

Original Research Article

Effect of dexamethasone with granisetron or ondansetron for prevention of post-operative nausea vomiting in patients undergoing laparoscopic gynaecological surgery

Shailendra Kumar Sharma¹, Shalendra Singh², Debashish Paul^{2*}, Nihar Ameta³, Priya Taank⁴, Tina Singh⁵

¹Department of Anaesthesiology and Critical Care, Military Hospital, Bhopal, Madhya Pradesh, India

²Department of Anaesthesiology and Critical Care, Armed Forces Medical College Pune, Maharashtra, India

³Department of Anaesthesiology and Critical Care, 160 Military Hospital, Masimpur, Assam, India

⁴Department of Ophthalmology, Command Hospital (Southern Command) Pune, Maharashtra, India

⁵Department of Obstetrics and Gynaecology, INHS Asvini, Mumbai, Maharashtra, India

Received: 22 January 2020

Revised: 02 February 2020

Accepted: 28 February 2020

*Correspondence:

Dr. Debashish Paul,

E-mail: drdpaulamc@rediffmail.com

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ABSTRACT

Background: Post-operative nausea and vomiting (PONV) is generally self-limiting, associated with high level of patient dissatisfaction and may delay hospital discharge. The anaesthetist is usually blamed, despite evidence that PONV results from a variety of factors and variety of antiemetic drug available in market. With this issue we aim to compare the effectiveness of dexamethasone with granisetron or ondansetron in patients undergoing laparoscopic gynaecological surgery.

Methods: 120 patients were registered in this prospective, randomized double blind study. Group I (n=60) received ondansetron 4 mg intravenously (IV)+dexamethasone 8mg I/V or II (n=60) received granisetron 1 mg IV+dexamethasone 8 mg I/V prior to anaesthesia. Post-operative data of PONV was recorded at pre-defined intervals.

Results: The majority of the patients were of the age group 20-25 years (55.83%). The mean score of Group I subjects was 0.30 ± 0.72 and that of Group II was 0.20 ± 0.57 ($p=0.43$). There are 3.33% of patients in group-I having vomiting episodes, and 1.67% of patients in group-II having vomiting episodes, none of the patients developed 2nd episodes of vomiting in either group. Thus it appears that dexamethasone in combination with ondansetron and granisetron is effective in decreasing the number of episodes of PONV. The occurrence of sickness episodes within 24 hours of surgery revealed no significant different in both groups. Haemodynamic variables showed no significant difference recorded in postoperative care unit between the study groups. The most common complaint was headache 16.67% in both groups.

Conclusions: Dexamethasone 8 mg with either granisetron 1 mg or ondansetron 4 mg showed no significant difference in antiemetic efficacy with minimal side effects and excellent patient satisfaction.

Keywords: General anaesthesia, Laparoscopic surgery, Post-operative nausea vomiting

INTRODUCTION

Post-operative nausea and vomiting (PONV) is generally self-limiting, associated with high level of patient

dissatisfaction and may delay hospital discharge. Despite continuing advances in anesthetic and surgical techniques, both the incidence and severity of PONV have remained relatively unchanged. The etiology of

PONV is complex and depends upon a variety of factors, including patient characteristics, types of surgery, anaesthetic techniques and postoperative care.^{1,2} Since laparoscopic surgery is an obvious risk factor for PONV in patients, prophylactic prescription of antiemetic is justifiable and has been described in literature.³ This increased risk of PONV is due to pneumo-peritoneum causing stimulation of mechanoreceptors in the gut. Various antiemetic therapies are being used routinely during intraoperative and postoperative periods, but its use has not completely eliminated the incidence of PONV which still remains a pressing problem in laparoscopic surgeries. Literature revealed PONV as the most unacceptable symptom after laparoscopic surgeries.⁴ It results in electrolyte imbalance, dehydration, aspiration of gastric contents, bleeding and suture dehiscence. In addition, it raises hospital costs, discharge time and a frequent concern voiced by patients in preanaesthetic check-up setting.

The introduction of 5-hydroxy tryptamine receptor antagonist like ondansetron was a major advancement in the treatment of PONV because of less adverse effects that were observed than commonly used traditional antiemetics. Granisetron, another 5-hydroxy tryptamine receptor antagonist, with stronger 5HT₃ binding, is more potent and a longer acting antiemetic agent compared to ondansetron against emesis associated with chemotherapy with less side effects.⁵ Dexamethasone is glucocorticoids that produce strong antiemetic effect by an undetermined mechanism. It may act through prostaglandin antagonism, serotonin inhibition in the gut and by releasing endorphins. The prophylactic antiemetic effect of dexamethasone is documented in laparoscopic surgery.⁵

None of the currently available antiemetic is not capable of completely eliminating the incidence of PONV. However, current understanding of risk factors for PONV is incomplete, in part because much remains to be elucidated about the pathophysiology of these symptoms, particularly their molecular biology. With this issue we aim to compare the effectiveness of dexamethasone with granisetron and ondansetron in patients undergoing laparoscopic gynaecological surgery.

METHODS

After obtaining institutional ethics review board approval and informed parental consent, this prospective randomised control trial was carried out in a tertiary care hospital. Out of a total of 164 laparoscopic gynaecological surgery patients listed for surgery during the study period from February 2014 to July 2016, 35 patients did not meet inclusion criteria and 03 patients were not included due to parental refusal and 06 cases were cancelled. A total of 120 patients in American society of anaesthesiologist physical status (ASA) grade I or II, between 20-35 years of age, undergoing laparoscopic gynaecological surgery were enrolled.

Patients with known allergy or hypersensitivity to the study drug, history of motion sickness, prior severe PONV and on long term steroid therapy were excluded from the study. Patients having history of acid peptic disease, gastrointestinal, liver or renal diseases and diabetes mellitus or on any anti-emetic medication within 24 hours before surgery were also excluded.

After computer-generated randomisation, patients were assigned in either group I (n = 60) who received ondansetron 4mg intravenously (IV) + dexamethasone 8mg I/V or group II (n = 60) received granisetron 1mg IV + dexamethasone 8mg I/V. Patients were kept Nil by mouth for 12 hours before surgery. In the preoperative room, intravenous line was secured. In the operation theatre routine monitoring devices pulse oximetry, non-invasive blood pressure (NIBP), electrocardiogram (ECG) monitors were attached, and baseline blood pressure, heart rate (HR) and O₂ saturation values (SpO₂) were recorded. Later capnography was attached after securing airway. General anaesthesia (GA) was given as per standard protocol to all the enrolled patients in either group. Maintenance of anaesthesia was achieved by sevoflurane (0.4-2%) and oxygen: nitrous oxide mixture (1:3). The study medications were administered immediately after induction of anaesthesia in all treatment groups. Neuromuscular blockade was reversed at the end of surgery with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) IV. All patients received analgesia in the form of paracetamol 15mg/kg IV, patients were monitored in post-op care unit for any sequel at 1 hour, 6 and 24 hours. To assess severity of PONV the scoring system was evolved which was as following (No nausea- 0, Nausea only -1, Nausea with retching -2, Vomiting - 3).⁶ In case patients had an episode of vomiting, rescue medicine was planned, inj metoclopramide 10 mg IV bolus dose. Symptoms of nausea and retching were not treated with rescue antiemetic. Nausea and Vomiting assessment was done up to 30 minutes following rescue medication administration and response was defined as improvement or resolution of PONV symptoms. Complete response (i.e., emesis free) was also defined as not emetic symptoms and no need for another rescue antiemetic medication. The details of any other adverse effects were noted throughout the study after general questioning of the patients by the anaesthesiologist.

Sample size was calculated based on previous studies considering the incidence of PONV as the primary outcome, a minimum of 50 patients in each group were required to attain the power of more than 80% of the study with an alpha error of 5%.⁷ Data was analyzed using computer software SPSS version 20. Demographical data was compared using independent t test and chi-square test. Haemodynamic parameters were compared using independent t test. Overall incidences were compared using fisher exact test. Adverse effects of study drugs were compared using chi-square test and

fisher exact test. A p-value of <0.05 was considered as significant.

RESULTS

Efficacy of dexamethasone with granisetron or ondansetron for prevention of post-operative nausea vomiting in patients undergoing laparoscopic gynaecological surgery was studied in 120 patients. Both

the groups were comparable with respect to demographics, ASA Physical status grade, duration of surgery and type of surgery (Table 1).

The majority of the patients were of the age group 20-25 years (55.83%). The mean score of Group I subjects was 0.30±0.72 and that of Group II was 0.20±0.57. There was no significant association found between both groups (Mann Whitney U test, p value=0.437) (Table 2).

Table 1: Demographic profile and clinical characteristics of patients in both the group (all values expressed as mean±sd or as expressed otherwise).

Parameter	Group I (n = 60)	Group II (n = 60)	p-value
Age in years	25.53±3.51	26.13±3.84	0.37
Weight(Kg)	54.41±6.63	54.78±6.64	0.76
ASA Status (I/II)	53/7	55/5	0.54
Duration of anaesthesia	41.62±5.45	43.25±7.28	0.16
Type of surgery			
Diagnostic hysterolaprosopic	43 (71.67%)	47 (78.33%)	0.54
Laparoscopic sterilization	17 (28.33%)	13 (21.67%)	

GA-General anaesthesia, ASA-American society of anaesthesiologist.

Table 2: Postoperative observation in both groups.

		Group I (n = 60)	Group II (n = 60)	p- value
Post-operative sickness	Nausea	6 (10%)	5 (8.33%)	
	Retching	3 (5.0%)	2 (3.33%)	
	Vomiting	2 (3.33%)	1 (1.67%)	
Mean PONV Score		0.30±0.72	0.20±0.57	0.43
Number of vomiting episode	0	58 (96.67%)	59 (98.33%)	
	1	2 (3.33%)	1 (1.67%)	
	2	0 (0%)	0 (0%)	
Incidence of overall sickness	Nausea (0-1 hr)	2 (3.3%)	2 (3.3%)	
	Retching (0-1 hr)	2 (3.3%)	1 (1.7%)	
	Vomiting (0-1 hr)	1 (1.7%)	1 (1.7%)	
	Nausea (1-6 hr)	2 (3.3%)	2 (3.3%)	
	Retching (1-6 hr)	1 (1.7%)	1 (1.7%)	
	Vomiting (1-6 hr)	1 (1.7%)	00	
	Nausea (6-24 hr)	2 (3.3%)	1 (1.7%)	
	Retching (6-24 hr)	00	00	
	Vomiting (6-24 hr)	00	00	

PONV-postoperative nausea and vomiting

(Since data was skewed so median were compared using Mann Whitney u test). There are 3.33% of patients in group-I having vomiting episodes, and 1.67% of patients in group-II having vomiting episodes, none of the patients developed 2nd episodes of vomiting in either group (Table 2). Thus it appears that dexamethasone in combination with ondansetron and granisetron is effective in decreasing the number of episodes of PONV. The occurrence of sickness episodes within 24 hrs of surgery revealed no significant different in both groups (Fisher’s Exact Test, p>0.05) (Table 2).

Systolic blood pressure (SBP), diastolic blood pressure (DBP), HR and SpO₂ showed no statistically significant difference recorded in postoperative care unit between the study groups (Table 3).

The incidences of post-operative adverse effects were noted in both study groups. In group - I, 10%patients had headache, 5% dizziness, 3.33% sedation, 6.67% constipation and abdominal distress and 3.33% facial flushing. In group-II, 6.67% patients had headache, 3.33% dizziness, 3.33% sedation, 3.33% constipation and abdominal distress and 1.67%facial flushing. None of the

antiemetic in our study leads to any significant hemodynamic changes or serious adverse effects. The most common complaint was headache 16.67% in both groups.

Table 3: Patients haemodynamic parameters at different time interval in post-operative period.

S BP 10	Group-I (O+D)	122.5±13.3	0.3
Min	GROUP-II (G+D)	120.1±12.4	
D BP 10	Group-I (O+D)	77.8±8.6	0.3
Min	GROUP-II (G+D)	76.2±8.9	
HR 10	Group-I (O+D)	76.43±8.04	0.37
Min	GROUP-II (G+D)	77.7±7.9	
SPO ₂ 10	Group-I (O+D)	99.2±0.5	0.09
Min	GROUP-II (G+D)	99.3±0.6	
S BP 30	Group-I (O+D)	115.7±10.9	0.93
Min	GROUP-II (G+D)	115.9±10.9	
D BP 30	Group-I (O+D)	72.33±6.8	1
Min	GROUP-II (G+D)	72.3±6.8	
HR 30	Group-I (O+D)	76.1±7.05	0.73
Min	GROUP-II (G+D)	76.5±7.1	
SPO ₂ 30	Group-I (O+D)	99.2±0.5	0.86
Min	GROUP-II (G+D)	99.2±0.5	

SBP-Systolic blood pressure, DBP-Disystolic blood Pressure, HR-Heart rate, SpO₂-Oxygen saturation

DISCUSSION

In present study the factors that would have contributed to PONV may be pneumoperitonium, use of inhalational drugs, use of fentanyl or use of nitrous oxide. In the study, patients of aged 20-35 years with BMI <35 kg/m² included. Young age, obese patient in laproscopic surgeries were included because study done by Pearman et al showed that PONV are more common among young age group and obese patients.⁸ Laparoscopic surgery was chosen because of high incidence of PONV associated with it. Naguib et al demonstrated that the incidence of PONV after laparoscopic surgeries in their placebo group was remarkably high (72%).⁹

In the study, incidences of PONV were reported maximum in first 12 hours and there were no differences in incidence in later 12 hours. Vishal et al demonstrated in their study that incidences of PONV were minimal in first 12 hours and there were no statistical differences in later 12 hours in study groups.¹⁰

Raphael et al observed that after 6 hours of surgery 2 mg granisetron is more effective than 4 mg ondansetron for preventing PONV.¹¹ 4mg ondansetron and 1 mg granisetron dose with 8 mg dexamethasone was used to prevent PONV and found granisetron plus dexamethasone is more effective compare to ondansetron plus dexamethasone but not any statistically significant difference. Chidambaram et al concluded that the prophylactic IV administration of granisetron is more effective than ondansetron for controlling PONV with

fewer incidences of side effects.¹² Naguib et al, concluded that granisetron is more potent and long acting than ondansetron against emesis associated with chemotherapy, and found to be very effective for preventing PONV after laparoscopic cholecystectomy.⁹ Wadaskar A et al, in their study concluded that granisetron is more effective than ondansetron and placebo in controlling PONV after laparoscopic gynaecological surgery.¹³ Pearman concluded in his study that there were no differences between treatment groups with respect to vital signs, laboratory values, or adverse events and concluded that intravenous ondansetron is safe and effective at preventing PONV in male and female patients undergoing day case surgery.⁸ Gigilla reported some hemodynamic variation in SBP, DBP and HR. Ondansetron mediated bradycardia and hypotension was reported in his study group.¹⁴ The study shows no statistically significant difference in the baseline values of hemodynamic variables between the two groups before, during or after giving study drug.

Study concluded that dexamethasone 8 mg with either granisetron 1 mg or ondansetron 4 mg showed no significant difference in antiemetic efficacy with minimal side effects and excellent patient satisfaction.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sharma SK, Singh S, Paul D, Ameta N, Taank P, Singh T. Effect of dexamethasone with granisetron or ondansetron for prevention of post-operative nausea vomiting in patients undergoing laparoscopic gynaecological surgery. *Int J Res Med Sci* 2020;8:1331-5.