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Comparison of Dexamethasone-Diphenhydramine and Dexamethasone-Ondansetron in Preventing Post-Operative Nausea and Vomiting after Laparoscopic Cholecystectomy

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ABSTRACT

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

Methodology: A total of 160 patients were enrolled, 80 patients each to either group D for the Dexamethasone-Dimenhydrinate group or group O for Dexamethasone-Ondansetron. The **s**tudy was carried out over a period of six months from 01-01-2022 to 30-06-2022. The study was held at the Department of Anaesthesia, Holy Family Hospital, Rawalpindi Medical University and Allied Hospital.

Results: The mean age of the patients was 42.3±13.2 and 42.4±14.0 in group D and group O, respectively. There were 40 (50%) males and females in Group D while 29 males (36.3%) and 51 females (63.7%) in Group o. Efficacy of combination dexamethasone+ dimenhydrinate with dexamethasone ondansetron in preventing PONV showed at 30 minutes (5.0% vs 12.5%; p=0.093), at 60 minutes (7.5% vs 20.0%; p=0.022), at 120 minutes (6.3% vs 17.5%; p=0.028) and 24 hours (5.0% vs 18.8%; p=0.007).

Conclusions: In conclusion, our study demonstrated that the dexamethasone–dimenhydrinate combination was more effective than the dexamethasone–ondansetron combination in preventing nausea and vomiting after laparoscopic cholecystectomy.

Keywords: Dexamethasone, dimenhydrinate, Ondansetron, Postoperative nausea and vomiting.

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [3,4] Critical analysis and manuscript review; [5]Data analysis; Manuscript Editing.

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Introduction

Anesthesiologists care for surgical patients in the perioperative and postoperative periods.[1] Postoperative nausea and vomiting (PONV) are one of the most common postoperative concerns with an incidence of up to 80% in high-risk patients, depending on the type of surgery and anaesthesia[1]. It is of great concern than even postoperative pain, to the surgical patients[2].PONV may lead to serious surgical complications such as wound dehiscence or surgical site bleeding, hematoma, aspiration and choking probability, and water and electrolyte disturbances resulting in increased healthcare costs due to lower patient satisfaction and delayed hospital discharge[3]. It is believed that PONV has a multifactorial origin[4]. These factors can be divided into patient-related characteristics (age, gender,

obesity and smoking status as well as the history of motion sickness or previous PONY), anaesthetic-related (volatile anaesthetics, intraoperative use of opioid and blood. transfusion) and surgical-related factors (type and duration of surgery and use of postoperative analgesic opioids[5].

Administration of antiemetic drugs to prevent and manage PONV is an important tool that should be used properly and regularly[6]. Considering the multifactorial aetiology of this complication, multimodal therapy is recommended for the prevention of PONV in high-risk patients[7]. Therefore, various drug combinations have been tried and found to be effective for this issue, albeit they had some side effects[8].

The study done by Kizilcik et al., suggested that the dexamethasone-dimenhydrinate combination was more effective than dexamethasone-ondansetron in the prevention of nausea and vomiting after rhinoplasty operations[1]. The additional antiemetic need in the dexamethasone-ondansetron group was significantly higher at 30 min after surgery (p=0.001). However, the difference in the reported incidence of vomiting after 60 minutes of surgery, which was 16.7% in the dexamethasone-ondansetron group versus 3.3% in the dexamethasone-dimenhydrinate group (p=0.195), was statistically insignificant[1].

Niazi et al reported that the efficacy of the Dimenhydrinate-dexamethasone combination was 88% while dexamethasone-ondansetron achieved efficacy in 65% of cases, which was statistically significant (<0.05)[9]. In perioperative medicine, Dimenhydrinate and ondansetron are the two most frequently used medications for PONV prophylaxis. There is still no medication that provides complete PONV prophylaxis. Numerous trials have compared ondansetron and dimenhydrinate in the prevention of PONV following laparoscopic surgery. Their findings are inconsistent, and there is no agreement on which drug is superior for PONV prophylaxis. Studies carried out in the Pakistani population are quite a few. We want to compare the efficacy of combination dexamethasone=dimenhydrinate with dexamethasone-ondansetron in preventing postoperative nausea and vomiting (PONV) after laparoscopic cholecystectomy. This will not only help in providing data for the Pakistani population in this regard as well as providing a cost-effective means in government setups to deal with this issue with evidence.

Methodology

This was a randomized control trial conducted between 01-01-2022 and 30-06-2022. The study was conducted at the Department of Anaesthesia, Holy Family Hospital affiliated with Rawalpindi Medical University (RMU). The sample size was calculated using the OpenEpi sample size calculator, sample size was calculated from a reference study [1] taking the incidence of vomiting after 60 min of surgery to be 16.7% in the dexamethasone-Ondansetron group versus 3.3% in the Dexamethasone-Dimenhydrinate group. Keeping the power of study at 80%, and the level of significance at 5%, the minimally required sample size was calculated as 160 with at least 80 in each group. A consecutive non-probability sampling technique was used. Male and female patients aged between 18-65 years; ASA grade 1 & 2 who were planned for elective laparoscopic cholecystectomy were included. Exclusion criteria included allergies, pregnant ladies or patients taking any acute or chronic dexamethasone, ondansetron and dimenhydrinate.

Data Collection: After approval from the Institutional Research Forum of Rawalpindi Medical University, all patients fulfilling the selection criteria were registered through the anaesthesia department of Holy Family Hospital, RMU and Allied Hospital, Rawalpindi. Demographic history including age (in years) and sex (male or female) were taken. Informed written consent was taken by patients after explaining to them the purpose and procedure of the study and the randomization

process. Randomization was done through a random number list already generated using SPSS software equally but randomly allocating 80 patients each to either group D for the Dexamethasone-Dimenhydrinate group or group O for Dexamethasone-Ondansetron. 80 patients in group D received 8 mg of dexamethasone and 50 mg of dimenhydrinate while group 0 received 8 mg of dexamethasone and 4 mg of ondansetron at 15 min post induction of general anaesthesia. General anaesthesia with intermittent positive pressure ventilation with endotracheal intubation was employed in all patients. Anaesthesia was maintained using isoflurane, oxygen/nitrous oxide mixture and nalbuphine. Postoperative pain was managed using ketorolac 0.5 mg/kg and tramadol 1.5 mg/kg. After completing the operation, the patients were evaluated for PONV at the 30th and 60th min in the postoperative period in the recovery room and at the 120th min and 24 hr in the ward by anaesthetic nurses. The patients were able to request antiemetic medications, and the drugs along with their doses will be recorded. The findings were recorded in structured pro forma attached as Annexure 1.

Data analysis: All the collected data were entered and analyzed using the statistical package of social sciences (SPSS version 22). Descriptive statistics were recorded for qualitative and quantitative variables. Qualitative variables like gender and PONV were measured as frequency and percentage. Quantitative data like age (in years) was presented as mean and standard deviation: Effect modifiers like age and gender were controlled by stratification. Post-stratified chi-square test was used. Efficacy between groups was compared by chi-square test. P-values less than 0.05 were considered statistically significant.

Results

A total of 160 patients (80 in each group) were enrolled in the study. Group D received Dexamethasone-Dimenhydrinate while Group O administered a Dexamethasone-Ondansetron combination.

Patients ranged between 18-65 years of age with a mean age of 42.3±13.2 and 42.4±14.0 in group D and group-O, respectively. There were 40 (50%) males and females in Group D while 29 males (36.3%) and 51 females (63.7%) in Group o.

The efficacy of combination dexamethasone+dimtenhydrinate with dexa+methasone+ondansetron in preventing PONV showed at 30 minutes (5.0% vs 12.5%; p=0.093), at 60 minutes (7.5% vs 20.0%; p=0.022), at 120 minutes (6.3% vs 17.5%; p=0.028) and 24 hours (5.0% vs 18.8%; p=0.007) (Table III-VI).

Table I: Comparison of efficacy between two groups at 30 minutes

Postop PONV	Group-D (Dexamethasone+ Dimenhydrinate)		Group-O (Dexamethasone+ Ondansetron)	
	No.	%	No.	%
Yes	4	5.0	10	12.5
No	76	95.0	70	87.5
Total	**80**	**100.0**	**80**	**100.0**
Chi square	2.818			
P value	0.093			

Table II: Comparison of efficacy between two groups at 60 minutes

Postop PONV	Group-D (Dexamethasone+ Dimenhydrinate)		Group-O (Dexamethasone+ Ondansetron)	
	No.	%	No.	%
Yes	06	07.5	16	20.0
No	74	92.5	64	80.0
Total	**80**	**100.0**	**80**	**100.0**
Chi square	5.270			
P value	0.022			

Table III: Comparison of efficacy between two groups at 120 minutes

Postop PONV	Group-D (Dexamethasone+ Dimenhydrinate)		Group-O (Dexamethasone+ Ondansetron)	
	No.	%	No.	%
Yes	05	6.3	14	17.5
No	75	93.7	66	82.5
Total	80	100.0	80	100.0
Chi square	4.838			
P value	0.028			

Table IV: Comparison of efficacy between two groups at 24 hours

Postop PONV	Group-D (Dexamethasone+ Dimenhydrinate)		Group-O (Dexamethasone+ Ondansetron)	
	No.	%	No.	%
Yes	04	05.0	15	18.8
No	76	95.0	65	81.2
Total	80	100.0	80	100.0
Chi square	7.227			
P value	0.007			

Discussion

Postoperative nausea and vomiting a well-described side effects related to the patient, anaesthetic and surgical factors. There are a lot of medications to prevent PONV, such as metoclopramide, dimenhydrinate, serotonin antagonists and dexamethasone. Although an antiemetic prophylaxis might not eliminate the risk of PONV, it can significantly reduce the incidence of nausea and vomiting[10]. However, no single excellent medication or method is there to describe. Various antiemetic drugs can be used for the treatment of PONV. Dexamethasone can decrease the incidence of PONV[11]. However, some authors emphasize that the combination of antiemetic drugs can further reduce PONV compared to single-agent treatment[12], especially for high-risk patients[13].

Dexamethasone is well-documented as an effective antiemetic. A single dose of dexamethasone administered perioperatively is rarely associated with significant side effects[15]. Preoperative dexamethasone 8 mg significantly reduces PONV and the use of rescue antiemetic[16]. Karanicolas et al published a systematic review and meta-analysis of 17 randomized controlled trials that evaluated the impact of prophylactic corticosteroid administration on PONV. The authors concluded that dexamethasone decreases the incidence of nausea and vomiting and that higher doses of dexamethasone (8–16 mg) are more effective than smaller doses (2–5 mg) in patients undergoing laparoscopic cholecystectomy[17]. Vomiting is the forceful expulsion of gastrointestinal contents through the mouth. Retching is the rhythmic action of the respiratory muscles preceding vomiting. Both retching and vomiting are objective patient experiences. Nausea is a subjective experience which may or may not be associated with vomiting[18]. The mechanism of the vomiting reflex was first described by Borison and Wang (1953) to be a complex act involving the respiratory, gastrointestinal, and abdominal musculature

controlled by the vomiting center. The vomiting center is situated in the lateral reticular formation close to the tractus solitarius in the brain stem. The vomiting center can be triggered by stimuli from the periphery: the oropharynx, the gastrointestinal tract, the mediastinum, renal pelvis, peritoneum and genitalia, and centrally from the CNS: cerebral cortex, labyrinthine, the visual center, the vestibular portion of the eighth cranial nerve, and the chemoreceptor trigger zone (CTZ) located in the area postrema at the base of the fourth ventricle[19]. As the area postrema has no effective blood-brain barrier, CTZ can be directly stimulated by chemicals in the cerebrospinal fluid (CSF) and blood[19].

The CTZ has high concentrations of encephalin, dopamine, and opioid receptors. The area postrema is rich in opioid, dopamine (D) and serotonin (5-hydroxytryptamine (5-HT)) receptors. The nucleus of the solitary tract contains high concentrations of encephalin, histamine, muscarinic (M), and cholinergic receptors. Recently, substance P and neurokinin-1 (NK1) receptors were found to be involved in the regulation of emesis. At present it is generally accepted that the key to control PONV is the blocking of all the recognized receptors involved in emesis[19]. A combination of dexamethasone with other antiemetics is more effective than any single drug alone[20].

Ondansetron is a carbazalone derivative that is structurally related to serotonin and possesses specific 5-HT3 subtype receptor antagonist properties without altering dopamine, histamine, adrenergic, or cholinergic receptor activity. The most serious side effects of ondansetron are rare hypersensitivity reactions. Other more commonly reported side effects are headache, light-headedness, dizziness, flushing at the i.v. site, transient increases in the plasma concentrations of liver transaminase enzymes, a warm epigastric sensation, and constipation. Cardiac dysrhythmias have been reported after i.v. administration of ondansetron and metoclopramide [68]. It can be used effectively in PONV. However, it might not eliminate PONV, probably because it acts through the blockage of one receptor[21].

In current study we compared the efficacy of combination dexamethasone+dimtenhydrinate with dexa+methasone-ondansetron in preventing PONV at 30 minutes (5.0% vs 12.5%; p=0.093), at 60 minutes (7.5% vs 20.0%; p=0.022), at 120 minutes (6.3% vs 17.5%; p=0.028) and 24 hours (5.0% vs 18.8%; p=0.007). Our findings are comparable with a study carried out by Kizilcik et al. [1]

Conclusion

In conclusion, our study demonstrated that the dexamethasone–dimenhydrinate combination was more effective than the dexamethasone–ondansetron combination in the prevention of nausea and vomiting after laparoscopic cholecystectomy

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