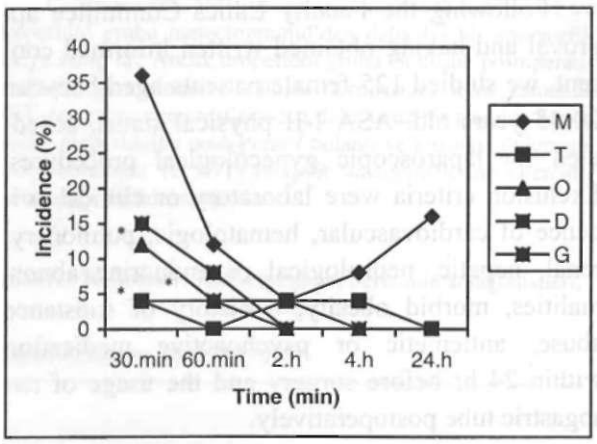


Figure 2. The percentage of vomiting.
(*)p<0,05 when compared with metoclopramide group

Group D (%12) and Group T (%4). Group O and G had same antiemetic requirement (%32). Group D also had lowest postoperative analgesic requirement (%24) but it wasn't significant (p>0,05).

When the complications were compared, no patient experienced hypertension, hypotension,

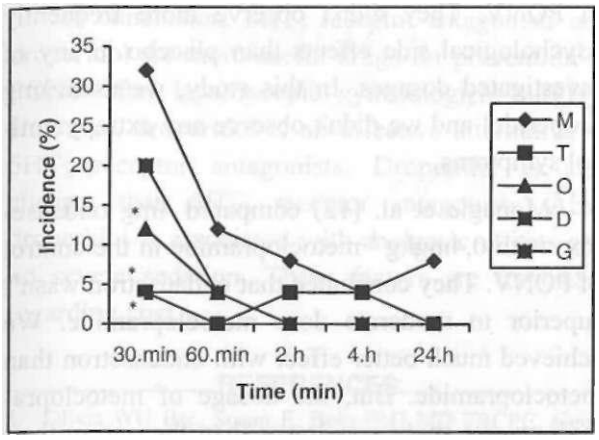
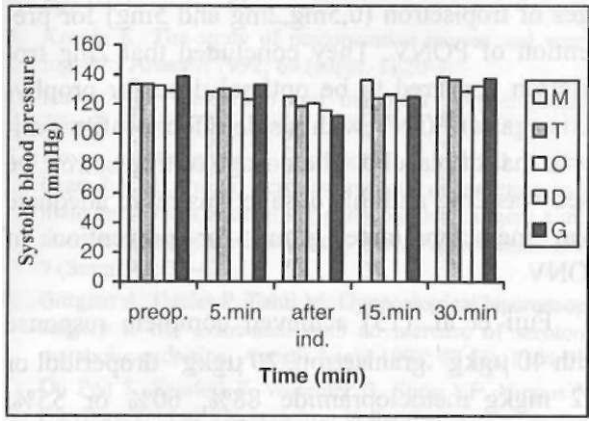


Figure 3. The percentage of nausea and vomiting.
(*)p<0,05 when compared with metoclopramide group



cough, hiccup or headache. Dry mouth was observed in all groups 16%, 12%, 24%, 12% and 32% respectively. No patient experienced sedation or extrapyramidal symptoms.

Discussion

Gynecological laparoscopic surgery is associated with a high incidence of PONV (6). Although routine antiemetic prophylaxis is clearly unjustified, patients at high risk for postoperative emesis should receive special considerations with respect to the prophylactic use of antiemetic drugs (2).

The more commonly used antiemetics are associated with side effects including sedation, dry mouth, hypotension and extrapyramidal reactions (5). These symptoms can cause a prolonged recovery time and increased patient morbidity. An effective antiemetic which could be used to treat nausea and emesis, without extending recovery time, would be a valuable tool for the anaesthesiologist (7).

In this study, we investigated the effectiveness and side-effects of droperidol and $5HT_3$ receptor antagonists over metoclopramide. We observed better antiemetic effect in group D and $5HT_3$ receptor antagonists than group M.

The newest class of antiemetics used for the prevention and treatment of PONV are the serotonin receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron). The seratonin recep-

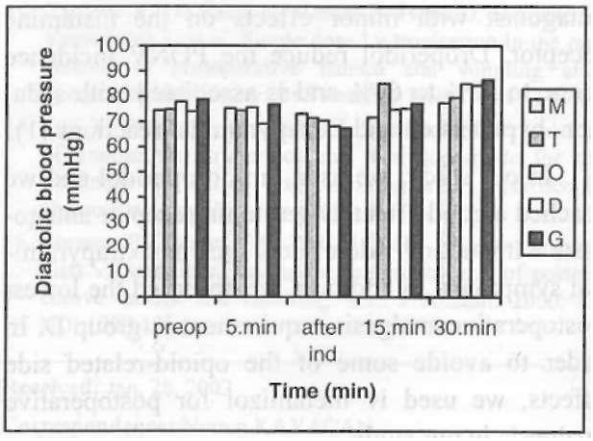


Figure 5. The values of diastolic blood pressure.

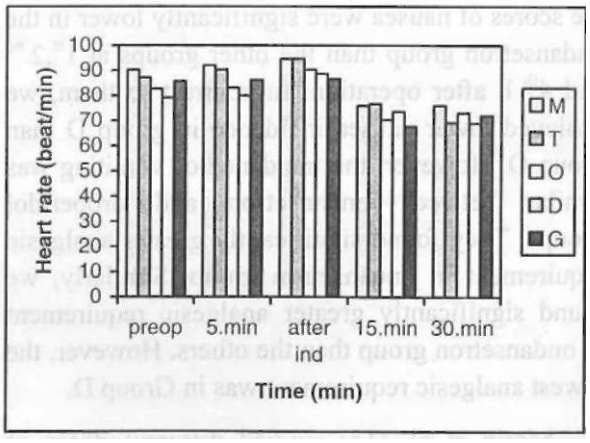


Figure 6. The values of heart rate.

tor antagonists have improved antiemetic effectiveness but are not as completely efficacious for PONV as they are for chemotherapy-induced nausea and vomiting (4). According to our results, $5HT_3$ receptor antagonists highly improved PONV.

Bilgin at al. (8) investigated the effect of ondansetron and tropisetron versus saline for PONV. They found that ondansetron and tropisetron were similarly efficient in prevention of PONV. We attained adequate and similar effect among the $_5HT_3$ receptor antagonists. In contrast to our results, Kafah et al. (9) found that the differences between ondansetron and metoclopramide were not significant. But, they had same opinion with us with respect to $_5HT_3$ receptor antagonists were much expensive.

Droperidol is primarly a dopamine-2 receptor antagonist with minor effects on the histamine receptor. Droperidol reduce the PONV incidence range to 22% to 60% and is associated with sedation, hypotension and extrapyramidal reactions (1).

In our study, we used lmg droperidol and we reached a good effect as serotonin receptor antagonists without any side effects such as extrapyramidal symptoms. In addition, we observed the lowest postoperative analgesic requirement in group D. In order to avoide some of the opioid-related side effects, we used iv metamizol for postoperative analgesia in our study.

Paxton et al. (10) investigated ondansetron 4mg, metoclopramide lOmg, droperidol lmg or placebo in the control of PONV. They found that the scores of nausea were significantly lower in the ondansetron group than the other groups at 1^{st}, 2^{nd} and 4 h after operation. In contrast to them, we achieved lower nausea incidence in group D than group O. However, the incidence of vomiting was similar between ondansetron and droperidol groups. They found significantly greater analgesic requirement in ondansetron group. Similarly, we found significantly greater analgesic requirement in ondansetron group than the others. However, the lowest analgesic requirement was in Group D.

Morin et al. (11) studied different doses of droperidol (0,625mg,l,25mg, 2,5mg respectively) in PONV. They didn't observe more frequently psychological side effects than placebo in any of investigated dosages. In this study, we used lmg droperidol and we didn't observe any extrapyramidal symptoms.

Monagle et al. (12) compared 4mg ondansetron with 0,4mgkg"' metoclopramide in the control of PONV. They concluded that ondansetron wasn't superior to moderate dose metoclopramide. We achieved much better effect with ondansetron than metoclopramide. But, the dosage of metoclopramide in our study was lower than the one in their study. Similar to our results, Polati et al. (13) concluded that 4mg ondansetron was more effective than lOmg metoclopramide.

Capovet et al. (14) investigated different dosages of tropisetron (0,5mg,2mg and 5mg) for prevention of PONV. They concluded that 2mg tropisetron appeared to be optimal dose for prophylaxis against PONV with a side effect profile similar to that of placebo. The dosage of tropisetron we used was 2mg and this dosage was more adequate than metoclopramide group for prevention of PONV.

Fuji et al. (15) achieved complete response with 40 M-gkg"' granisetron, 20 figkg"' droperidol or 0,2 mgkg"' metoclopramide 88%, 60% or 55%, respectively. Droperidol and tropisetron groups were superior to metoclopramide (40%) with respect to requirement of rescue antiemetic. Ondansetron and granisetron groups were similar regarding to the requirement of rescue antiemetic.

Loewen et al. (16) suggested that $5HT_3$ receptor antagonists were superior comparing with droperidol and metoclopramide. We observed that droperidol had similar effect compared with $5HT_3$ receptor antagonists. Group metoclopramide had inadequate effect. Also, the lowest need for analgesic was observed in group droperidol.

The present study demonstrated that $5HT_3$ receptor antagonists and droperidol are superior effects during the 24h period postoperatively when given prophylactically in laparoscopic surgery. Droperidol group had also the lowest requirement of analgesic.

In conclusion, $5HT_3$ receptor antagonists and droperidol are more useful drugs for prevention of PONV after laparoscopic gynecological surgery. However, droperidol is an effective alternative to $5HT_3$ receptor antagonists. Droperidol is also cheaper than $5HT_3$ receptor antagonists. Also, droperidol is associated with analgesic effects and no severe sedation. These factors are important regarding cost.

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