The Comparative Study of Ondansetron and Metoclopramide Effects in Reducing Nausea and Vomiting After Laparoscopic Cholecystectomy

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Abstract- Postoperative nausea and vomiting (PONV) are one of the most common complications of anesthesia and without prophylactic intervention occurs by about one-third of patients under general anesthesia. The aim of this study was to compare the efficacy of ondansetron and metoclopramide in reducing PONV after laparoscopic cholecystectomy. In this study, 60 patients undergoing laparoscopic cholecystectomy were randomly allocated into two equal groups (n=30), and in the first group 10 mg metoclopramide and in the second group 4 mg ondansetron preoperatively were injected. Nausea and vomiting and the need for rescue antiemetic treatment in recovery and 6 hr. and 6-24 hrs. After surgery were evaluated. Data were analyzed by SPSS software with chi-square test and analysis of variance (ANOVA). The incidence of nausea in metoclopramide was 43.3 % and in ondansetron was 33.3 %. The difference between two groups was not significant (*P*=0.6). The incidence of vomiting in metoclopramide was 20% and in ondansetron was 26.7%, and there was not any significant difference between intervention groups (*P*=0.12). For prevention of PONV after laparoscopic cholecystectomy, both metoclopramide and ondansetron are effective, and in preventing of nausea, ondansetron is more effective than metoclopramide, whereas there was not any significant difference between two drugs in preventing of vomiting.

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Introduction

Postoperative nausea and vomiting (PONV) is a common complication of general anesthesia. PONV is still a clinical problem after anesthesia and surgery that will cause a delay in discharge from hospital (1). Without preventive interventions, PONV occurs in about one-third of patients (10-60%) under general anesthesia, and its complication includes wound dehiscence, bleeding, increased the risk of gastric contents aspiration, patients' delayed discharge, rehospitalisation, and decreased patient satisfaction. The most patients believe that PONV can be even more disturbing than postoperative pain (2). Several factors are involved in the etiology of PONV, so its extensive prevention is not cost effective. The ability to identify high-risk patients for preventive intervention could significantly improve the quality of patient care and satisfaction after surgery. In various studies, various factors such as female gender, history of motion sickness, previous history of PONV, nonsmoking and use of postoperative opioids have been reported as risk factors for PONV (1).

Preventive interventions to reduce PONV include modification of anesthesia techniques and pharmacological intervention. Although preventive interventions to prevent PONV are significantly more effective than treatment, some patients need to be treated after surgery even after adequate preventive interventions. Both the drug categories and administration time are important factors to choose the appropriate drug for the prevention of this complication. In several studies, the effects of traditional medications

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(metoclopramide, perphenazine, prochlorperazine, droperidol, and cyclizine) and 5-hydroxy tryptamine receptor antagonists (ondansetron, dolasetron, granisetron, and tropisetron) have been compared in terms of preventing PONV, and the results have been different and in some cases contradictory (3). From among these medications, metoclopramide by inhibiting dopamine receptors at the center of medulla oblongata chemoreceptor trigger zone (CTZ) reduces or inhibits nausea and vomiting. Ondansetron reduces the activity of the vagus nerve, which deactivates the vomiting center in the medulla oblongata, and also blocks serotonin receptors in the chemoreceptor trigger zone (4). Ondansetron is an effective drug in the prevention and treatment of PONV by having low side effects (5).

Due to the minimally invasive nature and fewer complications, comparing with open surgery, laparoscopic surgery is preferable in many patients. Because of its less complication, laparoscopic cholecystectomy has been selected for treating acute cholecystitis. However, it has some complications such as PONV, and this leads us to identify a good way to control them (6). In addition, since the aim of laparoscopy is a reduction of hospitalization time, if we are able to control the PONV after laparoscopic cholecystectomy, we will be better able to achieve our purpose. The aim of this study was to compare the effects of metoclopramide and ondansetron in preventing PONV after laparoscopic cholecystectomy.

Materials and Methods

In this double-blind clinical trial study (registered at Iranian Registry of Clinical Trials; registration code: IRCT201111094093N3), after approval of the university ethical committee, written, informed consent to participate in the study was obtained from 60 patients who were aged 15-80 years, classified as ASA physical status I or II, and scheduled for elective laparoscopic cholecystectomy surgery. The exclusion criteria included gastroesophageal reflux, severe obesity, difficult airway management, pregnancy, breastfeeding, liver or kidney disease, history of opioid addiction and alcoholism, Body Mass Index (BMI)>30, neuromuscular diseases, mental diseases, diabetes, and gastrointestinal obstruction. Using double-blind randomization technique these patients were given either group M (metoclopramide 10 mg) or group O (ondansetron 4 mg).

The drugs were prepared in the same 2 cc syringes, and the injection was immediately before anesthesia induction performed by an anesthesiologist who was unaware of the drug kind. All patients received 1 mg of intravenous midazolam as premedication; the anesthetic induction was similarly conducted on each two groups by 2 μg/kg of fentanyl, 2 mg/kg of propofol and 0.5 mg/kg of atracurium. After tracheal intubation, the maintenance of anesthesia was established by propofol infusion 100 μg/kg/min. Muscle relaxation maintained with injection atracurium 0.25 mg/kg with intermittent positive pressure ventilation to maintain ETCO2 between 4.6-5.2 Kpa. At the cessation of the surgical procedure, 0.02 mg/kg atropine and 0.04 mg/kg neostigmine were administered by IV to reverse muscle relaxation, and the trachea was extubated when the patient was awake, and respiration was adequate and regular. The patients in the recovery room were evaluated in terms of the incidence rate of nausea and vomiting, a number of vomiting, the need for rescue antiemetic treatment, opioid pain therapy, and shivering incidence rate by anesthesiology assistant who was unaware of the type of medication prescription. In addition, the patients were evaluated during 6 and 6-24 hours after surgery, in terms of the incidence of nausea, vomiting, and the need for rescue antiemetic treatment. For each case of vomiting, or nausea for more than 5 minutes, metoclopramide 10 mg was intravenously injected.

Considering 40% reduction in the incidence of nausea and vomiting (from 70% to 30%) in previous studies, and the rate of α=0.05 and β=20%, the sample size was calculated as the number of 30 patients per group.

The collected data in previously prepared checklists was entered into statistical software SPSS version 18, analysis of variance (ANOVA) was used for comparison of all continuous variables between the groups. *Chi*-square test was used for analysis of categorical demographic data. Differences were considered significant when $P<0.05$.

Results

The main demographic and clinical characteristics of the patients under investigation were not significantly different between the two groups (Table 1).

Table 1. Demographic and clinical characteristics of patients

Variables		Ondansetron (n=30)	Metoclopramide (n=30)	*P*
Gender	**Male**	7(23.3)	4(13.3)	0.5
	Female	23(76.7)	26(86.7)	
Age (yr)		45.97±13.07	46.27±15.19	0.93
Weight (kg)		72.47±7.91	69.97±8.82	0.25
Residency	**Urban**	16(53.3)	23(76.7)	0.103
	Rural	14(46.7)	7(23.3)	
Smokers		5(16.6)	3(10)	0.71
Duration of operation (min)		84.67±16.01	79.23±13.42	0.16
Systolic Blood Pressure(mmHg)		128.5±10.14	132.47±11.45	0.16
Diastolic Blood Pressure(mmHg)		77.10±7.21	81.43±9.67	0.06
Heart Rate(beat/min)		81.33±12.82	82.20±13.17	0.8

Data presented as mean±SD or number (%)

The incidence of PONV and need for rescue antiemetic medication in the recovery room, during the first 6 hrs, and during 6-24 hrs after surgery is summarized in Table 2.

Table 2. Incidence (%) of PONV and proportion (%) of patients requiring the antiemetic medication

Outcome		Ondansetron (n=30)	Metoclopramide (n=30)	*P*
In recovery	**Nausea**	1(3.3)	9(30)	0.012
	Vomiting	0(0)	1(3.3)	1
	Antiemetic medication	0(0)	6(20)	0.024
During 6 hrs	**Nausea**	7(23.3)	13(43.3)	0. 17
	Vomiting	6(20)	5(16.7)	1
	Antiemetic medication	7(23.3)	8(26.8)	1
During 6-24 hrs	**Nausea**	3(10)	0(0)	0.24
	Vomiting	2(6.7)	0(0)	0.5
	Antiemetic medication	3(10)	0(0)	0.23
Entire 24hrs	**Nausea**	10(33.3)	13(43.3)	0.6
	Vomiting	8(26.7)	6(20)	0.7
	Antiemetic medication	10(33)	11(36)	1

In terms of the incidence rate of nausea in the recovery room, we found the significant statistical difference between ondansetron and metoclopramide groups (*P*=0.012). The incidence of nausea during the first 6 hrs (*P*=0.17) and during 6-24 hours after surgery was not statistically significant between two groups (*P*=0.24). In terms of the entire 24 hrs period incidence of nausea, we don't saw the statistically significant difference between ondansetron and metoclopramide groups (*P*=0.6).

The incidence rate of vomiting during recovery room (*P*=1), the first 6 (*P*=1), 6-24 hrs after surgery (*P*=0.5) and the entire 24 hrs period was not a significant difference among the two groups (*P*=0.7).

In terms of the need for rescue antiemetic medication during recovery room, there was a statistically significant difference between ondansetron and metoclopramide groups (*P*=0.024). However, we couldn't see a statistical difference during the first 6 (*P*=1) and during 6-24 hrs after surgery between two groups (*P*=0.23).

Among the patients, 5 patients (16.7%) from ondansetron group, 3 patients (10%) from metoclopramide group had more than once vomiting during the first 6 hours after surgery, and the difference between the mentioned groups was not statistically significant (*P*=0.06). This rate in two groups during 6-24 hrs after surgery was reduced to the first 6 hrs, and the number of vomiting between groups was not statistically different (*P*=0.66).

The incidence rate of postoperative shivering was not a significant difference among the groups (*P*=0.7).

In terms of the different factors' effect on PONV, smoking (*P*=0.03) and surgery duration greater than 90

minutes (P=0.01) significantly reduced the incidence of this complication in the two groups. However, there was no statistically significant difference between the incidence of this complication and gender and age of patients in different groups (P>0.05).

Discussion

PONV is amongst the most common complications following anesthesia and surgery with a selectively high incidence after laparoscopic cholecystectomy. The cause of PONV after laparoscopic cholecystectomy is complex and multifactorial and depends on various factors such as patients' demographic characteristics, type of anesthetic drugs and techniques, and postoperative cares (7,8).

In this clinical trial, patients were similar in terms of demographic variables, duration of surgery and basic vital signs. In the study of entire 24 hrs period incidence of PONV among the two groups, it was observed that nausea incidence rate and the incidence rate of vomiting in both ondansetron and metoclopramide groups wasn't statistically significant.

Many studies reported that ondansetron is statistically superior to metoclopramide for prevention of PONV (9,10,11,12). Other published studies that evaluated the efficacy of ondansetron and metoclopramide administered intravenously have shown similar reductions in the incidence of PONV during the 24 h post recovery period (13,14,15).

In a separate survey of postoperative nausea in some studies, as well as our study, the effect of ondansetron was higher than metoclopramide (12), however, in other studies, there was no significant difference between the two drugs (13). In terms of the incidence of postoperative vomiting, the result of our study was similar to some studies (13) and was different from other studies (12).

In this study, the effect of smoking history on the incidence rate of PONV was statistically significant, and it had reduced this rate in two groups. This result is similar to results from other studies (1,16) investigating the risk factors for PONV.

In entire 24 hrs period incidence of PONV based on gender, this rate was higher in females although there were no significant differences between different groups. In previous studies female gender is known as one of the risk factors for PONV (1,17).

In our study, the patients were studied in four different age groups. Although the age group above 70 years compared to other age groups had a lower incidence of PONV, this difference was not statistically significant. Other studies also confirm high incidence of PONV in young people (1).

Like most of the studies, this study had also some limitations including the duration of the patients' follow-up. If the duration of follow-up were longer, results that are more accurate would be obtained.

This study shows that both ondansetron and metoclopramide are effective in reducing PONV after laparoscopic cholecystectomy. Effectiveness rate of ondansetron in reducing nausea is more than metoclopramide, but in terms of reducing postoperative vomiting, there was no significant difference between two drugs.

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