

A Comparative Study for the effect of ondansetron and metoclopramide in prevention of postoperative nausea and vomiting

Zahraa Abdul Kareem Mohammed¹, Samir Ahmed Jawad², Maysa Salih Mahdi³, Wafaa Fowzi Ibrahim⁴

1: Department of Pharmacology College of pharmacy Karbala University / Iraq

2: Head of intensive care unit in Al-Hussein medical city/ Iraq

3: Department of clinical laboratories College of applied medical sciences Karbala University / Iraq

4: Department of Pharmacology College of pharmacy Karbala University / Iraq

ملخص

خلفية الدراسة: ان معالجة الغثيان والتقيؤ بعد العملية الجراحية يزيل المعاناة ويؤدي الى عدم البقاء في المستشفى مما يقلل النفقات ويزيد من رضى المريض. ان الهدف الرئيسي هو ايجاد دواء اكثر فعالية مع اقل تأثيرات جانبية في منع الغثيان والتقيؤ بعد العملية الجراحية .

اهداف الدراسة: مقارنة الفعالية في معالجة الغثيان والتقيؤ لكل من الميتكلوبرومايد مع الديكساميثازون مقابل الاندسترون مع الديكساميثازون.

الطريقة: اشترك في هذه الدراسة ستون مريضاً من كلا الجنسين تتراوح أعمارهم بين 20 و50 سنة. تم انجاز الدراسة في مدينة الامام الحسيني (ع) الطبية في كربلاء العراق في الفترة بين 1 ايلول 2015 وحتى 1 كانون الثاني 2016. المرض استلموا مضادات التقيؤ قبل عملية رفع المرارة بالجراحة المنظارية وزع المرضى على مجموعتين : أ، ب، (ثلاثون مريض لكل مجموعة)، كل مجموعة أعطيت العلاج قبل العملية، مجموعة (أ) اخذت الميتكلوبرومايد (10 ملغم) مع الديكساميثازون (8ملغم) ومجموعة (ب) اخذت اوندانسترون (4ملغم) مع الديكساميثازون (8ملغم) مباشرة بعد التخدير في منع الغثيان والتقيؤ بعد استئصال المرارة بالمنظار . وقد تم مراقبة الفعالية لمنع الغثيان والتقيؤ لهذه الادوية بعد العملية باستخدام ورقة استبيان. تم جمع المعطيات تحليلها احصائياً.

النتائج: لا يوجد اختلاف مميز بين المجموعة أ والمجموعة ب في العمر والجنس والعلامات الحيوية ووجد ان المجموعة ب كانت اكثر فعالة في منع الغثيان حيث كانت نسبة حدوثه (8.6%) والتقيؤ (3.33%) مقارنة بالمجموعة أ مع حدوث الغثيان (91.4%) والتقيؤ (30%).

الاستنتاج: يمتلك اوندانسترون مع الديكساميثازون فعالية ضد التقيؤ بعد العملية الجراحية للمرضى الذين اجرؤا عملية رفع مرارة بالناظور أفضل من الميتكلوبرومايد مع الديكساميثازون.

Abstract

Background: Management of postoperative nausea and vomiting relieve suffering and leads to shortened hospital stay, reduced hospital costs, and increased patient satisfaction. The major goal is to find the most effective treatment with the least side effects in prevention of post operative nausea and vomiting (PONV) .

Objectives: To compare the anti-emetic effect of (metoclopramide+ dexamethasone) versus (ondansetron + dexamethasone) in patient undergoing laparoscopic cholecystectomy.

Methods: 60 patients of both sex were involved in this study, aged from 20 to 50 years old. The study was performed at Imam Hussein medical city, Karbala, Iraq during the period from the first of September 2015 to the first of January 2016. Patients received antiemetic preoperatively for laparoscopic cholecystectomy. They were divided into two groups A & B (30 patients each), each group received combination of two antiemetic drugs , group A received IV (metoclopramide 10mg + dexamethasone 8mg), B received IV (ondansetron 4mg + dexamethasone 8mg) given just before

induction of anaesthesia in preventing PONV following laparoscopic cholecystectomy. They were monitored for their nausea and vomiting activity by using questionnaire form postoperatively.

Results:

It was found that there was no significant difference between group A & group B in age, sex & vital signs and it was found that group B treatment was more effective in preventing nausea (9.9%) & vomiting (3.3%) as compared to group A with an prevention of nausea (99.9%) & vomiting (30 %).

Conclusion: Ondansetron with dexamethasone better antiemetic activity as compared to metoclopramide with dexamethasone in patient undergoing laparoscopic cholecystectomy.

Key words: postoperative nausea and vomiting, metoclopramide, Ondansetron.

Introduction: Postoperative nausea and vomiting (PONV) is one of the most commonly reported adverse effects of anesthesia remains a significant clinical issue that can detract from patients' quality of life in hospital ,as well as in the days immediately post discharge in addition, PONV may increase perioperative costs, increase perioperative morbidity, increase postanesthesia care unit stay, prolong hospital stays, length of stay/delay discharge, delay the time that the patient can go back to work, and lead to readmissions. Despite the existence of multiple tools to stratify patients and multiple PONV treatment guidelines, clinicians do not systematically address the treatment and/or prophylaxis of PONV in a uniform fashion with both pharmacologic and non pharmacologic strategies in attempts to minimize PONV occurrences^[1]. Various factors contributing to PONV include patient characteristics, anesthetic technique, type of surgery, and postoperative care^[2]. Women undergoing laparoscopic surgeries are particularly at risk ^[3] . Laparoscopic gallbladder surgery (cholecystectomy) is a standard treatment for patients with symptomatic gallstones and it has replaced open cholecystectomy. The application of this technique has spread worldwide due to the advantages of decreased pain and faster recovery times^[4]. It provides enormous benefits to patients, including quick recovery, shorter hospital stay and prompt return to regular activities^[5]. Despite the minimally incursive nature of laparoscopy, high incidence (53-70%) of post-operative nausea and vomiting (PONV) is still a significant cause of post-operative morbidity^[6]. Laparoscopic cholecystectomy is a procedure that requires necessity of carbon dioxide insufflation resulting in peritoneum distention, and increased pressure in the peritoneal cavity which is a very important risk factor inciting nausea and vomiting^[7] . Ondansetron binds to 5-HT₃ receptors both in the central chemoreceptor trigger zone and the gastrointestinal tract to inhibit emetic symptoms ^[8] . For both prevention and treatment of postoperative nausea and vomiting, intravenous (IV) ondansetron is an effective antiemetic when compared with placebo ^{[9][10]} . Metoclopramide is chlorobenzamide which was used commonly as an anti-emetic agent ^[11]. The antiemetic effect of the drug is related to dopamine-2 receptor antagonism in the chemoreceptor trigger zone^[12] . Initially metoclopramide was used for the treatment of nausea and vomiting in migraine and in radiotherapy and chemotherapy. Today it is probably one of the most popular antiemetic drugs in anaesthetic practice for prevention of PONV ^[13] .

Patients and Methods:

Patients

Sixty patients of both sex were randomly allocated to participate in this study, aged (20-50) years, American Society of Anaesthesiologists (ASA) Grade I and II. More scheduled for elective laparoscopic cholecystectomy. The study performed at Imam- Hussein medical city, Karbala, Iraq from September 2015 to January 2016. Any patient with neurological or psychiatric disorders, drugs allergy, emergency surgery, pregnancy, any intraoperative or postoperative complication were excluded from the study. Each patient received midazolam i.v (0.01 mg/kg), ketamine i.v (0.5 mg/kg), propofol i.v (2mg/kg), and intubation was done with assist of muscle relaxant rocuronium (0.5 mg/kg) and maintains of anesthesia with isofurane. Verbal & written consent was obtained from all patients before enrolling them in the study. Pre, intra & post-operative data were collected by using pre-constructed form sheet including blood pressure, pulse rate, O2 saturation , nausea & vomiting.

Methods

Method of grouping patients

Sixty patients are allocated randomly into two groups (each 30 patients), group A were received intravenous ondansetron (4mg) with dexamethasone (8mg) & group B were received intravenous metoclopramide (10mg) with dexamethasone (8mg) given just before induction of anaesthesia in preventing PONV following laparoscopic cholecystectomy.

Method of nausea and vomiting assessment

By using a data sheet patients are monitored every 2, 4, 6, 8 and 10 hours postoperatively and ask the patients to assess their nausea. For example, the amount of nausea that a patient feels ranges from mild(+), moderate(++) and severe (+++). Patients assess their vomiting by yes or no.

Method of Statistical analysis

Data were collected and statically analyzed by SPSS version.

Table 1: Questionnaire form (pre-operation)

Name:	age:
ASA: (1) (2)	
Time of induction:	
Time of start of surgery:	
End of surgery:	
Time of recovery:	
Duration:	

Results

Beginning with patients Age and sex, the following table (table 3) shows the mean of age of the patients of each group, with the ratio of male to female patients and mean of duration of operation of the two groups participating in the study.

Table 3: Age mean, male to female ratio and duration of operation mean of the patients of two groups of the study.

Variable	Group A	Group B
N	30	30
Age	37.33±8.70 ^a	38.8±6.56 ^a
M/F	14/16	15/15
D	70.83±15.27 ^a	71.16±11.80 ^a

Results represents mean± standard deviation; group A:(metoclopramide + Dexamethasone) and group B: (Ondansetron + Dexamethasone); M/F: male to female ratio; D: duration of operation. Superscripts (a) represent non-significant change $P \leq 0.05$ between two groups.

Table 4: Blood pressure systolic and diastolic mean, pulse rate mean and O2 saturation of the patients of two groups of the study.

vital signs		Mean± Std. Deviation	P value
BPS	Group A (metoclopramide+Dexamethasone)	126.94 ±17.53 ^a	0.6
	Group B (Ondansetron + Dexamethasone)	126.34±13.30 ^a	
BPD	Group A (metoclopramide+Dexamethasone)	80.20±12.28 ^a	0.4
	Group B (Ondansetron + Dexamethasone)	79.02±10.59 ^a	
PR	Group A (metoclopramide+Dexamethasone)	84.68±13.31 ^a	0.6
	Group B (Ondansetron + Dexamethasone)	84.95±9.10 ^a	
SPO ₂	Group A (metoclopramide+Dexamethasone)	98.0±1.42 ^a	0.07
	Group B (Ondansetron + Dexamethasone)	97.77±1.28 ^a	

Superscripts (a) represent non-significant change $P \leq 0.05$ between two groups.

Table 5 : Post-operative percentage of nausea in patients of two group of the study.

		Group A	Group B	P value
N %	Mild nausea	23 76.6%	2 6.6%	0.05
	Moderat nausea	7 23.3%	1 3.3%	
	Severe nausea	0 0.0%	0 0.0%	
Total	30 99.9%	3 9.9%		

Results represents percentage of nausea (mild & moderate);group A:(metoclopramide + Dexamethasone) and group B: (Ondansetron + Dexamethasone); with significant change which **P** value ≤ 0.05 .

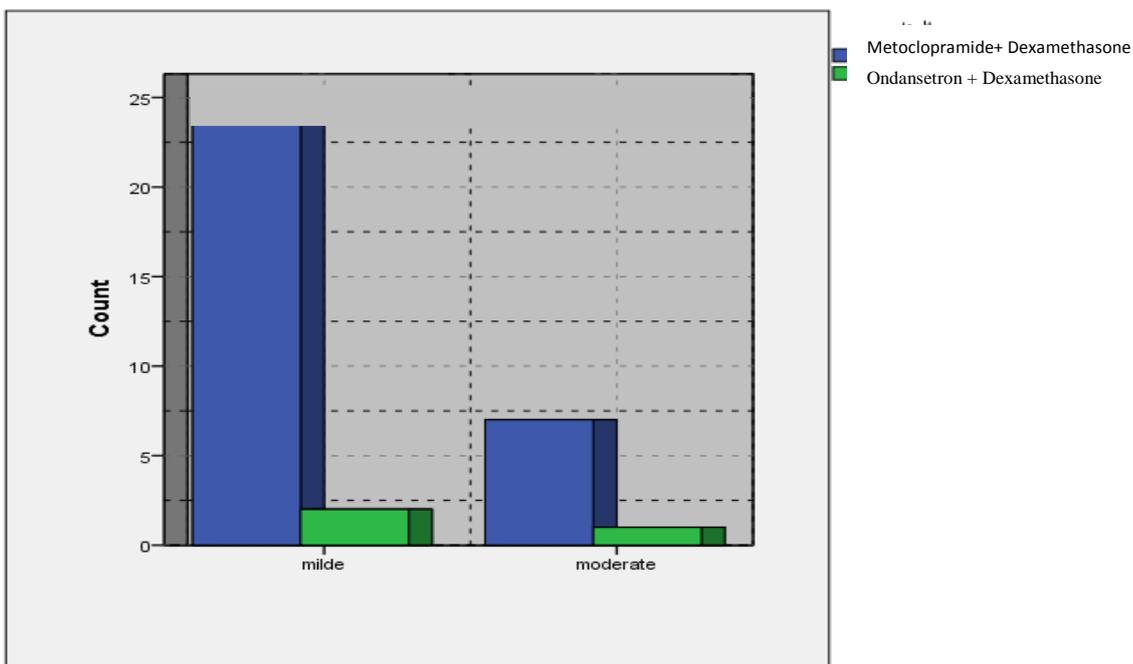


Fig. 1: The incidence of nausea for each combination .

Table 6: Post-operative percentage of vomiting of the patient of two group of the study.

					P value
			Group A	Group B	
V	yes	Count % V	9 30%	1 3.3%	0.05
Total		Count % V	9 30%	1 3.3%	

Results represents percentage of vomiting; group A:(metoclopramide + Dexamethasone) and group B: (Ondansetron + Dexamethasone); with significant change which **P value** ≤ 0.05 .

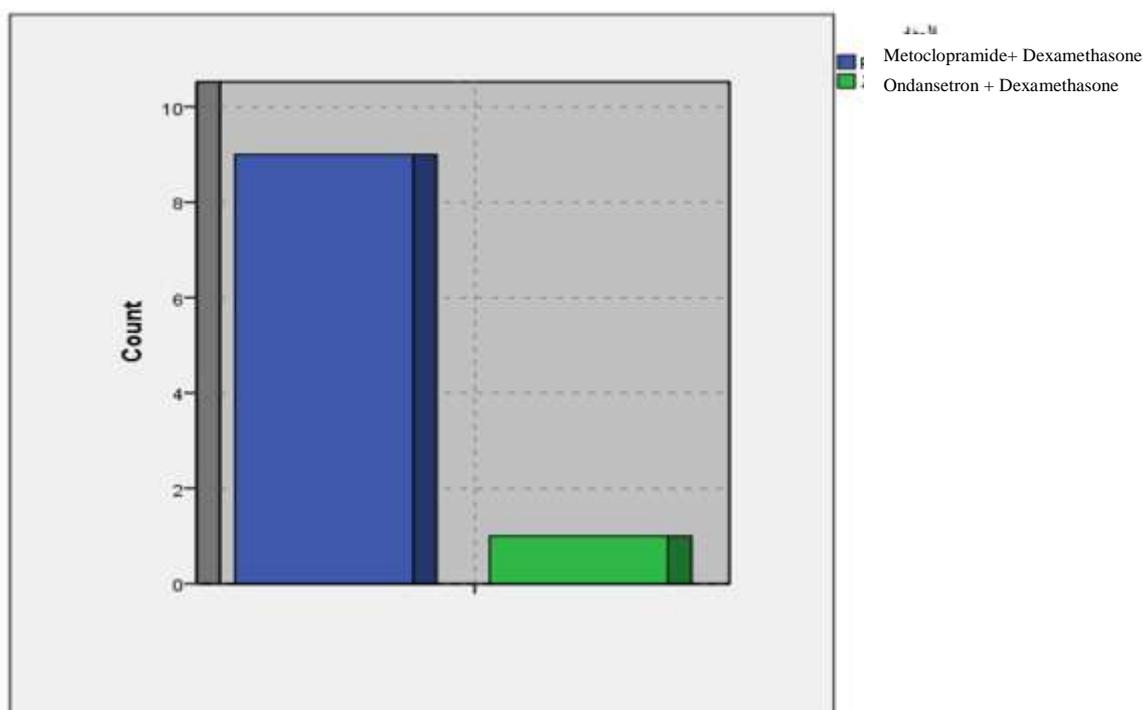


Fig. 2: The incidence of vomiting for each combination .

Discussion

Post operative nausea and vomiting (PONV) is still among the most common and troublesome complications of surgery, causing delays in patient discharge from hospital, especially in outpatient surgeries. Therefore, therapeutic strategies preventing this complication are of almost importance^[14]. PONV is amongst the most common complications following anesthesia and surgery with a selectively high incidence (up to 70%) after laparoscopic cholecystectomy^[15]. None of the available antiemetic is entirely effective for preventing PONV, especially in high-risk patients. A better prophylaxis might be achieved by using a combination of agents acting at different receptor sites^{[16][17]}. This study shows that combination of ondansetron with dexamethasone was more effective in preventing PONV following laparoscopic cholecystectomy than metoclopramide with dexamethasone. By using T-test of independent two samples, it was found that there was no significant difference between group A & group B in age, sex & vital signs. It was found that group B that received combination of ondansetron with dexamethasone have significant effect in preventing nausea (8.6%) & vomiting (3.33%) as compared to group A that received combination of metoclopramide with dexamethasone with an incidence of nausea (91.4%) & vomiting (30%). Our data were in agreement with other researches^{[18][19][20][21][22]}. While other studies show that dexamethasone alone was as effective and as safe as ondansetron in preventing PONV^[23].

References

1. **Howard S. Smith, Eric J. Smith, Benjamin R. Smith**, "Postoperative nausea and vomiting". *Ann Palliat Med* 2012;1(2):94-102.
2. **Gold BS, Kitz DS, Lecky JH, et al.** "Unanticipated admission to the hospital following ambulatory surgery". *JAMA*, 1989; Dec;262(21):3008-3010.
3. **Honkavaara P, Lehtinen AM, Hovorka J, et al.** "Nausea and vomiting after gynaecological laparoscopy depends upon the phase of the menstrual cycle". *Can J Anaesth*, 1991; Oct;38(7):876-879.
4. **Wang B, He KH, Jiang MB, et al.** "Effect of prophylactic dexamethasone on nausea and vomiting after laparoscopic gynecological operation: meta-analysis". *Middle East J Anesthesiol*. 2011;21(3):397-40.
5. **Gupta P, Khanna J, Mitramustafi AK, Bhartia VK.** "Role of preoperative dexamethasone as prophylaxis for post-operative nausea and vomiting in laparoscopic surgery". *J Min Access Surg*, 2006;2: 12-5.
6. **Wang JJ, Ho ST, Liu YH, Lee SC, Liu YC, Liao YC, et al.** "Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy". *Br J Anaesth*, 1999; 83: 772-5.
7. **Argiriadou H, Papaziogas B, Parlidis T, et al.** "Tropisetron versus ondansetron for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: a randomized double blind, placebo - controlled study". *SurgEndosc*, 2002;16: 1087-90.
8. **Bunce KT, Tyers MB.** "The role of 5-HT in postoperative nausea and vomiting". *British Journal of Anaesthesia*, 1992; 69: S60-2.
9. **Leeser J, Lip H.** "Prevention of postoperative nausea and vomiting using ondansetron, a new, selective 5-HT₃ receptor antagonist". *Anesth Analg*, 1991;72:751-5.
10. **Scu'dleri, Wetchler B, Sung YF, et al.** "Treatment of postoperative nausea and vomiting after outpatient surgery with the 5-HT₃ antagonist ondansetron". *Anesthesiology*, 1993;78:15-20.

11. **Yis U, Durgul O, Duman M, Unal N.** "Metoclopramide induced dystonia in children two case reports". *European J Emergency Medicine*, 2005;12: 117-9.
12. **Van Harten PN, Hoek HW, Kahn RS.** "Acute dystonia induced by drug treatment". *BMJ*, 1999;319: 623-6.
13. **Aziz N, Naz U, Ilyas M.** "A comparative study between metoclopramide and dexamethasone for prevention of postoperative nausea and vomiting in laparoscopic cholecystectomy". *J Med Sci*, 2011;19: 129-132.
14. **Garrett K et al.** "Managing nausea and vomiting". *Critical care nurse*, 2003; 23:31–50.
15. **Ahmed Nisar, Muslim M, Aurangzeb M, et al.** "Prevention of postoperative nausea and vomiting in laparoscopic cholecystectomy". *J Med Sci*, 2012; 20: 33-36.
16. **M. J. Sanchez-Ledesma, L. L´opez-Olaondo, F. J. Pueyo, et al.** "A comparison of three antiemetic combinations for the prevention of postoperative nausea and vomiting". *Anesthesia and Analgesia*, 2002;95(6):1590–1595.
17. **A. S. Habib, H. E. El-Moalem, and T. J. Gan.** "The efficacy of the 5-HT₃ receptor antagonists combined with droperidol for PONV prophylaxis is similar to their combination with dexamethasone". *Canadian Journal of Anesthesia*, 2004;51(4): 311–319.
18. **Farhat K, Pasha AK, Kazi WA.** "Comparison of Ondansetron and Metoclopramide for PONV Prophylaxis in Laparoscopic Cholecystectomy". *J Anesthe Clinic Res*, 2013;4 (3): 2155-6148.
19. **Dr. Hina Bashir, Dr. Umar Qadir Bacha, Dr. Shahid Bukhari, et al.** " A comparative evaluation of prophylactic single dose metoclopramide, single dose ondansetron and a combination of ondansetron plus dexamethasone in the reduction of post operative nausea and vomiting". *Journal of Dental and Medical Sciences*, 2015;14:20-24.
20. **Souvik Maitra, Anirban Som, Dalim K Baidya, et al.** "Comparison of ondansetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries" . 2015; 1-4.
21. **Fauzia Bano, Safia Zafar, Sadqa Aftab, et al.** "Dexamethasone plus ondansetron for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: a comparison with dexamethasone alone". *Journal of the College of Physicians and Surgeons Pakistan*, 2008; 18 (5): 265-269.
22. **Usha Daria and Vinod Kumar.** " qualitative comparison of metoclopramide, ondansetron and granisetron alone and in combination with dexamethasone in the prevention of postoperative nausea and vomiting in day care laparoscopic gynaecological surgery under general anaesthesia". *Asian J Pharm Clin Res*, 2012; 5(2), 165-167.
23. **Xian- xue wang, quan zhou , et al** "dexamethasone versus ondansetron in the prevention of postoperative nausea & vomiting in patients undergoing laparoscopic surgery: a meta-analysis of randomized controlled trials". *BMC anesthesiology*, 15 August 2015.