



Comparison of Dexamethasone and Ondansetron Use in Prevention of Post-operative Nausea and Vomiting

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Authors' contributions

This work was carried out in collaboration among all authors. Authors SA and HR conceived the idea, designed the project and did bench work. They also supervised the whole project. Author SKS and SA wrote the manuscript and done the statistics. Author SK, MAA and OH helped in handling the samples and also helped in bench work. All authors read and approved the final manuscript.

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ABSTRACT

Background: PONV remained the common cause of patient's discomfort after anaesthesia 30% in all post-surgical patients and 80% in high-risk patients. With other common and serious complications of surgeries vomiting and nausea remained unpleasant trigger for patients who underwent the surgeries that prolongs the hospital stay and also leads to recurrent admissions. Therefore in this study we want to compare the effectiveness of pre-operative single-dose dexamethasone versus ondansetron in reducing post-operative nausea and vomiting after laparoscopic surgeries.

Methods: Patients admitted for laparoscopic procedures at Ziauddin Hospital North site were recruited for this quasi-experimental study. All consecutive patients were assigned to one of the two groups (1 or 2) using computer generated simple randomised numbers and given either of the two treatments: single dose dexamethasone (5-8mg) or ondansetron (4mg). Researcher assessed

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post-operative nausea and vomiting at thirty minutes, two, four, eight, and twenty-four hours after the procedure. For statistical association the chi-square test and independent t-test were applied. Significant was defined as a P-value of less than 0.05.

Results: The mean age of patients was 42.9 ± 16.6 years with mean weight of 62.9 ± 8.8 kilograms. All the operation performed as laparoscopic and common procedure was cholecystectomy (72/98: 73.5%), followed by appendectomy (17/98: 17.3%). Patients with ondansetron had more episodes of vomiting after 30 minutes of laparoscopic surgery. In addition, we discovered a correlation between the two groups' nausea episodes 30 minutes after surgery. After 30 minutes of laparoscopic surgery, patients who took ondansetron reported more nausea episodes.

Conclusion: Prophylactic dexamethasone 8 mg i.v. significantly reduced the incidence of PONV in patients undergoing laparoscopic surgery.

Keywords: Laparoscopic; dexamethasone; ondansetron; nausea; vomiting; post-operative; PONV; cholecystectomy; appendectomy.

1. INTRODUCTION

PONV refers to nausea and vomiting that occurs in inpatients within the first 24–48 hours after surgery [1]. After the invention of anaesthesia, PONV was recognised as a surgical concern. Post-discharge nausea and vomiting (PDNV) develops following an outpatient operation. It's an uncomfortable sensation brought on by a strong desire to vomit but no expulsive muscular activity [2]. PONV remained the most common source of patient discomfort following anaesthesia, with recorded rates of 30% in all post-surgical patients and up to 80% in high-risk patients [3]. In addition to the other common and significant surgical side effects, vomiting and nausea remained an unpleasant trigger for patients who underwent surgery, lengthening hospital stays and leading to recurrent hospitalizations [4]. Postoperative nausea and vomiting (PONV) have become one of the most challenging and important concerns in anaesthetic medicine, thanks to the development of ambulatory and day-care surgeries [5] PONV has a complicated and poorly known physiology. Rather of being confined in an anatomically defined "vomiting centre," the brain regions implicated in the pathophysiology of vomiting, according to our current hypothesis, are dispersed throughout the medulla oblongata [6] The nucleus tractus solitarius (NTS), a vertical column of grey matter implanted in the medulla oblongata composed of solely sensory nuclei (clusters of nerve cell bodies), and the chemoreceptor trigger zone (CTZ), both found in the area postrema (a medullary structure), are at the root of PONV. The CRTZ does not have a blood–brain barrier, but it gets input from vagal afferents in the gastrointestinal tract and can detect emetogenic poisons, metabolites, and medications circulating in the blood and CSF fluid [7] The NTS receives information from the

vestibular and limbic systems, as well as vagal afferents, via the CRTZ. The NTS is stimulated by the rostral nucleus, the nucleus ambiguus, the ventral respiratory group, and the dorsal motor nucleus of the vagus, resulting in vomiting [8]. Because of changes in female hormone levels, women are two to four times more likely than males to develop PONV as adults and teenagers. Patients with a BMI greater than 35 have been associated to PONV [9]. This could be due to increased intra-abdominal pressure and the pharmacokinetic effects of lipophilic anaesthetics, which have longer half-lives in these patients [10]. Other risk variables have been identified, including the type of operation, drugs, anaesthetic, surgery duration, and anaesthesia. Antiemetics that act on the muscarinic (muscarinic), dopaminergic (D2), histaminergic (H1), or serotonergic (5HT3) receptors are currently available. Neurokinin-1 (NK-1) receptor antagonists are also being researched [11]. However, ondansetron and dexamethasone are widely used as treatment of PONV. The objective of current study was to compare the outcome of single dose dexamethasone pre-operatively with ondansetron in reducing post-operative nausea and vomiting after laparoscopic surgeries [12].

2. METHODOLOGY

After receiving approval from the ethical review committee, this quasi-experimental type of study was carried out at the Department of Surgery, Ziauddin Hospitals North location (2811120SASUR, December, 2020). Using the Open-Epi sample size calculator, the sample size was estimated, using the parent article and taking incidence of PONV following ondansetron to be 51.6% and incidence of PONV following dexamethasone to be 22.6%.

Sample Size: X-Sectional, Cohort, & Randomized Clinical Trials			
Two-sided significance level(1-alpha):	95		
Power(1-beta, % chance of detecting):	80		
Ratio of sample size, Unexposed/Exposed:	1		
Percent of Unexposed with Outcome:	52		
Percent of Exposed with Outcome:	22		
Odds Ratio:	0.27		
Risk/Prevalence Ratio:	0.44		
Risk/Prevalence difference:	-29		
	Kelsey	Fleiss	Fleiss with CC
Sample Size - Exposed	43	42	49
Sample Size-Nonexposed	43	42	49
Total sample size:	86	84	98

After taking written informed consent and explaining that they would receive either of the two medications, all consecutive patients presenting to the study setting and meeting the eligibility criteria were randomly assigned to one of the two groups (1 or 2) using computer generated simple randomised numbers and given either of the two treatments: single dose dexamethasone (5-8mg) or ondansetron (4 mg). The research medications were subsequently administered by the operating surgeon through slow (thirty second) IV injection one hour before to surgery. Patients having previous history of vomiting and nausea 24 hours prior to surgery, American society of anaesthesiology status III or higher, BMI more than 35 were excluded. Those who have history of CLD, renal abnormalities, DM, use of any anti-emetic within 24 hours of surgery and patients who are taking steroids or on any chemotherapy were also excluded from the study.

Single blinding was observed i.e., the patients were not known which of the experimental medication they have received, while the surgeon and anaesthetist were aware of the type of study drug administered. During procedures, the patient was supine, and the normal pressure for pneumoperitoneum was 12-16mmHg CO₂. The operations were carried out under general anaesthesia. All patients were monitored for PONV after surgery. The researcher assessed PONV at thirty minutes, two, four, eight, and twenty-four hours after the procedure (done under general anaesthesia). Antibiotics and pain relievers were given as needed, and rescue anti-emetics were given as necessary, all of which were noted on the study questionnaire.

3. RESULTS

At the start of the procedure, all 98 study participants were separated into two groups: one

took dexamethasone (5-8 mg) and the other received ondansetron (4 mg). Data was analysed by using SPSS version 21 and the outcomes of the study were examined using the unpaired "t" test, while categorical data was evaluated using the chi-square test. For statistical significance, p-value of less than 0.05 was used. The mean age of the study subjects was found to be 42.9±16.6 years ranged between 14 to 86 years. Mean weight of the patients included was 62.9±8.8 in the range of 35 to 75 kilograms. All the procedures were performed under general anaesthesia with the maximum duration of anaesthesia recorded was 240 minutes and minimum were 60 minutes with mean time of 103.3±37.4. All the operation performed as laparoscopic and the most common procedure was laparoscopic cholecystectomy (72/98: 73.5%), followed by the laparoscopic appendectomy (17/98: 17.3%). The comparative analysis of the two groups in which one group got the ondansetron and other had the dexamethasone with the type of procedure performed showed insignificant statistical association with p-value of 0.521. Majority of the patients needed the use of rescue anti-emetics (56/98: 57.1%) Figs. 1 and 2.

63 (64.3%) were females in the current study and 35 (35.7%) were males. It has also been found that even after use of prophylaxis anti-emetics 21 (21.4%) of the patients had the episodes of vomiting after 30 minutes of operation including the 01 who received dexamethasone and 20 patients who were given the ondansetron while 16 (16.3%) experienced vomiting at 2 hours post-operatively with the 15 patients who were treated with ondansetron and 1 in patients having the dexamethasone. 31 (31.6%) subjects also felt nausea after 30 minutes of operations among them 27 had ondansetron and 4 had the dexamethasone. However, 26 (26.5%) patients had nausea after 2 hours of operation within 3 patients who received dexamethasone and 23 who received ondansetron. Neither of the patient had vomiting nor nausea after 4, 8 and 24 hours respectively.

We further aimed to determine the statistical link between the two groups with the different study parameters used in research. We were able to generate the significant statistical link between the two groups with the use of rescue anti-emetics (p-value: 0.00). It shows that even after use of the prophylaxis use of dexamethasone and ondansetron many patients need the rescue anti-emetics after operations and more in the group

who received ondansetron. We also determined a positive link of vomiting episodes at 30 minutes after operation within the two groups. Patients with ondansetron had more episodes of vomiting after 30 minutes of laparoscopic surgery. In

addition, we discovered a correlation between the two groups' nausea episodes 30 minutes after surgery. After 30 minutes of laparoscopic surgery, patients who took ondansetron reported more nausea episodes Table 1.

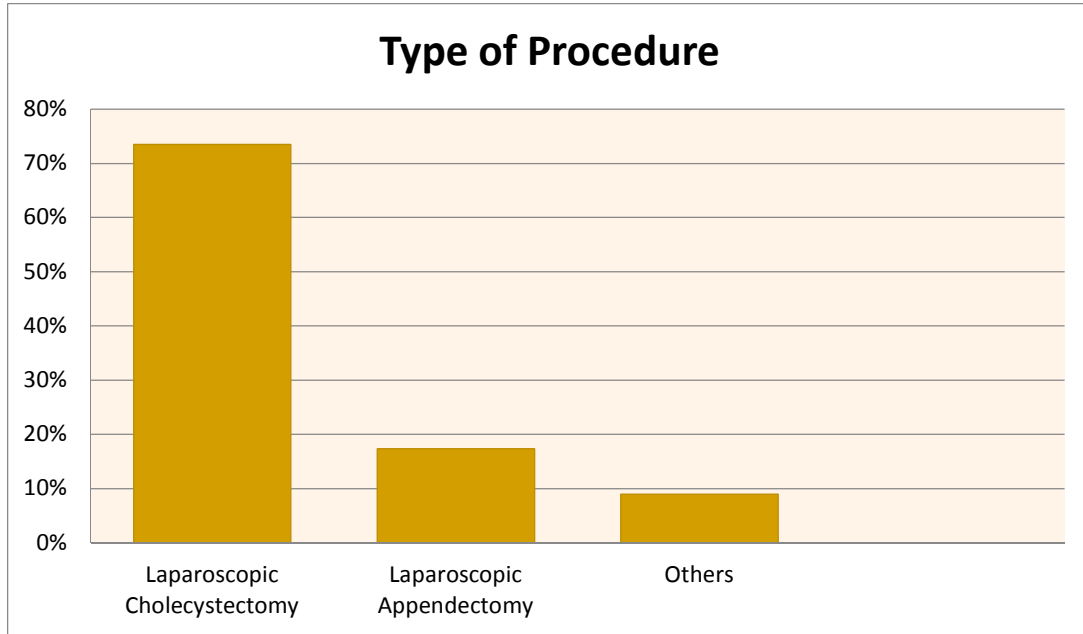


Fig. 1. Laparoscopic operation performed during the study

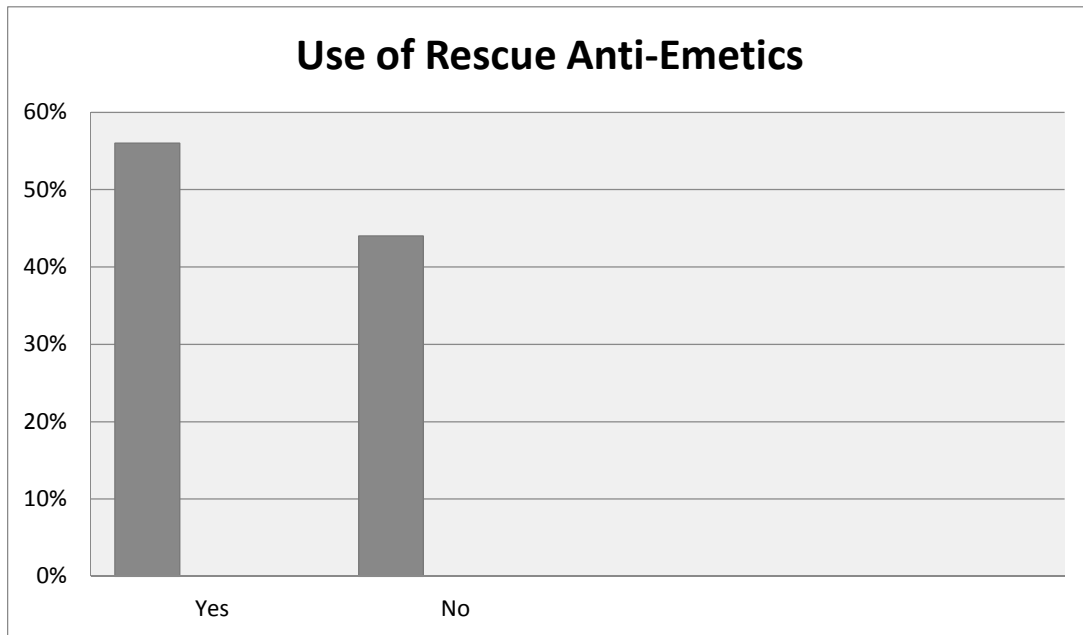


Fig. 2. Frequency of use of rescue anti-emetics

Table 1. Association of individual complication with two groups

Study Parameter	Groups		p-vaule
	Dexamethasone	Ondansetron	
Rescue Anti-Emetic	Yes	11	0.00 ^a
	No	33	
Vomiting after 30 Minutes	Yes	01	0.00 ^a
	No	48	
Vomiting after 2 Hours	Yes	01	0.00 ^a
	No	48	
Nausea after 30 Minutes	Yes	04	0.00 ^a
	No	45	
Nausea after 2 Hours	Yes	08	0.038 ^a
	No	41	

^aFischer's Exact Test

We further aimed to determine the statistical link between the two group's dexamethasone and ondansetron with the clinicopathological characteristics like age, weight, time of anti-emetic, duration of operation, insufflation and anaesthesia. We found insignificant association between two groups and each parameter except hospital stay Table 2.

4. DISCUSSION

PONV (postoperative nausea and vomiting) is a frequent postoperative complication that can be one of the most distressing elements of surgery [13] Patients who have had laparoscopic surgery frequently experience nausea and vomiting after the procedure (PONV). PONV prophylaxis is required for these patients. A multitude of drugs are used to prevent PONV in these patients, with dexamethasone being one of the most cost-effective. All patients had the same preoperative fasting and premedication, as well as the same standardised balanced anaesthesia without neuromuscular block and postoperative treatment, which included postoperative analgesic methods and drugs [14]. In 1981, dexamethasone was initially reported to be an effective antiemetic in cancer chemotherapy patients. Dexamethasone and other steroids have been found to be significantly superior to other medicines (metoclopramide, prochlorperazine, droperidol, domperidone) in reducing nausea and vomiting associated with chemotherapy in randomised, placebo-controlled studies [15]. The mechanism of antiemetic activity of dexamethasone is uncertain, however it may involve central inhibition of prostaglandin synthesis [16] Another theory involves changes in the blood CSF barrier's permeability to serum proteins or a decrease in 5-HT turnover in the central nervous system [17]. These statements, however, are not backed up by any experimental evidence. The cause of nausea and vomiting

during anaesthesia-assisted laparoscopic surgeries is unknown, however it is undoubtedly multifaceted. Because it promotes peritoneum stretching and elevated blood pressure in the peritoneal cavity, gas insufflation is a leading cause of nausea and vomiting [18]. PONV is hypothesised to be influenced by CO₂ insufflation that is delayed, as well as persistent p Delay in CO₂ insufflation, lingering pneumoperitoneum after CO₂ insufflation, peritoneum distension, stomach aggravation, and instinctive organ bothering and control are suggested to influence PONV [19]. A number of antiemetics have been demonstrated to be beneficial in the prevention and treatment of PONV in surgical patients [20].

Dexamethasone is also a more effective suppressor of nausea and vomiting in post-operative patients who have undergone laparoscopic surgery, according to the current study. According to a recent study published in 2021 by Vishwanath Mohire et al, patients who were given dexamethasone experienced much less nausea and vomiting in the first 2 hours after surgery, as well as between 2 and 6 hours following surgery [21]. McKenzie and colleagues studied the combination of ondansetron and dexamethasone in women undergoing major gynaecological surgery and discovered that it was more useful than ondansetron alone, as our findings revealed [22]. Fahri Eryilmaz et al. conducted another trial in 2021 that analyses the two groups' prevention of postoperative nausea and vomiting while on different dexamethasone and dexamethasone plus metoclopramide drugs. As a result, the findings were overwhelmingly in favour of dexamethasone treatment [23]. The best way to reduce the high risk of postoperative nausea and vomiting (PONV) following otologic surgical procedures is yet unknown. However, dexamethasone proved to be highly effective in reducing the incidences in many studies [24].

Table 2. Statistical links of clinicopathological parameters with two groups

Parameter	Group	N	Mean	Std. Deviation	P-Value
Age	Dexamethasone	49	43.37	18.466	0.827 ^c
	Ondansetron	49	42.93	14.555	
Weight	Dexamethasone	49	61.96	10.038	0.241 ^c
	Ondansetron	49	64.02	7.601	
Duration of Anaesthesia	Dexamethasone	49	105.71	32.733	0.557 ^c
	Ondansetron	49	101.22	41.743	
Duration of Operation	Dexamethasone	49	92.76	32.629	0.663 ^c
	Ondansetron	49	89.41	40.930	
Time of Anti-emetic	Dexamethasone	11	1.5909	.70065	0.125 ^c
	Ondansetron	45	1.2000	.75679	
Hospital Stay	Dexamethasone	49	1.3000	.67006	.000 ^c
	Ondansetron	49	2.0400	.80076	
Duration of Insufflation	Dexamethasone	49	90.70	34.700	0.302 ^c
	Ondansetron	49	83.40	35.620	

^cIndependent sample T-test

In some investigations, multiple antiemetic combination therapy has been shown to be more effective than single or double antiemetic preventive medicine [23] However, Hache et al. reported in a trial of high-risk patients that the incidence of PONV was the same whether aprepitant was given with one or two antiemetics, and that the incidence of PONV increased significantly when aprepitant was taken with three or four antiemetics [14] Another study indicated that oral aprepitant has similar effects to ondansetron in terms of lowering PONV, nausea severity, the number of rescue antiemetics taken, and the time to the first emetic episode in the first 24 hours following surgery [25].

In addition, abdominal surgeries, notably laparoscopy, bariatric, and gynaecological surgeries, have been associated to an increased occurrence of PONV. In the current investigation, we discovered no statistically significant link between laparoscopic abdominal operations and PONV. This could be explained by differences in risk exposures, environmental exposure, and genetic vulnerability. Wang et al. evaluated the antiemetic effect of dexamethasone 8 mg i.v. to saline in the prevention of nausea and vomiting after laparoscopic cholecystectomy. They observed that the whole occurrence of nausea and vomiting within inside the dexamethasone used changed into 23% in comparison to 63% with inside the saline used, and that dexamethasone eight mg i.v. notably decreased the occurrence of nausea and vomiting [26]. The number of obese people undergoing general anaesthesia is increasing as obesity becomes a global

epidemic. Obesity's possible link to an increased risk of PONV has become a source of concern. Obese patients are more likely to get larger doses of volatile anaesthetics and opioids due to their increased body weight and fat content [27].

One of the study's flaws is that confounding factors like the length and type of operation could have influenced the outcomes. The procedures varied from simple laparoscopic sterilisation with minimal manipulation and a 60-minute time limit to hysterolaparoscopy or laparoscopic ovarian cystectomy with more manipulation and a 210-minute time limit. This could have influenced the outcome. We did not collect data on post-discharge nausea and vomiting, which could have added to the assessment of PONV, because the research assessment was limited to the first four hours and did not include follow-up after discharge. Finally, rather than analysing rescue analgesia with opioids based on the emetic potential of particular opioids, we did not compare the number of patients receiving opioids for individual groups, which could be considered as another study error.

5. CONCLUSION

Prophylactic dexamethasone 8 mg i.v. significantly reduced the incidence of PONV in patients undergoing laparoscopic surgery. There is no link between PONV and gender, weight, type of procedure, or operation time. Patients who get IV dexamethasone have a lower risk of vomiting and nausea 30 minutes and 2 hours following their procedures.

CONSENT

Verbal and written informed consent were obtained from all patients.

ETHICAL APPROVAL

Ethical approval was taken from Ethics Review Committee (ERC) of Zia Uddin University Karachi accordance with institutional guidelines (3070121KZEM).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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