ORIGINAL ARTICLE

Comparison of ondansetron and dexamethasone combination with odensetron in preventing post-operative nausea and vomiting in patients of laparoscopic cholecystectomy

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Abstract

Objective: To compare the efficacy of ondansetron and dexamethasone combination with ondansetron alone in preventing post-operative nausea and vomiting in patients of laparoscopic cholecystectomy.

Material and Methods: This randomized controlled trial was conducted in Department of Anaesthesia and Surgery, Khyber Teaching Hospital, Peshawar from January, 2017 to June, 2018. 208 patients fulfilling the criteria were hospitalized for laparoscopic cholecystectomy. 104 patients were allocated in ondansetron and dexamethasone combination (group 'A') while 104 patients in ondansetron only (group 'B') by simple random technique. The incidence of nausea and vomiting was recorded for first 24 hours post-operatively. Data were compiled and analyzed with SPSS 20. Chi-square test was applied to compare efficacy in both groups, taken $P \leq 0.05$ as significant.

Result: Mean age in Group-A was 30±10.21 years and in Group-B was 3±9.27 years. Male to female ratio in Group-A was 3.2:6.8 and in Group-B was 3:7. Ondansetron and dexamethasone combination was effective in 90% patients where as Ondansetron alone was effective in 68% patients which was statistically significant with P-value=0.0001.

Conclusion: Combination of ondansetron and dexamethasone is more effective than ondansetron alone in preventing post-operative nausea and vomiting in patients of laparoscopic cholecystectomy and it's use should be encouraged in routine cases.

Keywords: Efficacy, Ondansetron and Dexamethasone, post-operative nausea and vomiting (PONV), laparoscopic cholecystectomy.

Introduction:

The diseases of gall bladder are common worldwide and among them, cholelithiasis affects about 10-15% of adult population with a higher prevalence in women.[1] Laparoscopic cholecystectomy is a minimally invasive procedure which offers many benefits like less hospital stay, less post-operative pain, shorter hospital stay and early resumption of normal activities.[2] Though the benefits of this procedure are more but post operative nausea and vomiting is the most common complication associated with laparoscopic surgeries and is the reason of prolonged hospitalization, more morbidity and delayed functional recovery.[3] The incidence of post-operative nausea and vomiting (PONV) after surgery is in the range of 20-30% but it may be up to 50-70% after laparoscopic surgeries.[4]

Prevention of PONV after laparoscopic surgeries is a challenge to the peri-operative physicians as it is distressing for the patients and much more such surgeries are performed on day care basis. Esophageal rupture, subcutaneous emphysema, and bilateral pneumothorax are additional complications of post-operative nausea and vomiting .[5]

There are certain factors which can predispose the patient to post-operative nausea and vomiting including administration of opioids, female

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gender, type of surgery, previous history of PONV, duration and drugs of anesthesia and carbon dioxide retention. Laparoscopic cholecystectomy requires insufflation of carbon dioxide for pneumo-peritoneum which can prove as a major cause for post-operative nausea and vomiting.[6]

Recent interest has focused on the use of a combination anti-emetic acting at different receptors and the adaptation of a multi-modal approach to tackle this problem. Many different types of anti-emetic drugs are used which includes serotonin receptor antagonists, phenothiazines, droperidol, steroids (dexamethasone) and 5-HT3 receptor antagonists (ondansetron, granisetrone and tropisetrone). Among these, 5-HT3 receptor antagonists are tvhe most widely used either alone or in combination with dexamethasone.[7] In a study by Gautam B, et al from Nepal has found that efficacy of ondansetron alone was 66.7% as compare to 89.4% in ondansetron and dexamethasone combination in preventing post-operative nausea and vomiting in patients of laparoscopic cholecystectomy.[8]

A number of studies have compared ondansetron with ondansetron and dexamethasone combination for post-operative nausea and vomiting prophylaxis after laparoscopic surgeries.[4] These studies are not unanimous in reporting their results and there is no consensus on which drug is better in PONV prophylaxis. In Pakistani population, there is a paucity of data and further evidence is needed in our local population on this subject. Results of our study results will help to select the best treatment in patients undergoing laparoscopic cholecystectomy in our local population.

Our objective was to compare the efficacy of ondansetron and dexamethasone combination with odansetron only in preventing post-operative nausea and vomiting in patients of laparoscopic cholecystectomy.

Material and methods:

This prospective randomized control trial was conducted at Department of Anesthesiology and Surgery, Khyber Teaching Hospital, Peshawar, Pakistan from January 2017 to June 2018. Patients suffering from symptomatic gallstones, age between 18 to 50 years were admitted for laparoscopic cholecystectomy from out patient department. Patients with ASA grade III to VI, have a history of motion sickness, receiving antiemetic, anti-histamine or steroid drugs within 24 hours prior to surgery were excluded from the study.

208 patients fulfilling the above criteria were included in the study after permission from ethical committee. Informed consent was taken from each patient, after explaining the risk and benefit of the study. Demographic information of patients (age, gender, BMI) was taken. All patients were randomly assigned by blind balloting into one of two groups of 104 patients each. Each patient had assigned a number at enrolment which defined a study drug assignment (ondansetron and dexamethasone combination/ ondansetron alone). 104 patients were in ondansetron and dexamethasone combination (Group-A) while 104 patients were in ondansetron alone (Group-B).

In group-A Ondansetron 4mg plus Dexamethasone 8mg and in group-B Ondansetron 4mg plus 2 ml normal saline was given just before induction of anesthesia. All patients were hydrated with 10ml/kg of ringer lactate. Anesthesia was induced with fentanyl 2µg/kg, followed by propofol 2mg/kg. Atracurium (0.6 mg/kg) was given intravenously to facilitate oro-tracheal intubation. Anaesthesia was maintained with isoflurane (1% inspired concentration) along with nitrous oxide 60% in O2 with controlled ventilation adjusted to maintain the end tidal CO2 at around 35-45 mm of Hg. Muscle relaxation for pneumo-peritonium and surgical procedures was provided with additional doses of atracurium. A naso-gastric tube was passed to empty the stomach which was suctioned and removed before extubation. During laparoscopy intra-abdominal pressure was maintained at 12 mmHg by CO2 insufflation and patients was placed in 15 – 20 degree head up position with little left lateral tilt. Patients were monitored during gen-

Table-1: Stratification of efficacy with respect to age , sex, bmi, asa grade and duration of procedure(n=208)

Variables		Efficacy	Group A	Group B	P-value
Age range in years	18 - 35	Effective	38(36.5%)	27(25.92%)	0.0103
		Not effective	04(3.8%)	13(12.5%)	
	36 - 50	Effective	56(53.8%)	44(42.24%)	0.0027
		Not effective	06(5.8%)	20(19.2%)	
Sex	Male	Effective	30(28.8%)	2120.16%()	0.0213
		Not effective	03(2.9%)	10(9.6%)	
	Female	Effective	64(61.44%)	50(48%)	0.0013
		Not effective	07(6.7%)	23(22.08%)	
BMI	≤ 25Kg/m^2	Effective	43(41.28%)	30(28.8%)	0.0052
		Not effective	04(3.8%)	14(13.44%)	
	> 25Kg/m^2	Effective	51(48.96%)	41(39.4%)	0.0052
		Not effective	06(5.8%)	19(18.24%)	
ASA Grade	Grade I	Effective	62(59.52%)	48(46.08%)	0.009
		Not effective	06(5.8%)	22(21.12%)	
	Grade II	Effective	32(30.72%)	23(22.08%)	0.0304
		Not effective	04(3.8%)	11(10.6%)	
Duration of Procedure	≤60 minutes	Effective	38(36.5)	30(28.8%)	0.0000
		Not effective	04(3.8%)	14(13.44%)	
	> 60 minutes	Effective	56(53.8%)	41(39.4%)	0.0026
		Not effective	06(5.8%)	19(18.24%)	

eral anesthesia by continuous ECG, NIBP, pulse oxymetry and capnometry. At the completion of surgery residual neuro-muscular blockade was antagonised with intravenous neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg. Trachea was extubated once the patient awake. All patients had receive supplementation of oxygen (3L/min) by a face mask in post-operative period for 3 hours and were monitored continuously in the recovery room. The incidence of nausea (if patient feel urge to vomit within 24 hours which lasts for 15 minutes after surgery on interview) and vomiting (forceful expulsion of gastric contents from mouth within 24 hours after surgery on interview) was recorded for first 24 hours post-operatively (0-4 hrs at recovery room, and 4-24 hours in ward) by the 4th year resident.

Efficacy (if no nausea and vomiting occur within 24 hours after surgery and no need for another anti-emetic drug i.e., metoclopramide) was noted as per operational definition and recorded on especially designed proforma.

Data was analyzed with statistical analysis program (IBM-SPSS V-20). Mean±SD was presented for quantitative variables like age, duration of procedure and BMI. Frequency and percentage were computed for qualitative variables like gender, history of diabetes, hypertension, PONV, ASA grade and efficacy. Chi-square test was applied to compare efficacy in both groups, taken p≤0.05 as significant. Stratification was done with regard to age, gender, duration of procedure, BMI, ASA grade to see the effect of these variables on efficacy. Post-stratification chi-square test for both groups was applied, p≤0.05 was considered statistically significant.

Results:

Age range in both group was 18-50 years with mean age 30±10.21 years in group-A and 33±9.27 years in group-B. In group-A 32% patients were male and 68% were female while in group-B 30% were male and 70% were female. Mean duration of procedure was 55±4.82 minutes in group-A while 60±5.34 minutes in group-B.

Mean BMI was 26±3.27 kg/m^2 in group-A while 27±4.12 kg/m^2 in group-B. 20% patients were diabetic in group-A while 22% in group-B. 20% patients were hypertensive in group-A while 18% patients in group-B. 68(65%) patients had ASA grade-I and 36(35%) patients had ASA grade-II in Group-A while 70(67%) patients had ASA Grade-I and 34(33%) patients had ASA grade II in Group-B.

10(10%) patients had post-operative nausea and vomiting and 94(90%) patients didn't had post-operative nausea and vomiting in group-A while 33(32%) patients had post-operative nausea and vomiting and 71(68%) patients didn't had post-operative nausea and vomiting in group-B. There was a significant difference between the efficacy (effectiveness of drugs) in both groups 90% in group-A while 68% in group-B with P-value 0.0001.

Stratification of efficacy with respect to age, gender, duration of procedure, BMI, ASA grade is given in table no 1.

Discussion:

The prevalence of post-operative nausea and vomiting ranges from 40% to 75% in patients undergoing laparoscopy. Post-operative nausea and vomiting is the most common complaint which leads to patient dis-satisfaction and prolong the hospital stay.[9] Various studies were conducted for more effective anti-emetic drugs without extra pyramidal side effects to reduce the occurrence of PONV. No single drug is doing well in preventing post-operative nausea and vomiting and with an assumption of using a combination of anti-emetic drugs effectively reduce the post-operative nausea and vomiting.[10]

Imam SM et al. observed no nausea and vomiting in 77.5% of (31/40) patients receiving combination of ondansetron and dexamethasone as compared to 47.5%(19/40) who received ondansetron alone. All these patients underwent elective caesarian sections ($p<0.05$). They found that 22.5% experienced post-operative nausea and vomiting either as nausea and vomiting in the combination group. This result is slightly higher than the current study (22.5% vs 12%). The incidence of post-operative nausea and vomiting was higher in the combination group in that study because all the patients were pregnant, while we had no pregnant patients.[11]

In our study group-A (ondansetron and dexamethasone combination) was effective in 90% patients and was not effective in 10% patients while in gxroup-B (ondansetron alone) was effective in 68% patients and was not effective in 32% patients which is statistically significant with p-value 0.0001.

Lopez-olaondo L et al. studied the efficacy of ondansetron 4mg plus dexamethasone 8mg for prophylaxis against PONV in 100 ASA I and II females undergoing major gynecological surgery with GA. They concluded that prophylactic combination anti-emesis is effective against PONV.[12] The results of the current study seem statistically comparable. A complete response in the combination group was 88% vs. 84% and in ondansetron group, it was 72% vs. 52%.

Bano F et al studied dexamethasone 8mg plus ondansetron 4mg combination with dexamethasone 8mg alone in patients undergoing laparoscopic cholecystectomy. They found that 81.6% patients didn't have nausea and vomiting postoperatively in the combination group, while 60.4% patients did not complain of either nausea or vomiting in the dexamethasone group.[13] The results of the current study are comparable with respect to the combination group i.e. 88% vs. 81.6%.

Ahmed N et al studied 67 patients undergoing laparoscopic cholecystectomy receiving combination of ondansetron and dexamethasone. They observed no nausea and vomiting in 85% patients.[14] Our results are comparable with respect to ondansetron and dexamethasone combination i.e. 88% vs. 85%.

Bhattarai B et al. compared the efficacy and safety of the combination of ondansetron 4mg and dexamethasone 4mg with ondansetron 4mg alone given as prophylaxis for PONV in 100 (50 in each group) ASA I and II adult patients undergoing laparoscopic surgery. They found that a complete response occurred in 92% patients in the combination group, while in the ondansetron group it was 76%.[15] The results of the current study seem statistically comparable. A complete response in the combination group was 88% vs. 92%, and in the ondansetron group, it was 72% vs. 76%.

Dabbous AS et al. enrolled 84 (42 in each group) patients and compared the effectiveness of dexamethasone 8mg with either granisetrone 1mg or ondansetron 4mg in patients undergoing laparoscopic surgery. They showed no statistically significant difference in anti-emetic efficacy in both groups.[16] Our results are comparable with respect to ondansetron and dexamethasone combination.

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Conclusion:

Our study concludes that combination of ondansetron and dexamethasone is more effective than ondansetron alone in preventing post-operative nausea and vomiting in patients of lapa-

roscopic cholecystectomy.

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Role and contribution of authors:
Dr Neelam Halimi, collected the data and references and did the initial write up.

Dr Munir Ahmad, collected the data and referecnes, went through the article, and made some changes.

Dr Hafiz Muhammad Waqas, critically review the article and did changes.

Dr Muhammad Basit, helped in collecting the data and references and helped in discussion writing.

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