COMPARING THE EFFECT OF MIDAZOLAM AND METOCLOPRAMIDE ON PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANESTHESIA

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ABSTRACT

Background

Postoperative nausea and vomiting is one of the most frequent complications of general anesthesia. The overall incidence of postoperative nausea and vomiting is currently estimated to be around 20 to 30% and in certain high-risk patients; this incidence may reach 70% .

Aims

The aim of the study is to compare the antiemetic efficacy of midazolam or metoclopramide in laparoscopic surgery under general anesthesia.

Methods

In this study 120 patients (ASA I–II) whom underwnet laparoscopic cholecystectomy in Sulaimani Teaching Hospital were evaluated as double-blinded randomized study, patients were allocated randomly to one of three main groups: Group 1 (n= 40) received midazolam (0.03 mg/kg) i.v as a premedication, Group 2 (n= 40) received metoclopramide (10 mg) i.v as a premedication and Group 3 (n= 40) received standard premedication. Anesthesia was standardized for all patients, follow up done for them up to 24 hrs. Data were interpreted by Chi-square test and Pearson's test, using Statistical Package of Social Sciences Software (SPSS).

Results

The incidence of postoperative nausea and vomiting was 20% with midazolam ($P < 0.05$), 35% with metoclopramide ($P > 0.05$), and 57.5% with none of two drugs.

Conclusion

Midazolam is more effective than metoclopramide in preventing post-operative nausea and vomiting.

Keywords: *Post operative nausea and vomiting, Midazolam and Metoclopramide.*

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INTRODUCTION

Postoperative nausea and vomiting is one of the most frequent complications of general anesthesia. Despite introduction of new antiemetic agents, the overall incidence of postoperative nausea and vomiting is currently estimated to be around 20 to 30% [(1)]. In certain high-risk patients; this incidence is still as high as 70% [(2)]. Postoperative nausea and vomiting (PONV) is one of the main complaints after laparoscopy (40-75% of patients) [(3)], it often comes before postoperative pain when patients are asked to rank their concerns [(4)]. PONV can cause prolonged post anesthesia care unit stay and unanticipated admissions following ambulatory surgery, therefore increasing medical costs [(5)]. It also regards the most unpleasant experiences associated with surgery and patient distress, aspiration of stomach contents, limitation of analgesia, poor surgical outcome, dehydration and/or requirement for intravenous fluids and one of the most common reasons for poor patient satisfaction rating in the postoperative period [(4, 6)].

Young age, female gender, patient with history of motion sickness, non-smoker, excessive anxiety, day of menstrual cycle, early pregnancy, diabetes and obesity are increase risk of postoperative nausea and vomiting, the incidence also increase in some type of surgery such as gynecological, ENT, laparoscopy, lithotripsy and strabismus surgery, also using some medications increase or decrease the incidence of PONV such as premedication like antiemetics, opioids, neostigmine or presence of some conditions like hypoxia, hypotension during regional anesthesia affect incidence of PONV[(3,4)].

The aim of this study is to compare the antiemetic efficacy of midazolam against metoclopramide in laparoscopic surgery under general anesthesia.

PATIENTS AND METHODS

After the approval of the proposal of by the Scientific and Ethical Committee of University of Sulaimani/ College of Medicine, a written informed consent was taken from 120 patients (ASA physical status I or II) (ASAI a normally healthy individual, ASAII a patient with mild controlled systemic disease) which scheduled for elective laparoscopic cholecystectomy at Sulaimani Surgical Teaching Hospital.

All patients were fasting to a minimum of eight hours. Anesthesia was standardized for all patients, induction with thiopental sodium (3-5 mg/kg) and fentanyl (1-2 μg/kg). Tracheal intubation was facilitated with Rocuronium (0.5 mg/kg)

Anesthesia was maintained with Isoflurane (1–2.5%) in100% O2; intermittent doses of Rocuronium (0.15 mg/kg) were given during anesthesia to maintain adequate muscle relaxation throughout the procedure.

Close circuit (aeonmed 7300A) was used for controlled mechanical ventilation in all patients and to maintain an end-tidal carbon dioxide tension at 35–40 mmHg. The fresh gas flow was set at (2-2.5 L/min).

ECG, noninvasive blood pressure, and pulse oximetry were used for monitoring, fluid replacement achieved with crystalloids.

Patients were positioned in the reverse Trendelenburg position with the right side of the table elevated.

Any patients on drugs with known antiemetic effect, morbid obesity (> 75% above ideal body weight), cardiac arrhythmias, Parkinson's disease, nausea and vomiting within 24 hrs prior to surgery, and allergic to benzodiazepines and metoclopramide, were excluded from the study.

Patients were randomly assigned to one of three groups (each group: n = 40): patients of (group 1) received (0.03 mg/kg) midazolam i.v, (group 2) (10 mg) metoclopramide i.v (both as premedication agents 3 minutes before induction) and (group 3 or control) received no any drugs as premedication.

At the end of surgery, atropine 1 mg and neostigmine 2.5 mg were given i.v to reverse the effect of neuromuscular blocking agent.

Post-operative pain management done with acetaminophen (i.v) and Diclofenac sodium (i.m), and the patients were followed up for next 24 hrs.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.

Vomiting was the forceful expulsion of gastric contents from the mouth.

Nausea and vomiting were evaluated on a three-point (1 = none, 2 = nausea, 3 = vomiting).

Statistical analysis

Data were interpreted by Chi-square and Pearson's test, using SPSS software, P-values < 0.05 were considered as statistically significant.

RESULTS

During the first 24 hr after anaesthesia, observing all patients for PONV and we found eight of 40 (20%) patients of group 1 who had received midazolam had nausea and vomiting (1 nausea and 7 vomiting) in whom 2 were males, fourteen of 40 (35%) patients of group 2 who had received metoclopramide had nausea and vomiting (2 nausea and 12 vomiting) just one of them was male, twenty-three of 40 (57.5%) patients of group 3 who had received non of two drugs had nausea and vomiting (6 nausea and 17 vomiting) in whom 4 were male (Table 1, Figure 1).

Comparing both groups (1 and 2) with group3 the incidence of PONV in patients who had received midazolam which was significantly ($P<0.05$) lower than the group that received metoclopramide which was non-significant ($P>0.05$) in compare to control group.

The number of males included in the study were 26 patients, 7 of them had nausea and vomiting (26.9%) (2 nausea and 5 vomiting), the remainder 94 patients included in study were female, 38 of them had nausea and vomiting (40.4%) (7 nausea 31 vomiting cases) (Table 2, Figure 2, 3).

The causing factor of nausea and vomiting in group 1; was pain in 2 of patients and remainder 6 patients were due to change in position, in group 2; change in position was the cause for 9 of patients and the other 5 patients were due to pain, in group 3; position changing was the leading cause in 19 patients, while pain was the cause in remainder 4 patients.

Table 1. Incidence of nausea and vomiting according to groups.

Groups	Age (years)		Sex		Nausea	Vomiting	P-value
1	A B C	2 (5%) 25 (62.5%) 13 (32.5%)	M 9 F 31	(22.5%) (77.5%)	1	7	0.02
2	A B C	2 (5%) 33 (82.5%) 5 (12.5%)	M 11 F 29	(27.5%) (72.5%)	2	12	0.093
3	A B C	0 (0%) 35 (87.5%) 5 (12.5%)	M 6 F 34	(15%) (85%)	6	17	

A (20-30) years, B (31-50) years and C (51-60) years, M (male), and F (female).

Table 2. Incidence of nausea and vomiting according to gender.

Groups	NO. of patients%		Nausea and Vomiting%		P- value
	Male	Female	Male	Female	
1	9(22.5%)	31(77.5%)	2(22.2%)	6(19.35%)	0.8
2	11(27.5%)	29(72.5%)	1(9%)	13(44.85%)	0.1
3	6(15%)	34(85%)	4(66.6%)	19(55.88%)	0.39

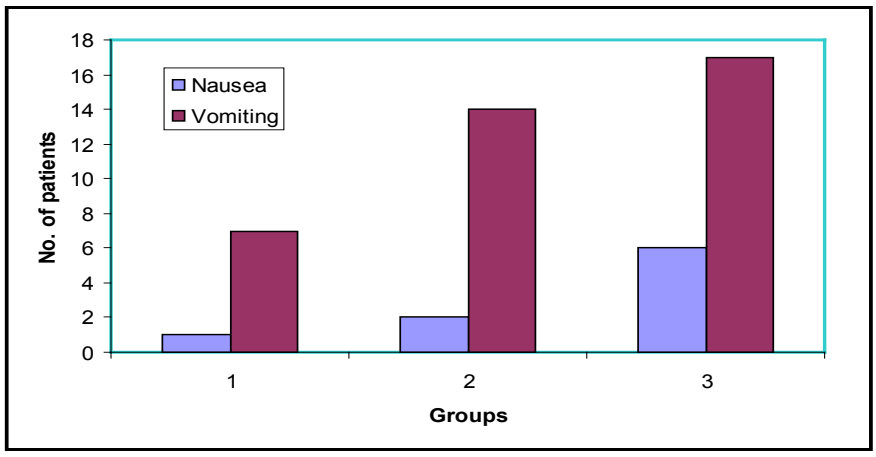

Figure 1. Incidence of PONV among groups.

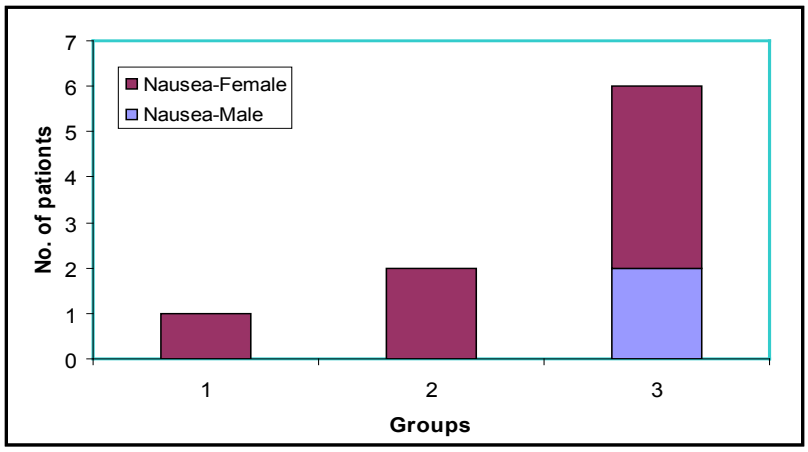

Figure 2. Comparison in incidence of nausea between male and female.

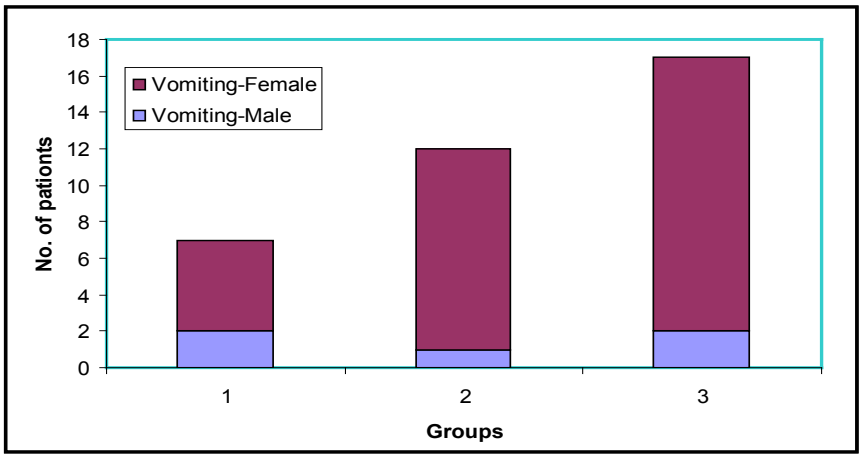

Figure 3. Incidence of vomiting between male and female.

DISCUSSION

The result of this study was a significant reduction in the incidence of PONV in group 1 when compared with group 2 and group 3.

The use of benzodiazepines in the management of PONV has been reported in the literature, both for prophylaxis and treatment [7].It has been postulated that a possible mechanism for the anti-emetic effect of benzodiazepines could be an action at the chemoreceptor trigger zone reducing synthesis, release and postsynaptic effect of dopamine [8].

Dopaminergic neuronal activity and 5 hydroxytryptamine release may also be reduced by binding of midazolam to the GABA benzodiazepine complex [9-11] thus, anxiolysis as a secondary effect may also contribute to antiemesis.

Midazolam has antiemetic effect compare with placebo as mentioned by (Heidari SM) he performed a study on eighty-two adult patients undergoing cholecystectomy[11], and (Safavi and Hunarmand 2009) said i.v midazolam 30 minute before extubation in sixty patients with lower abdominal surgery is effective more than placebo in reducing PONV [12].

Midazolam could be more effective antiemetic than other drugs as seen with (Sanjay) when compare midazolam with ondansetron for preventing post operative nausea and vomiting in two hundred patients after cardiac surgery and midazolam was more effective than ondansetron [13] and the same was shown by (Ha et al. 2007) with one hundred nineteen patients after thyroidectomy [14].

Metoclopramide has been used for almost 40 years to prevent PONV [15]. The affinity for dopaminergic D2-receptors explains the antiemetic effect of metoclopramide [16]. Although it may provoke extra pyramidal symptoms, metoclopramide is still used in clinical practice [15, 17].

It was suggested that PONV is approximately two to three times more frequent in women than in men [18]. In this study, PONV was predominant in women, in common with most other studies on PONV [19, 20], which was about one and half fold increase in the incidence of PONV in women (all the women who participated in this trial were not in menstrual cycle and were not receiving any hormone-replacement therapy) as compared with men but statistically was not significant; this could be attributed to the unequal sex distribution.

This overwhelming incidence of PONV in women suggests that women should be a target population to receive prophylactic antiemetics before laparoscopic surgery.

Conclusion

The result of data collection and analysis appear that midazolam is more effective than metoclopramide as premedication agent for prevention PONV in laparoscopic surgeries.

Recommendation

Because of high incidence of PONV in patients undergoing laparoscopic surgeries [3], so prophylactic anti emetics is advised to decrease PONV, especially in high risk patients. Midazolam can be given as premedication agent to prevent PONV; and it could be more effective than metoclopramide.

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