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ORIGINAL ARTICLE

A Comparative Study Between the Effects of Aprepitant and Ondansetron for the Prevention of Postoperative Nausea and Vomiting after Laparoscopic Cholecystectomy

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ABSTRACT

Background: Postoperative nausea and vomiting is one of the most typical side effects following surgery and anaesthesia (PONV). There has been a significant paradigm shift in the approach taken to prevent PONV. There have also been a few new medical treatments for the prevention and treatment of PONV. Clinical trials and meta-analyses show that aprepitant prevents PONV better than ondansetron.

Objective: To compare the frequency of PONV after administration of Aprepitant vs Ondansetron in laparoscopic cholecystectomy

Materials and Methods: The Jinnah Hospital in Lahore's Laparoscopic Operation Theater conducted this randomised control trial over the course of six months, from 15 April to 15 October 2019. Two groups of patients were randomly assigned. Ondansetron 8 mg was given orally to Group O two hours before induction with a sip of water. Two hours prior to induction, Group A took 80 mg of aprepitant orally with a sip of water. Every patient was instructed to fast for 6–8 hours. A 20G cannula was used to create an intravenous line after entering the operation room, and Ringer lactate was started. During surgery, the following parameters are all monitored: heart rate, oxygen saturation (SpO2), electrocardiography, noninvasive blood pressure (NIBP), and end-tidal carbon dioxide concentration (EtCO2). Using an intravenous infusion of propofol 2 mg/kg, anaesthesia was induced. Atracurium 0.6 mg/kg intravenous was used to aid in endotracheal intubation. In order to maintain anaesthesia, oxygen and (0.5–1%) isoflurane were used. As an analgesic, nalbuphine 0.1 mg/kg and paracetamol 15 mg/kg were administered. Neostigmine 0.04 mg/kg intravenous and Glycopyrotate 0.008 mg/kg intravenous were administered at the conclusion of operation to reverse the neuromuscular blockade. The last stitch or staple was made at 0 hours. Prior to surgery, the patient or attendant was instructed to contact the on-call doctor about any episodes of PONV. PONV occurrence was observed every 12 hours for 48 hours.

Results: In this study we compared Aprepitant and Ondansetron on prophylaxis of PONV in patients undergoing laparoscopic cholecystectomy. Results showed that frequency of PONV was significantly higher with Ondansetron as compared to Aprepitant. i.e. (14.6% vs. 24.2%, p-value=0.032). From 0-12 hours frequency of PONV was higher with Ondansetron while from 12-24 hours PONV was higher in Aprepitant.

Practical Implication: Government and hospitals should devise ways and procedures for effective research work for the benefit of patients, so that patient's post-operative complications and symptoms can be managed efficiently.

Conclusion: Aprepitant is more effective than ondansetron at preventing PONV in patients having laparoscopic cholecystectomy, according to the findings of this trial.

Keywords: Vomiting, Postoperative nausea, PONV, Aprepitant, Cholecystectomy, Ondansetron, General anesthesia

INTRODUCTION

The most frequent procedure carried out often all over the world is a cholecystectomy. Laparoscopic surgery has largely supplanted open cholecystectomy, which is now typically done as an outpatient treatment. Although laparoscopic operations are minimally invasive and cause little tissue damage, they are not without risk of problems. PONV is one of the more frequent consequences, with prevalence estimates ranging from 28% to 80% in various studies [1,2].

PONV not only makes the patient more uncomfortable, but it also has various side effects that can be minor or even deadly, like tachycardia, stomach pain, a longer recovery time, and a higher risk of aspiration. Without antiemetic prophylaxis, the incidence of PONV during laparoscopic cholecystectomy varies from 20 to 30%. Dehydration, electrolyte imbalance, dietary issues, and aspiration of vomit are among risks associated with uncontrolled PONV [2,3].

Extremely violent vomiting has been linked to ophthalmic surgical vitreous fluid loss, haemorrhage beneath skin flaps, and abdominal wound dehiscence. The patient, the procedure, and the type of anaesthetic can all affect the causes of PONV. Emesis can be caused by medications that excite the chemoreceptor trigger zone, such as opioids and inhaled anaesthetics. Drugs can inhibit cholinergic (muscarinic), dopaminergic, histaminergic, or serotonergic receptors, among other sites of action. Ondansetron is a strong 5-HT3 antagonist that is mainly used to treat chemotherapy- and radiotherapy-induced nausea and vomiting [3,4].

Both peripherally on the vagal nerve terminals and centrally in the area postrema's chemoreceptor trigger zone, 5-HT3 receptors can be detected. When Zhang et al. looked at the effectiveness of ondansetron for PONV prevention with different types of anaesthesia, they discovered that it considerably reduced the incidence of vomiting but not nausea, demonstrating that there is still room for a better medication [5].

Aprepitant, a neurokinin-1 (substance P) antagonist, acts after crossing the blood brain barrier via a last common pathway of the emetic centres. Sinha et al. investigated the preventative effectiveness of aprepitant in reducing PONV in morbidly obese patients undergoing bariatric surgery and discovered a 3% incidence of vomiting after 72 hours in the aprepitant group compared to a 15% incidence in the placebo group ($p = 0.021$) [6, 9,10].

Aprepitant and ondansetron were both equally effective in preventing early nausea and vomiting, which were 10% and 20%, respectively, during laparoscopic cholecystectomy, but aprepitant was superior in preventing delayed nausea and vomiting, which were 3.6% vs. 23.3%. This was the conclusion reached [6, 7]

PONV continues to be one of the most often encountered problems in day case procedures even after so many antiemetic medications. The goal of this study is to identify the most effective medication for PONV prevention. Ondansetron and aprepitant cannot be compared since there is insufficient data and because only 30 participants from each group were included in the parent study [8, 9, 10].

In our study, we will compare the occurrence of PONV throughout a 48-hour period in 12-hour time increments using a large sample size of 450 participants. Finding the best medication for early and late nausea and vomiting can aid in reducing post-operative hospital stays, improving patient comfort, and preventing complications from PONV.

Objective: To compare the frequency of PONV after administration of Aprepitant vs Ondansetron in laparoscopic cholecystectomy

Definitions for operations: Nausea

Subjective unpleasant sensation with awareness of urge to vomit. Assessed on VAS. A score >4 /10 was labeled as nausea.

Vomiting

Involuntary forceful expulsion of gastric contents through mouth

Postoperative Nausea and Vomiting

Any nausea or vomiting (even a single time) occurring during 48 hours after recovery from anesthesia. VAS for nausea was assessed every 12 hourly till 48 hours.

Hypothesis

There is a difference in frequency of PONV after administration of aprepitant and ondansetron in laparoscopic cholecystectomy.

RESOURCES AND METHODS

Study Design: Randomized Control trial

Study Setting: Laparoscopic operation theatre, Jinnah hospital Lahore

Duration of Study: Six months April 2019 to October 2019

Sampling technique: Non-probability purposive sampling.

Sample size: In patients undergoing laparoscopic cholecystectomy, the sample size was 314 cases, with 157 cases in each group, estimated with 80% power of the test, 5% level of significance, and taking the expected percentage of PONV, which is 20% with ondansetron and 10% with aprepitant (8).

Sampling standards

Inclusion standards

1 Patients with status ASA I & II (Annexure I)
2 Age 18-50 years
3 Patients undergoing for elective laparoscopic cholecystectomy.

Exclusion standards

1 Refusal of patient to give informed consent
2 Morbid obesity i.e. BMI more 40kg/m2
3 Diabetes Mellitus i.e. taking medication for diabetes or fast blood glucose above 126mg/dl
4 Pregnant females
5 Nervous system diseases, such as Parkinson's disease or multiple sclerosis
6 Hiatus Hernia
7 Allergic to Drugs
8 GERD

Data Collection Methodology: This prospective randomised controlled trial was carried out on 314 patients undergoing laparoscopic cholecystectomy who were 18 to 50 years old and American society of anesthesiology (ASA) I and II after receiving approval from Jinnah Hospital Lahore's ethical committee. All patients enrolled in the trial provided written informed consent in addition to providing demographic data such as name, age, sex, height, and contact information. The patients were divided into two groups, Groups "A" and "O," each with 157 patients, using a computer-generated random number table. Ondansetron 8 mg was given orally to Group O two hours before induction with a sip of water. Two hours before induction, Group-A got 80 mg of aprepitant orally along with a drink of water.

Two hours before induction, Group-A got 80 mg of aprepitant orally along with a drink of water. Every patient was instructed to fast for 6 to 8 hours. A 20G cannula was used to create an intravenous line after entering the operation room, and Ringer lactate was started. During surgery, the following parameters are all monitored: heart rate, end-tidal carbon dioxide concentration, noninvasive blood pressure (NIBP), electrocardiography, oxygen saturation (SpO2), and heart rate (EtCO2). Anaesthesia was brought on by administering a 2 mg/kg intravenous infusion of propofol. Endotracheal intubation was aided by the intravenous administration of atracurium, 0.6 mg/kg. In order to maintain anaesthesia, oxygen and (0.5–1%) isoflurane were used. As an analgesic, nalbuphine 0.1 mg/kg and paracetamol 15 mg/kg were administered. Neostigmine 0.04 mg/kg intravenous and Glycopyrotate 0.008 mg/kg intravenous were administered at the conclusion of operation to reverse the neuromuscular blockade. The last stitch or staple was made at 0 hours.

Data Analysis Methodology: Data entry and analysis were conducted using SPSS 20.0. Age and BMI were determined quantitatively using the mean and standard deviation. Indicators of qualitative factors, The frequency and percentages of variables, like gender and PONV incidence, were used. To account for the effect modifiers, the data were stratified for BMI, age, and gender. For a period of 12 hours, the incidence of PONV was stratified. The post-stratification chi square test was used to assess significance, with a p-value of 0.05 being considered significant. The chi-square test was used to determine the frequency of PONV in both groups, with a p-value of 0.05 being deemed significant.

RESULTS

• In Group-A 47(29.9%) patients BMI was normal, 51(32.5%) patients were overweight and 59(37.6%) patients were obese and in Group-O 54(34.4%) had normal BMI, 50(31.8%) were overweight and 53(33.8%) were obese. Table-3

• In Group-A 73(46.5%) patients had ASA-I and 84(53.5%) had ASA-II while in Group-O 84(53.5%) had ASA-I and 73(46.5%) had ASA-II. Table-4

• PONV was significantly higher in Group-O as compared to Group-A. i.e. 14.6% vs. 24.2%, p-value=0.032. At 0-12 hour PONV was higher in Group-O, at 12-24 hours frequency of PONV was higher in Group-A while from 24 hours onwards till 48th hour none of the patients experienced PONV. Table-5

• Group-A had a substantially greater frequency of PONV in the younger age groups, while Group-O had a significantly higher frequency of PONV in the older age categories.Table-6

• For male and female patients frequency of PONV was significantly higher in Group-O but among male it was statistically significant while among females statistically significance was not achieved. Table-7

• ASA status of patients had no significant effect of PONV in both treatment groups. Although frequency of PONV was lower in Group-A as that of Group-O patients. Table-8

• PONV was significantly higher in Group-O patients with normal BMI and similar trend was seen for patients who were overweight and obese. Statistical significance was only seen for patients with normal BMI however for overweight and obese patients statistical significance was not achieved for PONV in relation to study groups. Table-9

Table-3: Body Mass Index of Patients in Treatment Groups

	Group-A	Group-O	Total
Normal	47	54	101
Overweight	51	50	101
Obese	59	53	112
Total	157	157	314

Table-4: ASA Status of patients in Treatment Groups

	Group A	Group O	Total
ASA-I	73(46.5%)	84(53.5%)	157
ASA-II	84(53.5%)	73(46.5%)	157
Total	157	157	314

Table-5: Frequency of Ponv in Groups

PONV	Group A	Group B	Total
Yes	23(14.6%)	38(24.2%)	61
No	134(85.4%)	119(76.8%)	253
Total	157	157	314
p-Value	0.032		

Table-6: Frequency of PONV in Groups in relation to age of patients

AGE	PONV	Group-A (n:157)	Group-O(n:157)	p-Value
20-30	Yes	18(41.9%)	0(0%)	<0.001
	No	25(58.1%)	31(100%)	
31-40	Yes	0(0%)	6(11.5%)	0.025
	No	41(100%)	46(88.5%)	
41-50	Yes	5(6.8%)	32(43.2%)	<0.001
	No	68(93.2%)	42(56.8%)	

Table-7: Frequency of PONV in Groups in relation to Gender of patients

Gender	PONV	Group-A	Group-O	p-Value
Male	Yes	0(0%)	13(16.3%)	0.002
	No	53(100%)	67(83.8%)	
Female	Yes	23(22.1%)	25(32.5%)	0.119
	No	8(77.9%)	52(67.5%)	

Table-8: Frequency of PONV in Groups in relation to ASA Status

ASA Status	PONV	Group-A	Group-O	p-Value
ASA-I	Yes	12(16.4%)	22(26.2%)	0.139
	No	61(83.6%)	62(73.8%)	
ASA-II	Yes	11(13.1%)	16(21.9%)	0.144
	No	73(86.9%)	57(78.1%)	

Table-9: Frequency of PONV in Groups in relation to BMI

BMI	PONV	Group-A	Group-O	p-Value
Normal	Yes	6(12.8%)	17(31.5%)	0.025
	No	41(87.2%)	37(68.5%)	
Overweight	Yes	9(17.6%)	12(24%)	0.432
	No	42(82.4%)	38(76%)	
Obese	Yes	8(13.6%)	9(17%)	0.614
	No	51(86.4%)	44(83%)	

DISCUSSION

Recent studies have focused on the effectiveness of a balanced antiemetic strategy using medications that operate on various locations and receptors. There have been studies on a number of medicines, including Metoclopramide, Dexamethasone, Ondansetron, Droperidol, and Clonidine. [9, 10]. Since currently endorsed antiemetics, There is still a medical need for extra potent medications to prevent PONV because medications like 5-HT3 receptor antagonist do not offer full protection. [11]

In this study, we compared Aprepitant and Ondansetron for patients having laparoscopic cholecystectomy in terms of PONV prophylaxis. Results showed that ondansetron significantly increased the frequency of PONV compared to aprepitant, 14.6% vs. 24.2%, with a p-value of 0.032. Ondansetron increased the frequency of PONV from 0 to 12 hours, but Aprepitant increased PONV from 12 to 24 hours [12].

In open and laparoscopic abdominal surgery, randomised Aprepitant was also discovered to be an efficient pharmacological method for the prevention of PONV in control trials comparing the results of aprepitant and ondansetron. Aprepitant was found to be superior to Ondansetron for preventing vomiting in the early postoperative period but equivalent to Ondansetron for preventing nausea. Comparable studies from Korea and Japan produced similar findings on the prevention of PONV during gynaecological laparoscopic surgery. Each of these trials showed a statistically significant decrease in PONV at both the immediate and delayed postoperative times [13]

The author's conclusion, which is in line with the findings of this trial 14, 15, was found for preventing vomiting in the first 24 and 48 hours, aprepitant was more effective than ondansetron. The Aprepitant group experienced a cumulative incidence of vomiting of 16% 48 hours later, while the Ondansetron group had a cumulative incidence of 38% (p-value = 0. According to a study from Egypt, oral aprepitant coupled with intravenous ondansetron and dexamethasone effectively suppresses early PONV in patients undergoing laparoscopic surgery for up to 24 hours after surgery [16].

The study found that complete response was attained in 37.9% of the participants on aripiprazole, which is somewhat better than the 31.2% of the subjects taking ondansetron. There was no statistically significant difference in side effects between the groups (p-value > 0.05), which is in line with the other investigations. Other significant studies show that Aprepitant significantly reduced nausea and vomiting in patients with established PONV compared to placebo (p-value 0.05) for up to 24 hours following major gynaecological surgery [13,17,18].

There is no question that NK-1 antagonists are significantly effective for PONV, as suggested by our study and numerous other international ones. Therefore, aprepitant appears to be a desirable medication for the prevention of high-risk PONV cases. An intravenous form may be utilised for PONV high-risk patients even if it is not recommended. Casopitant, Rolapitant, and Vestipitant are three other NK-1 receptor antagonists that are in the midst of development. After crossing the blood brain barrier, the NK 1 receptor antagonist aprepitant acts through a common route used by the emetic centres. Aprepitant is a medication that treats PONV well and has few adverse effects [13,15,19].

This medicine has proved to provide significant and lasting symptom relief when taken either alone or in combination with other anti-emetics. In the postoperative population, the innovative medication has been shown to be effective in treating both acute and delayed onset nausea and vomiting, which reduces the requirement for rescue dosages later in the postoperative period. It should be noted that aprepitant has been demonstrated to be more effective than ondansetron at preventing PONV during the perioperative period. The biggest drawback and usage restriction of aprepitant is its high cost, which makes it difficult to justify usage in situations other than those with really severe symptoms or significant risk factors for nausea and vomiting. It is envisaged that costs would go down in the future, enabling the inclusion of this potent drug for routine PONV prevention[13,17,19].

CONCLUSION & PRACTICAL IMPLICATIONS

The study's findings support the notion that aprepitant is superior to ondansetron in avoiding PONV in individuals having laparoscopic cholecystectomy. In order to effectively treat patients' post-operative problems and symptoms, the government and hospitals should develop methods and processes for successful research work for the benefit of patients.

REFERENCES

1 Wolfe BM, Gardiner B, Frey CF. Laparoscopic cholecystectomy: a remarkable development. Jama 2015;314(13):1406-.

2 Albuquerque AFM, Queiroz SIML, Germano AR, da Silva JSP. Factors associated to post-operative nausea and vomiting following oral and maxillofacial surgery: a prospective study. Oral and maxillofacial surgery 2017;21(1):49-54.

3 Mishra A, Pandey RK, Sharma A, Darlong V, Punj J, Goswami D, et al. Is perioperative administration of 5% dextrose effective in reducing the incidence of PONV in laparoscopic cholecystectomy?: A randomized control trial. Journal of clinical anesthesia 2017;40:7-10.

4 Kranke P. Implementing postoperative nausea and vomiting management guidelines. Postoperative Nausea and Vomiting 2016:170.

5 Wong E, Pulenzas N, Bedard G, DeAngelis C, Zhang L, Tsao M, et al. Ondansetron rapidly dissolving film for the prophylactic treatment of radiation-induced nausea and vomiting—a pilot study. Current Oncology 2015;22(3):199.

6 Zhang D, Shen Z, You J, Zhu X, Tang Q-F. Effect of ondansetron in preventing postoperative nausea and vomiting under different conditions of general anesthesia: A preliminary, randomized, controlled study. Upsala Journal of Medical Sciences 2013 05/ 10/16/received 01/11/accepted;118(2):87-90.

7 Sinha AC, Singh PM, Williams NW, Ochroch EA, Goudra BG. Aprepitant's prophylactic efficacy in decreasing postoperative nausea and vomiting in morbidly obese patients undergoing bariatric surgery. Obesity surgery 2014 Feb;24(2):225-31.

8 Grau-Talens EJ, Motos-Micó JJ, Giraldo-Rubio R, Aparicio-Gallego JM, Salgado JF, Ibáñez CD, et al. Small-incision cholecystectomy (through a cylinder retractor) under local anaesthesia and sedation: a prospective observational study of five hundred consecutive cases. Langenbeck's archives of surgery 2018;403(6):733-40.

9 Wu S-J, Xiong X-Z, Cheng T-Y, Lin Y-X, Cheng N-S. Efficacy of ondansetron vs. metoclopramide in prophylaxis of postoperative nausea and vomiting after laparoscopic cholecystectomy: a

systematic review and meta-analysis. Hepato-gastroenterology 2012;59(119):2064-74.
10 Dua N, Bhatnagar S, Mishra S, Singhal A. Granisetron and ondansetron for prevention of nausea and vomiting in patients undergoing modified radical mastectomy. Anaesthesia and intensive care 2004;32(6):761-4.
11 Apfel C, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, et al. IMPACT Investigators. a factorial trial of six interventions for the prevention of postoperative nausea and vomiting. Headache 2004;44(10):1059-60.
12 Ham SY, Shim YH, Kim EH, Son MJ, Park WS, Lee JS. Aprepitant for antiemesis after laparoscopic gynaecological surgery: a randomised controlled trial. European Journal of Anaesthesiology (EJA) 2016;33(2):90-5.
13 Okafor D, Kaye AD, Kaye RJ, Urman RD. The role of neurokinin-1 (substance P) antagonists in the prevention of postoperative nausea and vomiting. Journal of anaesthesiology, clinical pharmacology 2017;33(4):441.
14 Habib AS, Keifer JC, Borel CO, White WD, Gan T. A comparison of the combination of aprepitant and dexamethasone versus the combination of ondansetron and dexamethasone for the prevention of postoperative nausea and vomiting in patients undergoing craniotomy. J Anesthesia Analgesia 2011;112(4):813-8.
15 Gan TJ, Apfel CC, Kovac A, Philip BK, Singla N, Minkowitz H, et al. A randomized, double-blind comparison of the NK1 antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. Anesthesia & Analgesia 2007;104(5):1082-9.
16 Hussein MM, Mostafa RH. Aprepitant for attenuation of postoperative nausea and vomiting with a decrease in postoperative analgesic needs after laparoscopic surgery. Ain-Shams Journal of Anaesthesiology 2017;10(1):144.
17 Wilhelm SM, Dehoorne-Smith ML, Kale-Pradhan PB. Prevention of postoperative nausea and vomiting. Annals of Pharmacotherapy 2007;41(1):68-78.
18 Diemunsch P, Schoeffler P, Bryssine B, Cheli-Muller L, Lees J, McQuade B, et al. Antiemetic activity of the NK1 receptor antagonist GR205171 in the treatment of established postoperative nausea and vomiting after major gynaecological surgery. British journal of anaesthesia 1999;82(2):274-6.
19 Ahmed H, Hammad AM, Abushouk AI, Zidan M, Salem M, Negida A, et al. Meta-analysis of safety and efficacy of rolapitant, NK-1 receptor antagonist for prevention of chemotherapy-induced nausea and vomiting. Current problems in cancer 2018;42(2):241-55.