Effects of ondansetron, metoclopramide and granisetron on perioperative nausea and vomiting in patients undergone bariatric surgery: a randomized clinical trial

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Research Article

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Abstract

Introduction

Post-operative nausea and vomiting (PONV) is a common problem after bariatric surgeries. In recent years, following the expansion of the number of this type of surgery, special attention has been paid to prevent this phenomenon. Also, several prophylaxis methods have been developed including Enhanced Recovery After Surgery (ERAS) and antiemetics. Nevertheless, PONV has not been completely eliminated and the clinicians are trying to reduce the incidence of PONV, yet.

Methods

After successful ERAS implementation, patients divided into five groups including control and interventional groups. Metoclopramide (MA), Ondansetron (OA), Granisetron (GA) and combination of Metoclopramide and Ondansetron (MO) were used as antiemetics for each groups. The frequency of PONV during first and second days of admission has been recorded.

Results

one hundred thirty patients were enrolled in this study. The MO group showed lower incidence of PONV (46.1%) in comparison to control group (53.8%) as well as other groups. Also, the MO group didn't require rescue antiemetic while one-third of control cases used antiemetics (0 vs 34%).

Conclusion

Using a combination of metoclopramide and ondansetron is a cost-effective antiemetic regimen for reducing PONV after bariatric surgeries. This combination is more helpful when implemented alongside ERAS protocols.

Introduction

Post-operative nausea and vomiting (PONV) is one of the leading causes of patient morbidity after laparoscopic bariatric surgeries. A wide variety of complications related to PONV has been described, such as prolonged length of stay (LOS) in hospital, unnecessary readmissions, delay in oral intake, and bad experience for patients [1]. Although several antiemetic regimens have been tried so far in different studies, the incidence of PONV is not significantly lowered, and it seems that it is impossible to totally eliminate it. On the other hand, the implementation of Enhanced Recovery After Surgery (ERAS) has greatly reduced the incidence of PONV and LOS. [2]. Therefore, a combination of ERAS and multiple antiemetic regimens is currently used to reduce the incidence of PONV. Nevertheless, the optimal regimen has not been found yet, and many trials are conducting to find out the best antiemetic regimen.[1, 2]. In this randomized clinical trial, we compare four different combined and single regimens alongside the implementation of ERAS to show which regimen is more effective.

Methods

After being approved by Iran National Committee for Ethics in Biomedical Research (IR.SBMU.MSP.REC.1399.784), a randomized clinical controlled trial was started with 130 patients in five groups. All the patients were proper candidates for laparoscopic bariatric surgeries, and structured informed consent was obtained from all participants.

All the operations were performed by board certified advanced laparoscopic surgeons in a minimally invasive educational center. All bariatric surgery was performed in our standardized institutional protocols as well as preoperative and postoperative care. Sleeve Gastrectomy (SG) surgeries were performed by using 44Fr Tubes.

To calculate the sample size in the clinical trial, we used the ANCOVA method with web-based tools. Twenty-six patients were estimated for each group [3]. Patients were divided into five groups:

Group 1: Patients who did not receive any antiemetic during hospitalization (NA).

Group 2: Patients receiving metoclopramide alone (MA).

Group 3: Patients who received ondansetron only. (OA)

Group 4: Patients receiving a combination of metoclopramide and ondansetron (MO).

Group 5: Patients who received granisetron alone (GA).

All patients were undergone ERAS protocols. In cases where the patient had PONV (including Group 1), intravenous Metoclopramide 0.2mg (Stat and BiD) was used as a rescue antiemetic.

To reduce the incidence of bias and confounding factors, all anesthetics and antiemetics used were provided from the same brand for each drug (see Appendix).

Patients with severe or moderate gastritis or duodenitis on esophagogastroduodenoscopy were excluded from the study, but patients with mild gastritis or positive rapid urease test on endoscopy, were treated for two weeks with three drugs of pentazole, amoxicillin, and metronidazole, and if the respiratory urease test was negative, they were included in the study and in refractory cases of H. Pylori, they were excluded. According to the American Society of Anesthesiologists (ASA) classification [4], patients with severe respiratory or cardiovascular problems (ASA III or higher) or a history of gastric or small bowel surgery were also excluded. Patients who underwent simultaneous cholecystectomy with bariatric surgery were also excluded (Figure 1).

Statistical Analysis

Information about demographic, clinical, and paraclinical variables, as well as intraoperative data, was [illegible] measure the demographic variables, identification

information, digital scales and meters, as well as obtaining a direct history of the patient were used. The duration of anesthesia was calculated in minutes from the moment of induction of anesthesia to the moment the patient regained consciousness and transferred to Post-Anesthesia Care Unit (PACU). Nausea and vomiting were also recorded by taking a history or direct observation.

Descriptive and analytical functions were used to analyze the information. Frequency, mean and median and standard deviation were used for variables of age, sex, weight, height, body mass index, incidence of nausea and vomiting, etc. (see Table1-6). To investigate the significant relationship between the variables, Correspondence Analysis was used. Partial correlation with Pearson formula was also used to investigate the confounding effect of other variables and their effect on nausea and vomiting.

Table 1
Demographic data

Variable	**Numbers (Percent)**
Total cases	130 (100%)
Age	36.3 (19-59)
Gender	
Men	31 (23.8%)
Women	99 (76.2%)
Weight (average, kilograms)	121.36
Height (average, centimeters)	164.6
Body mass index (average, $\frac{\varvec{k}\varvec{g}}{\varvec{m}^2}$)	44.6, Std = 5.22

Table 2
preoperative clinical infromation

Numbers (percent)	Variable
	Underlying diseases
83 (63.8%)	No UD*
19 (14.6%)	Hypothyroidism
14 (10.8%)	Type-2 Diabetes Mellitus
14 (10.8%)	Hypertension
13 (10%)	Two concurrent UD
3 (2.3%)	Equal or more than three UD
History of previous surgery (general anesthesia)	
55 (42.3%)	No surgeries
48 (36.9%)	One
19 (14.6%)	Two
8 (6.1%)	Three or more
*UD = Underlying disease(s)	

Table 3
preoperative paraclinical information

Variable	Numbers (percent)
Upper endoscopy findings	
Normal	80 (61.5%)
Antral gastritis	21 (16.2%)
Erosive gastritis	13 (10%)
Duodenal erythema	5 (3.8%)
Duodenal diverticula	2 (1.5%)
Biliary gastritis	4 (3.1%)
Esophagitis	4 (3.1%)
Stomach polyp(s)	1 (0.8%)
Respiratory urease test	
Negative	100 (76.9%)
Positive	28 (21.5%)
Fatty liver (based on abdominal ultrasonography)	
No fatty liver	20 (15.4)
Grade 1	41 (31.5)
Grade 2	49 (37.7)
Grade 3	20 (15.4)

Table 4
intra and postoperative information

Variable	Numbers (percent)
Surgery type	
Sleeve gastrectomy	115 (88.5)
Mini-bypass	15 (11.5)
Average time of anesthesia	141.8 (75 305)
Average dose of anesthetics	
Fentanyl	195.16
Midazolam	2.28
Lidocaine	91.9
Thiopental	498.3
Atracurium	63.05
Pain pumps	18 (13.8)

Table 5
incidence of PONV in the perioperative period

	Before oral intake (day 1)		After oral intake (day 2)		
Regimen	Nausea	Vomiting	Nausea	Vomiting	Rescue usage
Control	11	6	7	3	9
MA	12	8	7	2	2
OA	10	5	9	2	6
MO	7	6	2	0	0
GA	9	7	6	3	8

Table 6
total incidence of PONV during admission

Study group	*Total incidence of PONV (including days 1 and 2)*
Control group	53.8
MA	53.8
OA	61.5
MO	46.1
GA	61.5

Results

Demographics

One hundred thirty morbid obese patients were enrolled in this study from March 2021 to August 2021. They were divided into five groups of 26 participants. All demographic information is displayed in the Table 1.

Clinical and paraclinical findings

Information like the presence of underlying diseases, and history of previous episodes of anesthesia, esophagogastroduodenoscopy results, H-Pylori, and fatty liver grade has been described in Tables 2-3.

Perioperative variables

Table 4 indicates the distribution of the type of surgery, the average time of general anesthesia, and the mean dosage of anesthetic medications as well as usage of Patient-Controlled Anesthesia devices.

Also, the findings related to the incidence of nausea and vomiting in the postoperative period on days 1 and 2 are presented in Table 5. It can be quickly realized that the incidence of nausea and vomiting is generally higher on the first day after surgery than on the second day. On the other hand, the highest incidence of nausea on the first day (before starting a liquid diet) was in the metoclopramide group (n = 12) and the lowest was in the metoclopramide and ondansetron group (n = 7). The incidence of vomiting on the first day has a similar distribution; Thus, the highest level is in the metoclopramide group alone (n = 8) and the lowest level is in the ondansetron group alone (n = 5). On the second day, the lowest incidence of nausea and vomiting was in the metoclopramide and ondansetron groups (Table 5).

Results analysis

Table 6 shows the final incidence of nausea and vomiting during the entire hospital stay. As it turns out, the lowest incidence of nausea or vomiting is in the group that used metoclopramide and ondansetron together (46.1%). The highest incidence of nausea or vomiting is related to ondansetron or granisetron

elationship between each of the variables that may be

confusing the results of nausea and vomiting is indicated. In almost all fields, there is no significant relationship between age, sex, body mass index, duration of operation, types of drugs used during anesthesia, underlying diseases and previous surgery, and endoscopic findings with nausea and vomiting. A lower p-value (0.01) in variables such as duration of operation, usage of fentanyl, and thiopental drugs on the first day, means that these variables may have an effect on the incidence of nausea, but this change is not significant (see p values in Table 7)

Table 7
correlation between other variables in the incidence of PONV

	Before oral intake (day 1)		***After oral intake (day 2)***	
variable	**Nausea (p value)**	**Vomiting (p value)**	**Nausea (p value)**	**Vomiting (p value)**
Age	0.740	0.075	0.785	0.192
Gender[1]	0.474	0.027	0.501	0.285
BMI	0.974	0.358	0.162	0.477
Operation time	0.01*	0.905	0.933	0.137
Fentanyl	0.065	0.515	0.562	0.324
Midazolam	0.225	0.427	0.265	0.690
Lidocaine	0.186	0.099	0.046	0.000
thiopental	0.080	0.948	0.187	0.991
Underlying disease[1]	0.210	0.591	0.298	0.246
Number of previous surgeries[1]	0.591	0.260	0.602	0.375
Endoscopy findings[1]	0.029	0.031	0.723	0.540
1=this variable is qualitative and Correspondence Analysis was used to examine its correlation.				
*= negative correlation with Pearson's coefficient equal to -0,247				

Discussion

Our results indicate lower episodes of PONV in the MO group. Also, single drug regimens showed equal or higher in comparison to controlled group. Granisetron is a serotonin-receptor antagonist (5HTRA) and has a great reputation for treating nausea/vomiting after chemotherapy or radiotherapy. For this reason, little information is available about the effect of this drug on PONV after bariatric surgery. The only study in this area showed a 30% incidence of PONV after bariatric surgery. Also combining granisetron with

5]. However, in our study GA couldn't do this and the incidence

of PONV was 61.5%. Ondansetron is another 5HTA that, unlike granisetron, has been studied many times in PONV. Overall incidence of OA has been reported about 50% which is a little lower than our result [6–9]. On the other hand, there are a lot of data from combining ondansetron with other medications such as Aprepitant[10] and Dexamethasone[11] that could lower PONV more than OA. Our ondansetron combination was the MO group. Metoclopramide belongs to the group of medications known as dopamine-receptor antagonists and is widely used as an antiemetic. However, metoclopramide alone is used as an antiemetic for PONV prophylaxis[12], but it is seems that several clinicians use it as a rescue antiemetic[13]. Interestingly, although these two drugs alone are well known, the combination of the two has been less commonly used in PONV after bariatric surgery (see Appendix). More interestingly, this combination has been less used in other laparoscopic surgeries like cholecystectomy [14]. on the other hand, in our study, MO groups showed significantly lower incidence of PONV among other groups (46.1%). Given that, these two drugs have two different mechanism of action it seems that this combination can be a useful regimen for controlling PONV.

Conclusion

Using a combination of metoclopramide and ondansetron is a cost-effective antiemetic regimen for reducing PONV after bariatric surgeries. This combination is more helpful when implemented alongside ERAS protocols. However, there is a scarcity of randomized clinical trials using this combination, and further studies with a high volume of participants can help clinicians to improve their knowledge in PONV prophylaxis.

Declarations

Contributions

BO developed the concept and performed the surgery. ME reviewed and analyzed the cases and co-wrote the paper. NG reviewed and co-wrote the paper.

Conflict of interest

All of the authors declare that they haven't any conflict of interest.

Funding

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Consent for publication

An informed consent was taken from the patient.

Ethical Approval

This topic is approved by Iran National Committee for Ethics in Biomedical Research (IR.SBMU.MSP.REC.1399.784).

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Figures

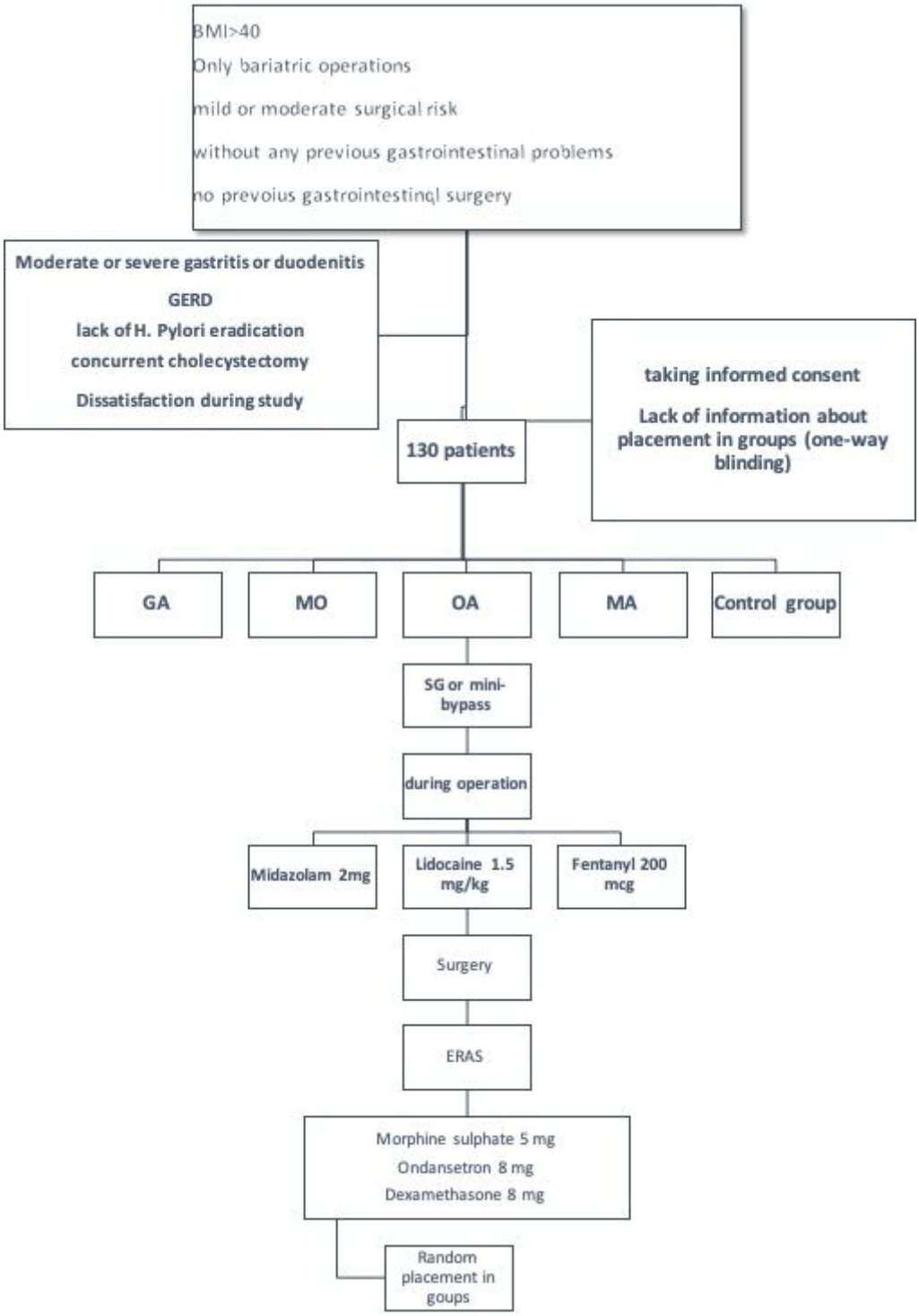

Figure 1

The Enrollment Flow Chart of the Patients