Original Article

PROPHYLACTIC ANTIEMETIC THERAPY WITH ONDANSETRON, DEXAMETHASONE AND COMBINED ONDANSETRON AND DEXAMETHASONE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA (GA)

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ABSTRACT:

OBJECTIVE: The aim of this study was to find a better prophylaxis against postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic cholecystectomy.

STUDY DESIGN: A randomized control study was carried out for comparison.

SETTING & DURATION: This study was conducted at department of anaesthesia and intensive care, Madinah Teaching Hospital, Faisalabad from January 2015 to July 2015.

SAMPLE SIZE: The study population consisted of 90 ASA I & II status patients undergoing laparoscopic cholecystectomy under general anaesthesia.

METHODS: The patients were randomly divided into three groups A, B and C. Group A patients were to receive prophylactic Dexamethasone, group B patients were to receive both Ondansetron and Dexamethasone and group C patients were to receive Ondansetron preoperatively. Postoperative nausea and vomiting was recorded and compared between three groups in PACU (Post anaesthesia care unit) for one hour and surgical ward for 23 hours respectively.

RESULTS: It was observed that group B (combined Dexamethasone and Ondansetron group) patients had significantly less postoperative nausea and vomiting as well as less requirement for rescue antiemetics postoperatively as compared to group A (Dexamethasone group) and C (Ondansetron group) patients. The frequency of nausea and vomiting was 0% and 3.3% in group B as compared to 30% and 30% in group A and 16.7% and 23.3% in group C respectively. Rescue antiemetics were used in 6.7% patients in group B as compared to 40% patients in group A and 23.3% patients in group C.

CONCLUSION: It is concluded that combined Dexamethasone and Ondansetron offer effective prophylaxis against postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy as compared to Dexamethasone and Ondansetron alone.

KEY WORDS: Laparoscopic cholecystectomy, PONV, dexamethasone, Ondansetron, antiemetic.

INTRODUCTION:

Laparoscopic cholecystectomy is a minimally invasive procedure which offers many benefits like small incision, less postoperative pain, shorter hospital stay[1] and early resumption of normal activities. Pain and nausea vomiting are found to be most distressing for patients during early postoperative period[2].

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Unfortunately incidence of postoperative nausea and vomiting (PONV) is higher after laparoscopic surgery. In some studies it is reported to be as high as 53-72%[3]. Higher incidence of PONV after laparoscopy is due to creation of pneumoperitoneum which causes stimulation of mechanoreceptors in the gut[4]. However etiology of PONV is multifactorial. Associated factors may be drugs used such as anesthetic or analgesic agents, surgical procedure itself and patient related factors such as female gender, obesity or a history of gastroesophageal reflux disease.

PONV poses extra burden on hospital physical as well as financial[5]. It is an independent reason for delayed discharge from hospital. It is a major reason for patient morbidity and increases the stress and anxiety of patient. It may lead to dehydration, electrolyte imbalance, wound dehiscence etc.

In the absence of prophylactic therapy the incidence of PONV is 20-30% in general surgical population and may increase up to 70-80% in high risk patients.

It has become a standard practice to use prophylactic antiemetics to minimize postoperative nausea and vomiting [6]. Various groups of drugs are available these days for treatment and prevention of PONV such as Dexamethasone, Butyrophenones, 5-HT3 antagonists, transdermal scopolamine etc.[7]. Nonpharmacologic methods such as acupuncture and adequate hydration are also being practiced. No single drug is found to be fully effective as a prophylactic agent in postoperative period. So we studied efficacy of combination of Ondansetron and Dexamethasone as compared to Dexamethasone and Ondansetron alone. Ondansetron is one of the most widely used selective 5-HT3 antagonist[8]. Dexamethasone alone or in combination with other drugs reduces PONV[9]. Although exact mechanism of action is unclear but it is suggested that dexamethasone exerts its antiemetic action through inhibition of prostaglandins, reduction in neural 5-hydroxytryptophan level and prevention of serotonin release in gut[10].

MATERIAL AND METHODS:

SETTING:

This study was conducted at department of anaesthesia and intensive care, Madinah Teaching Hospital.

DURATION OF STUDY:

The study was carried out from January 2015 to July 2015.

SAMPLE SIZE:

After fulfilling the inclusion criteria 90 ASA I & II status patients undergoing laparoscopic cholecystectomy under general anesthesia were selected. The patients were randomly divided into three groups A, B and C each consisting of 30 patients. Group A patients received prophylactic dose of dexamethasone, group B patients received both Ondansetron and Dexamethasone while group C patients received Ondansetron alone prior to induction of anesthesia.

SAMPLING TECHNIQUE:

Consecutive (Non Probability) sampling technique was used.

SAMPLE SELECTION:

INCLUSION CRITERIA:

- American society of anesthesia (ASA) grade I and II patients.
- Patients between 20 and 65 years of Age.

EXCLUSION CRITERIA:

- History of gastroesophageal reflux disease.
- Morbid obesity.
- History of any psychiatric illness.
- History of substance abuse.
- Hypersensitivity to drugs under study.

STUDY DESIGN:

Randomized control trial

DATA COLLECTION PROCEDURE:

After written informed consent 90 ASA I and II patients scheduled for elective laparoscopic cholecystectomy were selected according to inclusion criteria. Exclusion criteria was strictly followed.

Using lottery method patients were randomly divided into three distinct groups A, B and C each consisting of 30 patients. Group A patients received prophylactic dose of Dexamethasone, group B patients received both Ondansetron and dexamethasone while group C patients received Ondansetron alone prior to induction of anesthesia.

Detailed data of the patients was collected including gender, age, height, weight, ASA status, baseline heart rate, oxygen saturation and blood pressure.

Double blind technique was used. Senior anesthesiologist was responsible for patient randomization and drug administration while resident doctor was responsible for data collection. Both resident doctor and patient were unaware of the drug being used.

Group A patients were administered 8mg Dexamethasone, group B patients were given 4mg Ondansetron and 4mg Dexamethasone while group C patients received 4mg Ondansetron intravenously respectively prior to induction of anesthesia. Patients were preoxygenated. Anesthesia was induced using thiopentone sodium 5mg/kg. Tracheal intubation was facilitated with atracurium besylate 0.5mg/kg. Anaesthesia was maintained with 0.6% isoflurane in oxygen. Analgesia was given using nalbuphine sodium and ketorolac sodium. Additional muscle relaxants were administered if required. At the end of procedure residual muscle paralysis was reversed with neostigmine 0.04mg/kg and atropine 0.01mg/kg. Patients were extubated and shifted to PACU. In PACU patients were continuously monitored for vital signs as well as any episode of nausea and vomiting and discharged to parent ward after one hour.

In parent ward patients were observed for nausea and vomiting for next 23 hours. Nausea was defined as feeling of sickness with an urge to vomit. Vomiting was defined as forceful expulsion of gastric contents via mouth or nose. If patient had nausea for half an hour or an episode of vomiting rescue antiemetic was given as intravenous metoclopramide 10mg. Record was maintained regarding incidence of nausea and vomiting and administration of rescue antiemetics for 24hours postoperatively. Duration of hospital stay was also noted.

DATA ANALYSIS PLAN:

Data was analyzed using SPSS (version 23)

- Mean and standard deviation was calculated for quantitative variables i.e. age, weight, height and ASA status.
- Frequency and percentages were presented for qualitative variables i.e. nausea, vomiting and antiemetics used.
- Chi square test was applied to compare gender, ASA status, nausea, vomiting and rescue antiemetics used.
- ANOVA (Analysis of variance) was used to compare age, height, weight.
- P value < 0.05 was considered significant.

RESULTS:

The treatment groups were comparable with regards to patient demographics i.e. age, height, weight and ASA status. However despite random allocation group C consisted of female patients only. [Table 1]

Table 1: Demographic Data

Group	N	Gender [M/F]	Age (Years)	Height (cm)	Weight (Kg)	ASA Status [I/II]
Group A	30	3/27	39.3±10.56	159.13±6.03	68.73±7.95	18/12
Group B	30	3/27	41.83±10.3	158.63±6.38	70.3±7.76	17/13
Group C	30	0/30	41.5±10.47	157.23±3.09	69.2±10.83	18/12
p-value			0.596	0.369	0.786	

The incidence of vomiting was 3.3% in group B as compared to 30.0% in group A and 23.3% in group C which is statistically significant (p-value 0.023). [Table 2]

Table 2: Incidence of Vomiting

Group	N	Vomiting				p-value
		Yes		No		
		No of Pts.	%age	No of Pts.	%age	
Group A	30	9	30.0%	21	70.0%	0.023
Group B	30	1	3.3%	29	96.7%	
Group C	30	7	23.3%	23	76.7%	
Total	90	17	18.9%	73	81.1%	

The incidence of nausea was 30% and 16.7% in groups A and C respectively as compared to group B (0%). It is statistically significant (p-value 0.006). [Table 3]

Table 3: Incidence of Nausea

Group	N	Nausea				p-value
		Yes		No		
		No of Pts.	%age	No of Pts.	%age	
Group A	30	9	30.0%	21	70.0%	0.006
Group B	30	0	0%	30	100.0%	
Group C	30	5	16.7%	25	83.3%	
Total	90	14	15.6%	76	84.4%	

Rescue antiemetics were given to 40% patients in group A and 23.3% patients in group C as compared to 6.7% patients in group B which is statistically significant (0.009). [Table 4]

Table 4: Rescue Antiemetics Given

Group	N	Antiemetics				p-value
		Yes		No		
		No of Pts.	%age	No of Pts.	%age	
Group A	30	12	40.0%	18	60.0%	0.009
Group B	30	2	6.7%	28	93.3%	
Group C	30	7	23.3%	23	76.7%	
Total	90	21	23.3%	69	76.7%	

DISCUSSION:

There are a number of factors associated with postoperative nausea and vomiting. The incidence of PONV is high despite antiemetic therapy. It is particularly high after laparoscopic surgery[11] and in female patients. We studied PONV in laparoscopic surgery due to high incidence of PONV in surgical ward.

Although a number of antiemetic drugs are available, the incidence of PONV is still high. Since no single drug is effective, we tried combination of antiemetic drugs. We combined Ondansetron and Dexamethasone. Ondansetron is preferred as it is devoid of

serious side effects[12] like sedation, dysphoria and extrapyramidal signs[13]. Dexamethasone in single dose is not associated with harmful effects. For more than two decades Dexamethasone has been used as antiemetic after chemotherapy with very few adverse effects[14].

In our study it was observed that PONV is much less when Dexamethasone and Ondansetron are combined as prophylactic agents as compared to Dexamethasone or Ondansetron alone. In combined group the incidence of postoperative vomiting was 3.3% as compared to 30% in Dexamethasone and 23.3% in Ondansetron group respectively. While the incidence of nausea was also observed to be significantly less in combined group being 0% as compared to 30% in dexamethasone group and 16.7% in Ondansetron group. So it was associated with less postoperative morbidity, less rescue antiemetics as well as shorter hospital stay which in turn reduces burden on hospital staff. Our study is comparable to observations made by Ashwani Kumar et al[15]. They concluded that dexamethasone when combined with Ondansetron, offers better prophylaxis as compared to Ondansetron and Dexamethasone alone against PONV. Mohammad Eidy et al[16] concluded that combination of two drugs is more effective as compared to either drug alone. Similar observations were made by L. Sanjowal et al[17] and Ahsan K et al[18].

Vrinda Agarvat et al observed that Ondansetron given intravenously just prior to induction is safe and more effective than intravenous Dexamethasone in early nausea and vomiting while Dexamethasone reduces delayed post-operative nausea and vomiting in patients undergoing elective laparoscopic surgeries[19].

Souvik Maitra et al compared both drugs for PONV[20]. It was observed that Dexamethasone is superior to Ondansetron in preventing postoperative nausea after 4–6 hours of laparoscopic surgeries. However, both drugs are of equal efficacy in preventing postoperative vomiting up to 24 hours.

A study carried out by Mohammad Ali Hessami et al in 2012 compared Dexamethasone and Granisetron, another 5-HT 3 antagonist[21]. It was observed that both drugs are equally effective for prophylaxis of PONV after laparoscopic surgery.

Ahmed Waqas et al[22] conducted a study in 2011 for prophylaxis of PONV after laparoscopic cholecystectomy. They compared Ondansetron with combined Metoclopramide and Dexamethasone. It was observed that Ondansetron was more effective as compared to combined Metoclopramide and Dexamethasone.

S.Didehvar et al[23] conducted a study in patients undergoing bariatric surgery with high emetogenic risk. They compared Palonosetron, second generation 5-HT3 antagonist alone with Palonosetron combined with Dexamethasone. They observed that combined therapy did not significantly reduce the incidence of PONV as compared to Palonosetron alone.

Seung-hwa Ryoo et al observed effects of combined Palonosetron and Dexamethasone in prevention of PONV as compared to Dexamethasone alone[24]. Combined therapy was observed to be more effective in preventing PONV as compared to Dexamethasone alone in women receiving IV-PCA using fentanyl.

Fauzia Bano et al concluded that combination of Dexamethasone and Ondansetron is more effective in prevention of PONV after laparoscopic cholecystectomy as compared to Dexamethasone alone[25].

Glenn S. Murphy et al concluded that among the patients undergoing outpatient laparoscopic cholecystectomy preoperative Dexamethasone reduced nausea, pain and fatigue postoperatively[26].

CONCLUSION:

So it is concluded that incidence of postoperative nausea and vomiting is significantly less if both Ondansetron and Dexamethasone are used prophylactically in patients undergoing laparoscopic cholecystectomy and rescue antiemetics are required less frequently as compared to monotherapy with Ondansetron and Dexamethasone.

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