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Research Article

Ondansetron versus metoclopramide and hyoscine as prophylaxis for nausea and vomiting post sleeve gastrectomy: randomized controlled trial

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Abstract

Background: Since it began to be used intermittently in the 1950s, there has been an upward trend in bariatric surgery, with the use of this procedure increasing more than 20-fold since 2010. Among the adverse Postoperative Events, Nausea and Vomiting (PONV) following general anesthesia and surgery were recorded as the most distressing and frequent, affecting on average somewhere between 30%-50% of patients, though the frequency of these events varies considerably.

Aim: This study purports to determine which of the various drugs available were the most effective in controlling PONV in patients post sleeve gastrectomy.

Methodology: A prospective, randomized controlled study with parallel groups was conducted with 45 patients, all of whom had undergone laparoscopic sleeve gastrectomy under general anesthesia. The patients were enrolled in the study, and then 15 patients were allocated at random to each of three groups. Each patient was then carefully monitored for specific vital signs including Non-Invasive Blood Pressure (NIBP), peripheral capillary oxygen saturation (SpO₂), heart rate, temperature, and end-tidal CO₂ (ETCO₂). Episodes of nausea and vomiting were monitored and documented by the follow-up nurses. **Results:** The study included 45 patients divided into three groups. The mean systolic blood pressure was 132.8 ± 6.6 mm Hg among the first group, 131.3 ± 11.0 mm Hg for the second group, and 131.5 ± 12.3 mm Hg for the third group. The pulse rate was significantly higher among the first group. Regarding post-surgical complaints, abdominal pain was recorded among 13.3% of the first group, 20% of the second group, and 13.3% of the third group.

Conclusions and recommendations: In conclusion, the study revealed no significant difference between the different drugs under study in terms of effects on the vital signs of the patients, except for heart rate. Nausea was the effect most frequently experienced for all drugs, while bloody vomiting was more frequent among patients on 10 mg of metoclopramide.

Keywords: nausea, vomiting, prophylaxis, sleeve gastrectomy, hyoscine, ondansetron, metoclopramide

INTRODUCTION

Health-related behavior in early life leads to later risks for lifestyle disorders. It is therefore important to investigate health behaviors among young people. University students represent a major segment of the young adult population's health-related behavior in early life influences later risks for lifestyle-related disorders. It is therefore important to investigate health behaviors among young people. University students represent a major segment of the young adult population. Bariatric surgery can have the effect of limiting the quantity of food taken into the stomach, malabsorptive, limiting the number of nutrients absorbed, or a combination of both. Since it began to be used intermittently in the 1950s, there has been an upward trend in bariatric surgery, with the use of this procedure increasing more than 20-fold since 2010 [1]. Among the adverse Postoperative events, Nausea and Vomiting (PONV) following general anesthesia and surgery were recorded as the most distressing and frequent [2], affecting on average somewhere between 30%-50% of patients [3], though the frequency of these events varies considerably. Several factors influence PONV, including gender (female), smoking/non-smoking status, whether there is a history of using postoperative opioids, and motion sickness [4]. Together with a laparoscopic approach and induced pneumoperitoneum, the prevention of PONV in bariatric operations constitutes a major challenge. When a therapeutic intervention would be justified to prevent PONV, the first choice would be to use selective serotonin type-3 (5-HT₃) receptor antagonists-for example, ondansetron, because of their safety and efficacy compared to other medications [5]. For patients seriously likely to suffer from PONV, an acceptable solution to reduce the risk might be to use a combination of a 5-HT₃ receptor antagonist and other antiemetic medication [6].

Hyoscine, also known as scopolamine, is a medication used to treat motion sickness and PONV [7]. It may also be used before surgery to reduce salivation. Zofran, the brand name for Ondansetron, a drug used to control nausea and vomiting, may also be used following cancer treatments involving surgery, chemotherapy, and treatment involving radiation. It has also effectiveness in treating gastroenteritis [8,9], as well as little effect on motion sickness [10]. It can be administered orally or by Intramuscular (IM) or Intravenous (IV) injection.

Metoclopramide is a drug used mainly for stomach and esophageal problems as it has a prokinetic property [11]. It is also used to control and treat nausea and vomiting, to help empty the stomach in people with delayed stomach emptying (gastroparesis), to treat gastroenteritis, and to help patients with gastroesophageal reflux disease [12]. It is also used to treat migraine headaches, including nauseating attacks [13].

MATERIALS AND METHODS

A prospective, randomized controlled study with parallel groups was conducted from 15 November 2018 to 15 February 2019, with 45 patients of both sexes, at the Najran University Hospital. Ethical approval was obtained from the ethics committee, and the patients involved consented in writing after the purpose of the study and the potential risks and benefits had been explained to them. All patients had laparoscopic sleeve gastrotomies under general anesthesia.

The exclusion criteria were patients with known hypersensitivity or contraindicated for the study medications, those suffering from chronic nausea, vomiting, motion sickness, or retching in the 24 hours before receiving general anesthesia, patients with conditions that required the administration, of opioid drugs, and those with neuromuscular or gastrointestinal diseases.

STUDY DESIGN

After the 45 patients were enrolled, they were randomly divided, using Red Cap software, into three groups of 15. The first group received ondansetron 5 mg, the second group received metoclopramide 10mg,

and the third group received spinal (scopolamine) 20 mg. All drugs were given intravenously (IV), over one minute immediately after admission to the ICU, and every eight hours thereafter.

Each patient was then carefully monitored for specific vital signs, including Non-Invasive Blood Pressure (NIBP), peripheral capillary oxygen saturation (SpO₂), heart rate, temperature, and end-tidal CO₂ (ETCO₂). Episodes of nausea and vomiting were monitored and documented by the follow-up nurses.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit while vomiting itself was defined as 'the forceful expulsion of gastric contents from the mouth' [14].

Retching was defined as 'the labored, spasmodic, rhythmic contraction of the respiratory muscles, including the diaphragm, chest wall, and abdominal wall muscles, without the expulsion of gastric contents, and was classified as PONV' [15]. The follow-up nurses involved in the study noted and recorded any other adverse effects, observed at any time throughout the study, and including spontaneous complaints. Attacks of abdominal pain and any/all other adverse effects, such as tachycardia, dyspnoea, or extra-pyramidal manifestation, of any drug were similarly monitored and documented by nurses who interviewed the patients. Post-operative analgesia was provided using paracetamol 1 gm every 6 hours for moderate pain and meperidine 25 gm PRN for severe pain.

The data were extracted, revised, and coded, and the values fed into IBM SPSS version 22 software. Two-tailed tests, and an alpha error of 0.05, were used for all statistical analyses and p values \leq 0.05 were considered statistically significant. Descriptive analysis of frequency and percentage description was undertaken for all clinical data, while statistical analysis was based on the Intention to Treat (ITT) method. Differences between the groups and the patients' data were tested using Monte Carlo exact probability to confirm the comparability of the groups. Variances in the patients' vital signs were calculated and evaluated between the three groups, using one-way Analysis of Variance (ANOVA), while those between post-surgical complaints were assessed using the Monte Carlo exact test.

RESULTS

As has been said, the study involved 45 patients, in three groups of 15 patients each. Demographically, 13.3% of patients in the first group were aged 20-30 years, compared with 20% in the second group and 40% in the third group. In the first group, 13.3% of patients were aged 40 years or above, compared with 26.7% in both the second and third groups. (The difference was not statistically significant: $p=0.247$)

About gender, 80% of patients in the first group were male, compared to 53.3% in the second group and 80% in the third group ($p=0.177$). There were no significant differences between the groups in terms of nationality ($p=0.334$) (Table 1).

Concerning vital signs (Table 2), the mean systolic blood pressure was 132.8 ± 6.6 mm Hg in the first group of patients, compared to 131.3 ± 11.0 mm Hg for the second group and 131.5 ± 12.3 mm Hg for the third group (difference not significant: $p=0.914$). The mean level of diastolic blood pressure recorded for the first group of patients was 82.2 ± 5.9 mm Hg, compared to 81.0 ± 8.7 mmHg for the second group and 82.6 ± 8.5 mm Hg for the third group ($p=0.842$). The pulse rate was significantly higher in the first group patients (98 ± 12.6 beats/min) than the second group (86.3 ± 12.5 beats/min) and the third group (91.4 ± 12.7 beats/min) ($p=0.048$). The values for respiratory rate and temperature were nearly equal among the three study groups ($p=0.113$ and 0.353 , respectively). SpO₂ was $95.6\% \pm 1.8\%$ for the first group, compared to $94.9\% \pm 2.7\%$ for the second group and $95.2\% \pm 2.0\%$ for the third group ($p=0.701$).

Table 3 shows the difference in post-surgical abdominal pain recorded

Table 1. Demographic characteristics of sampled patients in the study

	Group							p	
	Scopinal 20 mg		Metoclopramide 10 mg				Ondansetron 5 mg		
	N	%	N	%	N	%			
Age in years								0.247	
20-	2	13.3	3	20	6	40			
30-	11	73.3	8	53.3	5	33.3			
40+	2	13.3	4	26.7	4	26.7			
Gender								0.177	
Male	12	80	8	53.3	12	80			
Female	3	20	7	46.7	3	20			
Nationality								0.334	
Saudi	13	86.7	13	86.7	15	100			
Non-Saudi	2	13.3	2	13.3	0	0			

p: Monte Carlo exact probability

Table 2. Vital signs among different patient groups

Vital signs		Group			p
		Scopinal	Metoclopramide	Ondansetron	
		20 mg	10 mg	5 mg	
SDP (mmHg)	Range	120-142	112-143	101-155	0.914
	Mean (SD)	132.8 (6.6)	131.3 (11.0)	131.5 (12.3)	
DBP (mmHg)	Range	67-89	65-94	70-96	0.842
	Mean (SD)	82.2 (5.9)	81.0 (8.7)	82.6 (8.5)	
Pulse rate (beats/min)	Range	71-122	60-102	73-120	0.048*
	Mean (SD)	98.0 (12.6)	86.3 (12.5)	91.4 (12.7)	
Respiratory rate	Range	20-22	22-22	20-24	0.113
	Mean (SD)	21.3 (1.0)	22.0 (0.0)	21.6 (1.0)	
Temperature	Range	36.9-37.9	37.0-37.9	36.9-37.7	0.353
	Mean (SD)	37.2 (0.3)	37.2 (0.3)	37.1 (0.2)	
SpO ₂	Range	91%-98%	90%-99%	91%-99%	0.701
	Mean (SD)	95.6% (1.8%)	94.9% (2.7%)	95.2% (2.0%)	

SBP: Systolic blood pressure; DBP: Diastolic blood pressure. p: One-way ANOVA. *p<0.05 (significant)

Table 3. Medical complaints among different patient groups

Complaints	Group						p
	Scopinal		Metoclopramide		Ondansetron		
	20 mg		10 mg		5 mg		
	N	%	N	%	N	%	
Abdominal pain							0.844
No	13	86.7	12	80	13	86.7	
Yes	2	13.3	3	20	2	13.3	
Nausea and vomiting							0.314
None	8	53.3	7	46.7	7	46.7	
Nausea	2	13.3	2	13.3	2	13.3	
Vomiting	2	13.3	0	0	1	6.7	
Nausea and vomiting	1	6.7	2	13.3	5	33.3	
Nausea and bloody vomiting	2	13.3	4	26.7	0	0	

p: Monte Carlo exact probability

for the three groups of patients-13.3% for the first group, 20% for the second, and 13.3% for the third (not a statistically significant difference at $p=0.844$). Nausea was recorded for 13.3% of patients in all groups, whereas 13.3% of patients in the first, none in the second, and 6.7% in the third recorded vomiting. For vomiting blood with nausea, however, 13.3% were again recorded for those in the first group, but 26.7% in the second but none in the third

DISCUSSION

The main aim of the research was to ascertain which drug was the most efficient for patients in the control of PONV following sleeve gastrectomy [16, 17]. This procedure is one of several bariatric methods, which also include gastric bandaging and gastric bypass. All these procedures are usually the choice of treatment for morbidly obese patients, due to the failure of other conservative methods to lose bodyweight [18, 19]. Postoperatively, bariatric patients appear to suffer from nausea and vomiting more frequently than normal weight or obese patients [20]. However, the average incidence of adverse events ranges from 30% to 50% depending on certain factors that may influence the occurrence of PONV. Such factors include gender (female), smoking/non-smoking status, and previous experience of PONV and travel sickness, while with abdominal surgery postoperative nausea is particularly prevalent following the laparoscopic intervention [16, 18]. In this research, although results recorded were similar to those in other studies [20, 22], about the frequency of incidence, more female patients than male suffered PONV [16, 22]. The reason for this is not immediately obvious, though it might be that more women than men have cosmetic surgery [20].

PONV is known to be a significant and the most frequent, negative consequence of surgery under general anesthetic, as has been demonstrated by previous clinical trials and research [23]. It may be that this increase in frequency results from the volatile agents in the anesthetics used for gastric surgery [24]. PONV incidence was, as anticipated, low in the control group, but not with those in the obese group, although IV anesthesia was administered to both groups [16,24]. PONV may also give rise to significant negative side effects. Vomiting may result in increased abdominal and thoracic pressure, leading to bowel anastomoses and the rupture of sutures and therefore anastomotic leakage and bleeding. A consequence of this may, in turn, be longer hospitalization and therefore greater costs for the treatment, quite apart from a deterioration in well-being [18,25].

As previous research has shown, combinations of antiemetic drugs may be more effective in the successful treatment and control of PONV with overweight patients. In a proportion of this research, however, such a combination of even two drugs proved ineffective [26,27]. This has been found using propofol instead of volatile anesthetic agents to maintain anesthesia [27].

Anticholinergics, butyrophenones, benzamine, and antihistamines are among the many antiemetics used in the control of PONV, though their indiscriminate use may have unintended and disagreeable consequences of prolonging the anesthesia, dysphoria, sedation, and extrapyramidal events, all of which may extend recovery times [28,29]. Research into such side effects, notable the extrapyramidal and

sedative concerns, has been driven by the need to discover new ways of controlling them without causing undesirable side effects [30]. In the management of nausea and vomiting among patients undergoing radiotherapy or chemotherapy, a 5-hydroxytryptamine subtype 3 (5HT₃) receptor antagonist-ondansetron has been identified as one such effective preventative [31].

Ondansetron is used extensively in the Middle East for economic reasons; however, in comparing its use, for the control of PONV following gastric sleeve surgery, with that of scopolamine and metoclopramide, this study could find no appreciable differences in effectiveness between the three drugs. Following treatment with ondansetron, the incidence of vomiting was lower than for those receiving metoclopramide (2.5% vs. 20%, $p=0.02$), while the incidence of nausea was also lower at 20% compared with 45%, though statistically, the difference was not significant ($p=0.05$).

Metoclopramide is a central dopaminergic D₂ receptor antagonist and prokinetic drug that increases both the speed at which the stomach empties and bowel transit time. Nevertheless, that droperidol and ondansetron are more effective than metoclopramide in preventing postoperative vomiting has been evidenced in a meta-analysis, while not only has metoclopramide been related to a high incidence of PONV (45%) but a 10mg dose is ineffective as an antiemetic in the prevention of postoperative vomiting [32,33]. Furthermore, in this study, no significant difference was noted between the PONV results comparing ondansetron and hyoscine with metoclopramide, a finding which might be explained by its short half-life.

Hyoscine is an ester of tropic acid and scopine. It is a racemic mixture in which only l-hyoscine is active. Hyoscine butyl bromide is presented as a clear solution for IV, IM, and SubCutaneous (SC) injection. It competitively antagonizes at muscarinic receptors. It is used for the prevention of travel (motion) sickness, and when given together with an IM opioid has been seen to decrease PONV [34]. Its antiemetic effect may also be due to its property of reducing gut secretions and muscle tone (anti-spasmodic). Other effects include initial tachycardia followed by bradycardia (reflected by an increased pulse rate in hyoscine-treated patients in our results), a reduction in bronchial secretions, mild bronchodilatation, respiratory stimulation, and sedation [34].

Although many physicians regard PONV, perhaps, as a minor irritation, 38% of patients who experience PONV perceive it to be as or more debilitating than the after-effects of the surgery itself [35]. This former should provide a major incentive to pursue further research aimed at identifying a truly efficacious treatment for this significantly problematic situation.

CONCLUSION

To conclude: about any substantial and important differences in the vital signs between the recipients of the different drugs involved in this study, apart from the heart rate-for which patients who had received 20 mg of spinal had more rapid pulses than those in the other two groups- none were observed. Whereas nausea was the most frequent medical complaint following the use of all drugs in the study, vomiting blood was more prevalent among those who had received metoclopramide 10 mg.

References:

- White S., Brooks E., Jurikova L., et al.: Long-term outcomes after gastric bypass. *Obesity surgery*. 2005;15:155-63.
- Kovac A.L.: Prevention and treatment of postoperative nausea and vomiting. *Drugs*. 2000;59:213-43.
- Sinclair D.R., Chung F., Mezei G.: Can postoperative nausea and vomiting be predicted?. *J Ame Society Anesthesiologists*. 1999;91:109-18.
- Apfel C.C., Greim C.A., Haubitz I., et al.: A risk score to predict the probability of postoperative vomiting in adults. *Acta Anaesthesiologica Scandinavica*. 1998;42:495-501.
- Gan T.J., Meyer T., Apfel C.C., et al.: Consensus guidelines for managing postoperative nausea and vomiting. *Anesthesia & Analgesia*. 2003;97:62-71.
- Apfel C.C., Korttila K., Abdalla M., et al.: A factorial trial of six interventions for the prevention of postoperative nausea and vomiting.

- New England J Med.* 2004;350:2441-2451.
7. Juo, P.S.: *Concise dictionary of biomedicine and molecular biology.* 2001, Crc Press.
 8. Freedman S.B., Ali S., Oleszczuk M., et al.: *Treatment of acute gastroenteritis in children: an overview of systematic reviews of interventions commonly used in developed countries. Evidence-Based Child Health: A Cochrane Review Journal.* 2013;8:1123-1137.
 9. Schnadower D., Finkelstein Y., Freedman S.B.: *Ondansetron and probiotics in the management of pediatric acute gastroenteritis in developed countries. Curr Opin Gastroenterol.* 2015;31:1-6.
 10. Sutton M., Mounsey A.L., Russell R.G.: *Treatment of motion sickness.* 2012.
 11. nlm.nih.gov/in
 12. Lucio S.D., Stevenson J.G., Hoffman J.M.: *Biosimilars: implications for health-system pharmacists. American J health-system pharmacy.* 2013;70:2004-2017.
 13. Becker W.J.: *Acute migraine treatment in adults. Headache: J Head Face Pain.* 2015;55:778-93.
 14. Watcha M.F., White P.F.: *Postoperative nausea and vomiting: its etiology, treatment, and prevention. J Amer Soc Anesthesiol.* 1992;77:162-84.
 15. Nguyen N.T., Goldman C., Rosenquist C.J., et al.: *Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. Annals Sur.* 2001;234:279.
 16. Apfel C.C., Heidrich F.M., Jukar-Rao S., et al.: *Evidence-based analysis of risk factors for postoperative nausea and vomiting. British J Anaesthesia.* 2012;109:742-753.
 17. Le T.P., Gan T.J.: *Update on the management of postoperative nausea and vomiting and postdischarge nausea and vomiting in ambulatory surgery. Anesthesiol Cli.* 2010;28:225-249.
 18. Maitra S., Som A., Baidya D.K., et al.: *Comparison of ondansetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries: a meta-analysis of randomized controlled trials. Anesthesiol Res Prac.* 2016.
 19. Groene P., Eisenlohr J., Zeuzem C., et al.: *Postoperative nausea and vomiting in bariatric surgery in comparison to non-bariatric gastric surgery. Videosurg Other Miniinvasive Techniques.* 2019;14:90.
 20. Apfel C.C., Läärä E., Koivuranta M., et al.: *A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. J Amer Soc Anesthesiol.* 1999;91:693
 21. Moussa A.A., Oregan P.J.: *Prevention of postoperative nausea and vomiting in patients undergoing laparoscopic bariatric surgery--granisetron alone vs granisetron combined with dexamethasone/droperidol. Middle East J Anaesthesiol.* 2007;19:357-367.
 22. Jędrzejewski E., Liszka M., Maciejewski M., et al.: *Age is not associated with increased surgical complications in patients after laparoscopic sleeve gastrectomy. Videosurg Miniinvasive Tech.* 2018;13:82.
 23. Apfel C.C., Kranke P., Piper S., et al.: *Nausea and vomiting in the postoperative phase. Expert-and evidence-based recommendations for prophylaxis and therapy. Der Anaesthetist.* 2007;56:1170-1180.
 24. Mendes M.N., de Souza M.R., da Cruz Martins F.A.: *Prophylaxis of postoperative nausea and vomiting in morbidly obese patients undergoing laparoscopic gastroplasties. A comparative study among three methods. Brazilian J Anesthesiol.* 2009;59:570-576.
 25. Groene P., Eisenlohr J., Zeuzem C., et al.: *Postoperative nausea and vomiting in bariatric surgery in comparison to non-bariatric gastric surgery. Videosurg Oth Miniinvasive Tech.* 2019;14:90.
 26. Bataille A., Letourneux J.F., Charmeau A., et al.: *Impact of a prophylactic combination of dexamethasone-ondansetron on postoperative nausea and vomiting in obese adult patients undergoing laparoscopic sleeve gastrectomy during closed-loop propofol-remifentanyl anaesthesia: A randomised double-blind placebo-controlled study. European J Anaesthesiol.* 2016;33:898-905.
 27. Benevides M.L., de Souza Oliveira S.S., de Aguilar-Nascimento J.E.: *The combination of haloperidol, dexamethasone, and ondansetron for prevention of postoperative nausea and vomiting in laparoscopic sleeve gastrectomy: A randomized double-blind trial. Obesity Surg.* 2013;23:1389-1396.
 28. Fortney J.T., Gan T.J., Graczyk S., et al.: *A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures. Anesthesia & Analgesia.* 1998;86:731-738.
 29. Vance J.P., Neill R.S., Norris W.: *The incidence and aetiology of post-operative nausea and vomiting in a plastic surgical unit. British J Plas Sur.* 1973;26:336-339.
 30. Bunce K.T., Tyers M.B.: *The role of 5-HT in postoperative nausea and vomiting. British J Anaesthesia.* 1992;69:605.
 31. Sandhu T., Tanvatharaphan P., Cheunjongkolkul V.: *Ondansetron versus metoclopramide in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy: a prospective double-blind randomized study. Asian J Surg.* 2008;31:50-54.
 32. Domino K.B., Anderson E.A., Polissar N.L., et al.: *Comparative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis. Anesthesia & Analgesia.* 1999;88:1370-1379.
 33. Nesek-Adam V., Grizelj-Stojčić E., Rašić Ž., et al.: *Comparison of dexamethasone, metoclopramide, and their combination in the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Surgical Endoscop.* 2007;21:607-612.
 34. Antor M.A., Uribe A.A., Ermyny-Falcon N., et al.: *The effect of transdermal scopolamine for the prevention of postoperative nausea and vomiting. Frontiers Pharmacol.* 2014;5:55.
 35. Kovac A.L., Pearman M.H., Khalil S.N., et al.: *Ondansetron prevents postoperative emesis in male outpatients. J Clinic Anesthesia.* 1996;8:644-51.