

COMPARISON OF PRE-OPERATIVE ONDANSETRON VERSUS COMBINATION OF DEXAMETHASONE AND ONDANSETRON FOR POSTOPERATIVE NAUSEA AND VOMITING IN ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY

Mansoor Tariq Azim, Syed Mukarram Hussain*, Muhammad Mudasir Saleem**, Eisha Mansoor***, Mishal Pervaiz****

142 Medical Battalion Gujranwala Pakistan, *Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan, **Combined Military Hospital Bahawalpur/National University of Medical Sciences (NUMS) Pakistan, ***Armed Forces Postgraduate Medical Institute/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, ****Ghurki Trust Teaching Hospital Pakistan

ABSTRACT

Objective: To compare the efficacy of ondansetron with a combination of ondansetron and dexamethasone after elective laparoscopic cholecystectomy in terms of postoperative nausea and vomiting.

Study Design: Randomized controlled trial.

Place and Duration of Study: Department of Surgery, Combined Military Hospital Rawalpindi Pakistan, from Apr 2014 to Mar 2015.

Materials and Methods: Two hundred and twenty two patients fulfilling the inclusion criteria were selected for study and divided into two groups of 111 each. Group A was given ondansetron while group B was given combination of ondansetron and dexamethasone at induction of general anesthesia. Patients of both groups were observed at 24 hours postoperatively for nausea and vomiting.

Results: Sixty six patients in group A had nausea as compared to 50 patients in group B (p -value 0.03), 46 patients in group A had vomiting as compared to 19 patients in group B (p -value <0.001), showing statistically significant difference between the two groups.

Conclusion: Postoperative nausea and vomiting is significantly lower in ondansetron and dexamethasone combination group as compared to ondansetron alone group after elective laparoscopic cholecystectomy.

Keywords: Dexamethasone, Elective laparoscopic cholecystectomy, Ondansetron, Postoperative nausea and vomiting.

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INTRODUCTION

First reported laparoscopic cholecystectomy was performed by Phillippe Mouret, a French surgeon in 1987 and now it is considered the gold standard treatment for symptomatic cholelithiasis¹. Laparoscopic cholecystectomy is the second most commonly performed general surgery procedure in United States². It is becoming more popular day by day in our country owing to the advantage of rapid recovery and shorter hospital stay³. However, laparoscopic surgery is found to be associated with a high incidence of postoperative nausea and vomiting (PONV) which impairs achieving the above mentioned benefits⁴. Its incidence can be as high

as 72% following laparoscopic cholecystectomy⁵. Many different factors like nature of surgery, uncorrected hypovolemia, pro-longed duration of general anesthesia and administration of opioid drugs can lead to PONV⁶. PONV is one of the major causes of patient dissatisfaction following surgery⁷. A number of pharmacological agents have been tried for prevention and management of PONV but no agent is found to be 100% successful⁸. It has been proved that combination pharmacological modality is better than monotherapy in this regard⁹. Selection of antiemetic drug is dependent upon its efficacy, safety and ease of dosing. Ondansetron is a selective 5-HT₃ receptor antagonist and dexamethasone is a corticosteroid with potent antiemetic properties¹⁰. We conducted this study to compare the efficacy of combination therapy using ondansetron and dexamethasone with monotherapy using ondan-

Correspondence: Dr Mansoor Tariq Azim, Dept of Gen Surgery, 142 Medical Battalion Gujranwala Cantt Pakistan

Email: mansurtariq@gmail.com

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setron alone for prophylaxis against nausea and vomiting after elective cholecystectomy.

PATIENTS AND METHODS

This study was randomized controlled trial conducted in department of Surgery Combined Military Hospital Rawalpindi from 1st April 2014 to 30th March 2015. Sample size was calculated by World Health Organization sample size calculator version 2.0. Even number of patients satisfying inclusion criteria were randomly selected on each operation list and divided into two groups by lottery. The same procedure was carried out on every operation list till the required sample size was achieved, 111 patients in each group. One group coded as "group A" received ondansetron alone (4mg) while the other group coded "group B" received combination of ondansetron (4mg) and dexamethasone (8mg). The study medications were prepared and presented to anesthetist as identical 2ml filled syringes, who administered drugs at the time of induction of anesthesia. The response was assessed for 24 hrs post operatively by resident house officer using a pre tested close ended structured questionnaire. Both the anesthetist and the resident house officer were kept blinded. Both male and female patients between 25-60 years of age undergoing elective laparoscopic cholecystectomy fulfilling American society of anesthesiology (ASA) class I and II were included. Patients having previous midline laparotomy, taking medicine with known anti-emetic activity, having history of hypertension or vertigo and those requiring conversion from laparoscopic technique to open approach were not included in this study.

After obtaining informed written consent, all relevant investigations were carried out in each patient. All patients underwent laparoscopic cholecystectomy after standard preparation under general anesthesia with endotracheal intubation. Group A was given ondansetron while group B was given combination of ondansetron and dexamethasone at the time of induction of anesthesia. Patients of both groups were

observed at 24 hours postoperatively for nausea and vomiting. antiemetic (meto-clopramide 10 mg I/V) was given if patient remained nauseous for more than 15 minutes or experienced vomiting. All the data was entered into the statistical package for social sciences (SPSS) version 18.0 and analyzed. Mean and standard deviation was calculated for quantitative variables like age. For qualitative variables like gender, nausea and vomiting, the frequency and percentage was calculated. Effect modifiers like age and gender were controlled by stratification. Chi-square test was applied and *p*-value of ≤ 0.05 was considered significant.

RESULTS

A total of 222 patients were included in the study during the study period. Out of total 222 patients, 18.9% (n=21) in group-A and 16.2% (n=18) in group-B were male and 81.1% (n=90) in group-A and 83.8% (n=93) in group-B were female. Age distribution of the patients showed that 23.4% (n=26) in group-A and 27% (n=30) in group-B were less than 40 years of age, whereas 76.6% (n=85) in group-A and 73% (n=81) in group-B were greater than 40 years of age, Mean \pm SD was calculated as 43.51 ± 5.97 and 44.21 ± 6.11 respectively. Statistical analysis of the study revealed that 59.5% (n=66) in group A developed nausea as compared to 45.0% (n=50) in group B with *p*-value of 0.03. Similarly 41.4% (n=46) in group A and 17.1% (n=19) in group B developed vomiting, calculated *p*-value being < 0.001 showing statistically significant difference between the two groups (table-I). Stratification for nausea and vomiting with regard to age (*p*-value < 0.013 and 0.018 respectively) and gender (*p*-value < 0.001 and 0.033) was done showing significant difference between the two groups (table-II & III).

DISCUSSION

PONV is one of the most common symptoms occurring after laparoscopic surgery⁸. PONV is found to be even more distressing than post surgical pain with cost of recovery increasing significantly in patients that develop it in post-operative period¹¹. Approximately one third of

surgical patients experience nausea and vomiting in postoperative period triggered by four main receptors in the body: histamine, serotonergic, dopaminergic and opiate¹². High incidence of PONV after laparoscopic surgery can be caused by the stimulation of mechanoreceptors of gut by pneumoperitoneum which places pressure on vagus nerve and in turn stimulates the vomiting center in brain¹³. Persistent PONV is associated with a number of complications such as fluid and electrolyte imbalance, wound disruption, delay in mobilization and prolonged hospitalization

dexamethasone being 4mg and 8mg respectively is recommended in literature¹⁵ and we conducted this study by using the same doses of these drugs. Ondansetron and dexamethasone have also well-accepted roles in the prophylaxis of PONV after gynecological, obstetric, pediatric and ophthalmic surgery¹⁶. In this study we compared the efficacy of ondansetron with and without dexamethasone in the prevention of PONV after laparoscopic cholecystectomy. Our results showed statistically significant difference of PONV between group A & B (p -value <0.001),

Table-I: Group wise incidence of nausea and vomiting

	Nausea		Vomiting	
	Yes	No	Yes	No
Group A	66	45	46	65
Group B	50	61	19	92
p -value	0.03		<0.001	

Table-II: Stratification of nausea with regard to age and gender.

Nausea	Group A				Group B			
	Age		Gender		Age		Gender	
	<40 Years	>40 Years	Male	Female	<40 Years	>40 Years	Male	Female
Yes	10	56	06	60	08	42	04	46
No	16	29	15	30	22	39	14	47
p -value	0.013		<0.001		0.018		0.033	

Table- III: Stratification of vomiting with regard to age and gender

Vomiting	Group A				Group B			
	Age		Gender		Age		Gender	
	<40 Years	>40 Years	Male	Female	<40 Years	>40 Years	Male	Female
Yes	06	40	04	42	12	07	06	13
No	20	45	17	48	18	74	12	80
p -value	0.030		0.021		<0.001		0.046	

causing significant adverse impact on patient well-being and health care resources¹⁴. Hence strategies for prevention of PONV are a vital component of enhanced recovery after surgery protocols.

Being multifocal in origin, multimodal combination pharmacological therapy is considered more appropriate for prophylaxis of PONV. Dexamethasone and ondansetron are the two most commonly used drugs for this purpose. Prophylactic dose of ondansetron and

PONV being significantly less in group receiving both the drugs. Our findings are in accordance with a study conducted by Bano and colleagues where they found that frequency of nausea and vomiting was significantly less in ondansetron and dexamethasone combination group as compared to dexamethasone alone group (p -value 0.035)¹⁷. A higher incidence of PONV was observed in females in both study groups, similar to the finding mentioned in literature¹⁸. Ondansetron is proved to be specifically effective against

vomiting. On the other hand, dexamethasone not only reduces the incidence of vomiting but is also effective in the prevention of nausea. This explains why the combined use of ondansetron and dexamethasone is very effective in reducing the overall incidence of both nausea and vomiting as both the drugs act as additive¹⁹. Similar results were found in studies conducted by Ahsan and colleagues (p -value 0.046)²⁰ and Ahmed *et al*²¹. Both studies involved patients undergoing laparoscopic cholecystectomy and combination versus only ondansetron was compared. In another study conducted by McKenzie *et al*²² comparison of ondansetron and dexamethasone (group-I) with ondansetron (group-II) was done in female patients undergoing gynecological surgery. A complete response, defined as no emesis and no need for rescue antiemetic during the 24-hour post-operative period, occurred in 52% patients in the combination group as compared to 38% in ondansetron group ($p=0.045$). Vomiting was statistically less in combination group than ondansetron alone group ($p=0.003$). They concluded that the combination of ondansetron plus dexamethasone was more effective than ondansetron alone for prophylaxis against PONV. Similar findings were observed by Eidy and colleagues where they found that incidence of nausea and vomiting was significantly less in dexamethasone and ondansetron combination group as compared to ondansetron alone group (p -value 0.01)²³. A number of concerns exist regarding the safety of dexamethasone in postoperative period but use of single dose dexamethasone is found to be free from any significant side effects including delayed wound healing. Furthermore, it is not only effective in decreasing postoperative pain after laparoscopic cholecystectomy but also helps in improving respiratory functions in early postoperative period²⁴.

LIMITATIONS OF STUDY

Study was carried out at single center and time frame was not considered when measuring incidence of PONV. Moreover, use of rescue

antiemetic was not quantified thus ignoring important data.

CONCLUSION

Laparoscopic cholecystectomy has become the treatment of choice for cholelithiasis in today's modern era. The high incidence of PONV after laparoscopic surgery is well documented and is the main reason for prolonged hospital stay following surgery significantly increasing the cost of treatment. Identification of high risk cases and prophylactic antiemetic measures are the best modality in countering PONV. Combination of ondansetron and dexamethasone is an effective prophylactic measure and should be offered to all patients undergoing laparoscopic cholecystectomy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Liu DS, Guan F, Wang B, Zhang T. Combined usage with intraperitoneal and incisional ropivacaine reduces pain severity after laparoscopic cholecystectomy. *Int J ClinExp Med* 2015; 8(12): 22460-68.
2. Zapf M, Denham W, Barrera E, Butt Z, Carbray J, Wang C, et al. Patient-centered outcomes after laparoscopic cholecystectomy. *Surg Endosc* 2013; 27(12): 4491-98.
3. Fujii Y. Management of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. *Surg Endosc* 2011; 25(3): 691-95.
4. Bhattarai B, Shrestha S, Singh J. Comparison of Ondansetron and combination of Ondansetron and Dexamethasone as a prophylaxis for postoperative nausea and vomiting in adults undergoing elective laparoscopic surgery. *J Emerg Trauma Shock* 2011; 4(2): 168-72.
5. Bhalla J, Baduni N, Bansal P. Comparison of palonosetron with ondansetron for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anesthesia. *J Minim Access Surg* 2015; 11(3): 193-97.
6. Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg* 2014; 118(1): 85-113.
7. Myklejord DJ, Yao L, Liang H, Glurich I. Consensus guideline adoption for managing postoperative nausea and vomiting. *WMJ* 2012; 111(5): 207-13.
8. Sharma ANG, Shankaranarayana P. Postoperative Nausea and Vomiting: Palonosetron with Dexamethasone vs. Ondansetron with Dexamethasone in Laparoscopic Hysterectomies. *Oman Med J* 2015; 30(4): 252-56.
9. Chatterjee S, Rudra A, Sengupta S. Current concepts in the management of postoperative nausea and vomiting. *Anaesthiosol Res Pract* 2011; 2011: 748031.
10. Kovac AL. Update on the management of postoperative nausea and vomiting. *Drugs* 2013; 73(14): 1525-47.

11. Parra-Sanchez I, Abdallah R, You J, Grady M, Cummings K. A time-motion economic analysis of postoperative nausea and vomiting in ambulatory surgery. *Can J Anaesth* 2012; 59(4): 366-75.
12. Kim MS, Lee JR, Choi EM, Kim EH, Choi SH. Association of 5-HT_{3B} Receptor Gene Polymorphisms with the Efficacy of Ondansetron for Postoperative Nausea and Vomiting. *Yonsei Med J* 2015; 56(5): 1415-20.
13. Turkistani A, Abdullah K, Manaa E, Delvi B, Khairy G, Abdulghani B, et al. Effect of fluid preloading on postoperative nausea and vomiting following laparoscopic cholecystectomy. *Saudi J Anaesth* 2009; 3(2): 48-52.
14. Singh BN, Dahiya D, Bagaria D, Saini V, Kaman L, Kaje V, et al. Effects of preoperative carbohydrates drinks on immediate post-operative outcome after day care laparoscopic cholecystectomy. *Surg Endosc* 2015; 29(11): 3267-72.
15. Paech MJ, Rucklidge MWM, Lain J, Dodd PH, Bennett EJ, Doherty DA. Ondansetron and dexamethasone dose combinations for prophylaxis against postoperative nausea and vomiting. *Anesthesia and Analgesia* 2007; 104(4): 808-14.
16. Szarvas S, Chellapuri RS, Harmon DC, Owens J, Murphy D, Shorten GD. A comparison of dexamethasone, ondansetron, and dexamethasone plus ondansetron as prophylactic antiemetic and antipruritic therapy in patients receiving intrathecal morphine for major orthopedic surgery. *Anesth Analg* 2003; 97(1): 259-63.
17. Bano F, Zafar S, Aftab S, Haider S. Dexamethasone plus ondansetron for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: a comparison with dexamethasone alone. *J Coll Physicians Surg Pak* 2008; 18(5): 265-69.
18. Honkavaara P, Lehtinen AM, Hovorka J, Korttila K. Nausea and vomiting after gynaecological laparoscopy depends upon the phase of the menstrual cycle. *Can J Anaesth* 1991; 38(7): 876-79.
19. Elhakim M, Nafie M, Mahmoud K, Atef A. Dexamethasone 8mg in combination with ondansetron 4mg appears to be the optimal dose for the prevention of nausea and vomiting after laparoscopic cholecystectomy. *Can J Anaesth* 2002; 49(9): 922-26.
20. Ahsan K, Abbas N, Naqvi SMN, Murtaza G, Tariq S. Comparison of efficacy of Ondansetron and Dexamethasone combination and Ondansetron alone in preventing post-operative nausea and vomiting after laparoscopic cholecystectomy. *J Pak Med Assoc* 2014; 64(3): 242-46.
21. Ahmed N, Muslim M, Aurangzeb M, Zarin M. Prevention of post-operative nausea and vomiting in laparoscopic cholecystectomy. *J Med Sci* 2012; 20(1): 33-36.
22. McKenzie R, Tantisira B, Jarambelker DJ, Riley TJ, Abdulhady H. Comparison of Ondansetron with Ondansetron plus Dexamethasone in the prevention of postoperative nausea and vomiting. *Anaesth Analg* 1994; 79(5): 961-64.
23. Eidy M, Vafaei HR, Rjabi M, Mohammadzadeh M, Pazouki A. Effect of ondansetron and dexamethasone on post-operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. *J Minim Invasive Surg Sci* 2012; 1(4): 138-43.
24. Sistla S, Rajesh R, Sadasivan J, Kundra P, Sistla S. Does single-dose preoperative dexamethasone minimize stress response and improve recovery after laparoscopic cholecystectomy? *Surg Laparosc Endosc Percutan Tech* 2009; 19(6): 506-10.