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Original Research Article

Efficacy of Ondansetron Alone and Combination with Dexamethasone in the Management of Post-Operative Nausea and Vomiting

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Abstract

Introduction: Ondansetron, a 5-HT3 antagonist, blocks the serotonin-induced depolarization of vagal afferent neurons to produce its antiemetic and antinauseant effects. It was first created to treat cancer chemotherapy and radiotherapy-induced vomiting, but it was later discovered to be useful for post-surgical nausea and vomiting (PONV). When PONV is severe, it can cause bleeding, dehydration, electrolyte imbalance, wound dehiscence, and pulmonary aspiration all of which lengthen hospital stays and raise medical expenses.

Aims and Objectives: To evaluate the efficacy of ondansetron alone and in combination with dexamethasone in the management of postoperative nausea and vomiting

Methods: This is a Prospective randomized double-blind control study conducted on 170 patients who had ASA grades I and II who were in the age group 20 to 65. 170 ASA grade I and II patients undergoing elective laparoscopic surgeries under general anaesthesia were explored in this randomized clinical study. All patients were randomly assigned to IPV. Preoxygenation was done and anaesthesia was applied and ventilated with the combination of O_2, air and isoflurane for 1 MAC for 3 minutes. $ETCO_2$ monitor was connected. Monitoring was done for PONV episodes within 24 hours at fixed intervals.

Results: Group A had a mean age of 41.5.13.54 vs. 40.74.11.76. 1. ($p>0.05$), which was statistically insignificant. Group A had 4 headaches, while group B had 3. Group A had no dizziness, while group B had 1. Both A and B had 1 patient with diarrhoea. No significant side-effect differences. ($p<0.05$). Group A had 4 headaches, while group B had 3. Group A had no dizziness, while group B had 1. Both A and B had 1 patient with diarrhoea. No significant side-effect differences. ($p<0.05$). In group A, 10 (11.76%) patients vomited in 0-4 hours, versus 2 (2.35%) in group B. 11 (12.94%) patients in group A vomited within 4-8 hours, compared to 2 (2.35%) in group B. 7 (8.24%) group A patients vomited in 8-12 hrs vs. 1 (1.18%) group B patient. 4.7% of group A patients vomited in 12-24 hours, compared to

1.8% in group B. 0-4 hours, 4-8 hours, and 8-12 hours have different statistics. 0-4- and 4-8-hours antiemetic rescue ($p>0.05$).

Conclusion: Ondansetron has shown to be a successful antiemetic drug in the prevention of postoperative vomiting and nausea (PONV), which is still a frequent perioperative complication.

Keywords: Postoperative Vomiting and Nausea, Ondansetron, Antiemetic.

Introduction

To qualify as post-surgical nausea and vomiting (PONV), a patient must experience nausea or vomiting within 24 hours of surgery [1]. PONV is known to dramatically increase the patient's discomfort, anguish, and dissatisfaction. It affects 21–32% of patients, and among high-risk groups including obese and female patients, patients with a history of PONV, patients who have had motion sickness in the past, etc., the prevalence can reach 70–80% [1-3]. The most frequent postoperative problems following general anaesthesia are nausea, vomiting, and retching [4,5]

According to patients, avoiding PONV and dealing with postoperative discomfort are equally important. When PONV is severe, it can cause bleeding, dehydration, electrolyte imbalance, wound dehiscence, and pulmonary aspiration all of which lengthen hospital stays and raise medical expenses [6-8]. There is a never-ending hunt for a solution to lessen both its prevalence and severity. According to the types of receptors at which they act, such as antagonists like acetylcholinesterase inhibitors, dopamine receptor antagonists, anti-histaminics, 5HT3 receptor antagonists, and corticosteroids, several anti-emetics have been researched for the prevention and treatment of PONV [9].

Ondansetron, a 5-HT3 antagonist, blocks the serotonin-induced depolarization of vagal afferent neurons to produce its antiemetic and antinauseant effects. It was first created to treat cancer chemotherapy and radiotherapy-induced vomiting, but it was later discovered to be useful for PONV. Glycopyrrolate is a powerful quaternary antimuscarinic with a long half-life and no central effects [10,11]. Its additional property of having an antisecretory effect on salivary and bronchial secretions makes it the favoured agent in anaesthetic treatment [12]. A powerful and extremely discriminating long-acting glucocorticoid is dexamethasone. Although the actual mechanism of its anti-emetic activity is unknown, it may be caused by endorphin release, serotonin suppression in the gut, and prostaglandin antagonism. It improves the effectiveness & lessens the negative side effects of other antiemetics [13-15].

After both inpatient and day surgery, nausea and vomiting are frequent and upsetting postoperative consequences, occurring 26–45% of the time. Gynaecological laparoscopy, a routine day care treatment, with a 51–82% incidence [16]. Since the causes of PONV are multifaceted, none of the existing antiemetics is completely effective in all individuals. A more successful alternative might be to employ a mix of antiemetic medications [17]. Following major gynaecological surgery, an ondansetron-dexamethasone combination has been utilized for PONV with positive results in reducing cisplatin chemotherapy-induced vomiting. After gynaecological laparoscopy, a technique with a high incidence of PONV, this combination has not been explored [18].

With few side effects, dexamethasone has been employed as an antiemetic for even more than 10 years in chemotherapy patients. Dexamethasone's antiemetic mechanism of action is unknown [19]. Because PONV is caused by a variety of stimuli, none of the existing antiemetics is completely effective in all individuals. There may be a way to manage situations with severe, frequent PONV using the combination of medications now used to treat nausea and vomiting in chemotherapy patients. Ondansetron and dexamethasone together have recently been demonstrated to be highly effective preventative strategies [19,20].

Materials and Methods

Research Design

This is a Prospective randomized double-blind control study which is conducted from July 2021 to June 2022 and was conducted on 170 patients who had ASA grades I and II, who were in the age group 20 to 65. This study was completed by different categories of a group such as the first 24h. Around 76% of patients had received ondansetron alone, 92% of patients had responded in a combined group, 80% of power and 95 % of confidence and the sample size was 81 in each group. It was conducted at the Narayana Hrudayalaya, Majumdar Shaw Medical Centre, Bommasandra, Bangalore.

170 ASA grade I and II patients undergoing elective laparoscopic surgeries under general anaesthesia were explored in this randomized clinical study. Participants were randomly assigned to Group A or Group B, each with 85 patients, using a computer-generated random list.

The pre-operative evaluation was done on the day previous to the surgical procedure including the Cardiovascular, respiratory, and central nervous systems were investigated. Routine lab tests included haemoglobin, total and differential count, random blood sugar, routine urine, blood urea nitrogen, serum creatinine, bleeding and clotting time, and ECG.

All patients were randomly assigned general anaesthesia with IPV. After 3 minutes of preoxygenation, anaesthesia was caused with 2 mg/kg propofol and comfortable with 0.1 mg/kg vecuronium. The patient was then ventilated with a combination of O_2, air and isoflurane for 1 MAC for 3 minutes, intubated, and an $ETCO_2$ monitor was connected.

Monitoring was done in the following fashion. At 0-4 hours, 4-8 hours, 8-12 hours, and 12-24 hours postoperatively. When there were 2 different or more PONV episodes within 24 hours, metoclopramide 10mg IV was given.

Inclusion and Exclusion criteria

Patients belonging to ASA (American Society of Anaesthesiologists) grades I and II. Patients between 20 to 65 years of age.

Patients belonging to ASA grades III and IV. Pregnant women. Patients with a history of motion sickness taking medicine currently. Patients who had received antiemetics within 24 hours of surgery. Patients on chronic steroid therapy. Patients suffering from diabetes mellitus, intestinal obstruction, hiatus hernia, and renal and hepatic diseases.

Statistical Analysis

The study used SPSS 25 and MS Excel for effective analysis. The continuous variables were expressed as mean±standard deviation. The discrete variables were expressed as counts and their respective percentage. The statistical method employed for analyzing continuous variables was ANOVA while for discrete variables was chi-square. The level of significance was considered to be $\alpha=0.05$.

Ethical Approval

The authors explained the study process to each participant thoroughly before data collection. The study obtained written

consent from each participant and received approval from the hospital's Ethical Committee.

Results

Randomized 170 patients into two groups of 80. Group A had a mean age of 41.5±13.54 vs. 40.74±11.76 years old, (p>0.05), which was statistically insignificant. Group A weighed 59.26 kg, while group B weighed 61.73 kg. (p>0.05). This was statistically insignificant. 10 patients in group A underwent laparoscopic appendectomy, 34 cholecystectomies, 4 ovarian cystectomies, 2 hysterolaparoscopy, 4 laparoscopic sterilization, 14 hernioplasty, and 2 hysterectomy. Group B had 7 laparoscopic appendectomies, 37 cholecystectomies, 4 ovarian cystectomies, 5 hysterolaparoscopy, 4 laparoscopic sterilization, 12 hernioplasty, and 1 hysterectomy (Table 1).

Table 1: Distribution of age in both groups

Parameters	**Group A N=85**		**Group B N=85**		**p-value**
Age (Mean ± SD)	41.5 ± 13.54		40.74 ± 11.76		0.695
Gender					
Male N(%)	37 (43.53)		40 (47.05)		0.644
Female N(%)	48 (56.47)		45 (52.95)		
Weight (in kgs; Mean ± SD	59.27 ± 8.08		61.73 ± 8.42		0.054
Procedure done	**Group A**		**Group B**		
	No.	**%**	**No.**	**%**	
Lap. Appendicectomy	10	11.76	7	8.24	
Lap. Cholecystectomy	34	51.76	37	55.29	
Lap. Ovarian cystectomy	4	4.7	4	4.7	
Hysterolaparoscopy	2	2.35	5	5.88	
Lap. Sterilisation	4	4.7	4	4.7	
Lap. Hernioplasty	14	22.35	12	20	
Lap. Hysterectomy	2	2.35	1	1.18	
Total	70	100	70	100	

A had 44 ASA I and 26 II patients. 70 Group B, 49 ASA I, 21 II (Table 2). It was not even significant (p>0.05). Group A's surgery lasted 103.15.47 minutes, while group B's lasted 98.59.18.35 minutes. p-value nonsignificant. Age, sex, weight, and surgery duration were comparable between groups. Major nausea (p>0.05). 20 (23.53%) group A patients had nausea within 0-4 hours vs. 6 (7.06%) group B patients. Group A (16.47%) had nausea in 4-8 hrs vs. B (5.88%). 7(8.24%) group A had nausea in 8-12 hrs vs. 1(1.18%) group B. Group A (4.71%) had nausea in 12-24 hrs; group B (1.18%) did not. p>0.05 for 0-4hrs, 4-8hrs, and 8-12hrs. In group A, retching occurred 4.7% in 0-4 hrs, 2.35 % in 4-8 hrs, 1.18 % in 8-12 hrs, and 1.18 % in 12- 24 hrs. In group B, there was no incidence in 8-12 hrs and 12-24 hrs. minor In group A, 10 (11.76%) patients vomited in 0-4 hours, versus 2 (2.35%) in group B. 11 (12.94%) patients in group A vomited within 4-8 hours, compared to 2 (2.35%) in group B. 7 (8.24%) group A patients vomited in 8-12 hrs vs. 1 (1.18%) group B patient. 4.7% of group A patients vomited in 12-24 hours, compared to 1.8% in group B. 0-4 hours, 4-8 hours, and 8-12 hours have different statistics. 0-4- and 4-8-hours antiemetic rescue (p>0.05). 7 patients (8.24%) in group A and 1 in group B needed rescue antiemetics in 4-8 hrs, and 3 in group A versus none in 8-12 hrs (Table

2). Group A had 4 headaches, while group B had 3. Group A had no dizziness, while group B had 1. Both A and B had 1 patient with diarrhoea. No significant side-effect differences. ($p < 0.05$).

Table 2: Distribution of patients by ASA grade in both groups

ASA Grade	**Group A**		**Group B**		**p-value**				
	No.	**%**	**No.**	**%**	0.417 (Not significant)				
I	44	63.53	49	69.41					
II	26	36.47	21	30.59					
Total	70	100	70	100					
Duration of surgical procedure (in minutes)	**Group A**		**Group B**		**p-value**				
Mean ± SD	103 ± 15.47		98.59 ± 18.35		0.092 (Not Significant)				
Group	**No. of cases with nausea at**								
	0-4 hours		**4-8 hours**		**8-12 hours**		**12-24hours**		
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Group A	20	23.53	14	16.47	7	8.24	4	4.71	
Group B	6	7.06	5	5.88	1	1.18	1	1.18	
p-value	0.003 Significant		0.028 Significant		0.03 Significant		0.173 Not Significant		
Group	**No. of cases of vomiting**								
	0-4 hours		**4-8 hours**		**8-12 hours**		**12-24hours**		
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Group A	10	11.76	11	12.94	7	8.24	4	4.71	
Group B	2	2.35	2	2.35	1	1.18	1	1.18	
p-value	0.017 Significant		0.009 Significant		0.03 Significant		0.173 Not Significant		
Group	**No. of cases requiring rescue antiemetic**								
	0-4 hours		**4-8 hours**		**8-12 hours**		**12-24hours**		
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Group A	6	7.06	7	8.24	3	3.52	3	3.53	
Group B	1	1.18	1	1.18	0	0	1	1.18	
p-value	0.054 Not Significant		**0.03 Significant**		**0.04 Significant**		0.301 Not significant		
	Overall incidence of complications in								
Complication	**Group A**				**Group B**				**p-value**
	Present		**Absent**		**Present**		**Absent**		
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Nausea	36	42.35	49	57.65	15	17.65	70	82.35	<0.001 Significant
Retching	8	9.41	77	90.59	2	2.35	83	97.65	0.05 Not significant
Vomiting	28	32.94	57	67.06	6	7.06	79	92.94	<0.001 Significant
Rescue antiemetic	20	23.53	65	76.47	3	3.53	82	96.47	<0.001 Significant
Any one	57	67.06	28	32.94	22	25.88	63	74.12	<0.001

complication									Significant
	Overall incidence of complications								
Complication	**Group A**				**Group B**				p-value
	Present		**Absent**		**Present**		**Absent**		
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Nausea	36	42.35	49	57.65	15	17.65	70	82.35	<0.001 Significant
Retching	8	9.41	77	90.59	2	2.35	83	97.65	0.05 Not significant
Vomiting	28	32.94	57	67.06	6	7.06	79	92.94	<0.001 Significant
Rescue antiemetic	20	23.53	65	76.47	3	3.53	82	96.47	<0.001 Significant
Any one complication	57	67.06	28	32.94	22	25.88	63	74.12	<0.001 Significant

Overall incidence of side effects					
Side effects	**Group A**		Group B		P value
	PRESENT		**PRESENT**		
	NO.	**%**	**NO.**	**%**	
Headache	4	4.7	3	3.53	0.699 (Not Significant)
Dizziness	0	0	1	1.17	0.238 (Not Significant
Diarrhoea	1	1.17	1	1.17	1 (Not Significant)
Constipation	0	0	1	1.17	0.238 (Not Significant)

General random blood sugar			
Time-Point	**Group A**	**Group B**	**P value**
Pre-op (Mean ± SD)	114.56 ± 13.6	110.66 ± 14.17	0.069 (Not Significant)
Post-op (Mean ± SD)	118.26 ± 17.28	115.67 ± 11.39	0.251 (Not Significant)

Discussion

For patients undergoing laparoscopic cholecystectomy, research was done to examine the effectiveness of ondansetron alone vs the combination of dexamethasone and ondansetron in avoiding postoperative nausea and vomiting. According to the study's findings, ondansetron and dexamethasone together were more effective than ondansetron by itself at preventing postoperative vomiting and nausea in patients having a laparoscopic cholecystectomy [21].

Recent research compared the effectiveness of intravenous dexamethasone to normal saline in reducing PONV in patients having laparoscopic cholecystectomy (lap-chole) (placebo). In the trial, the incidence of nausea and vomiting after surgery (PONV) was considerably lower in the dexamethasone-administered group than in the placebo group. The former should therefore be used more frequently in patients undergoing lap-chole because it is easily accessible, affordable, and has no severe side effects after a single dose [22].

Severe postoperative vomiting and nausea might be avoided with the help of a combination of antiemetic medications (PONV). Determining the lowest single optimal dose of dexamethasone in combination with ondansetron for the treatment of PONV in patients having laparoscopic cholecystectomy was the goal of the randomized double-blind, dose-ranging research. The number of analgesics consumed overall, the length of hospital stays, and side effects were comparable between groups. The findings imply that 8 mg of dexamethasone is the

lowest dose that, when paired with 4 mg of ondansetron, will avoid PONV in people treated with laparoscopic cholecystectomy [23].

The goal of the study was to examine how ondansetron alone and ondansetron combination with dexamethasone-treated patients undergoing laparoscopically assisted vaginal hysterectomy under general anaesthesia for PONV and pain. According to the study's findings, ondansetron coupled with dexamethasone is much more effective than ondansetron alone at reducing PONV in patients, who have undergone laparoscopic hysterectomy [20].

The recent evidence regarding the safety and effectiveness of dexamethasone in combination with other antiemetics against solo antiemetics for the avoidance of postoperative vomiting and nausea following laparoscopic cholecystectomy was updated through a comprehensive review and meta-analysis of published randomized controlled trials. The study finds that postoperative vomiting and nausea following laparoscopic cholecystectomy could be prevented more effectively with Dexamethasone in combination with other antiemetics than with antiemetics used alone. Further research should be done on the dexamethasone action mechanism and the best dosage [24-25,26].

Conclusion

Ondansetron has shown to be a successful antiemetic drug in the prevention of postoperative vomiting and nausea (PONV), which is still a frequent perioperative complication. In the study, the antiemetic impact of both one-time and repeated applications was assessed. According to the study's findings, none of the individuals' alleged complications existed. It has been established that ondansetron is a well-tolerated antiemetic and that it reduces PONV more effectively when administered as a single dosage than repeatedly. It appears that preventing vomiting is more beneficial than treating nausea.

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