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ORIGINAL ARTICLE

Comparison of Ondansetron, Metoclopramide and Dexamethasone for PONV Prophylaxis in Laparoscopic Surgeries.

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Abstract

Background

Postoperative nausea and vomiting (PONV) is one of the most frequently occurring complications occurring after administration of anaesthesia and surgery.

Objective

The present study was designed to compare the efficacy of the antiemetics- ondansetron, metoclopromide and dexamethasone and to look into the complications occurring in patients after elective laparoscopic surgeries under General Anesthesia.

Material and Methods

In this prospective, randomized, placebo-controlled, double-blind study we included 135 adults, ASA I or II patients, aged 20-50 years, undergoing elective laparoscopic surgery under GA. The technique, anaesthetic drugs, methods of monitoring were kept uniform in all the patients during the intra-operative period. The patients were then randomly assigned into three groups to ensure that any differences between and within the groups are not systematic at the outset of the experiment. Group A (n=45) received ondansetron 4 mg/2ml, Group B (n=45) received metoclopramide 10 mg/2 ml I/V, Group C(n=45) received dexamethasone 8mg/2ml just before induction of anaesthesia. Patients were observed at 6 hours, 12 hours and 24 hours after anesthesia. The presence of vomiting was assessed by the nursing staff double blind to the study. Anticipatory vomiting was assessed by direct questioning of the patient. The rescue antiemetic (Inj Promethazine 25 mg) I/V, was given, if patient suffered from nausea for more than 15 minutes, or experience retching or vomiting during study period.

Results

Group A showed lower frequency of vomiting and nausea when compared to Group B and Group C which was statistically significant. There was a higher use of rescue emetics in Group B

Conclusion

This study showed that the use of ondansetron is more effective in the control of nausea and vomiting in patients undergoing laparoscopic surgery. Group B was associated with the known adverse reactions mainly those of extrapyramidal symptoms.

Keywords

Laparoscopic surgery, PONV

INTRODUCTION

Anaesthesia is derived from the Greek word *anaísthçt(os)* and means' without feeling or senseless' thus allowing invasive and painful procedures to be performed with little distress to the patient. The side effects of anesthesia can occur peri-operatively or postoperatively. The type of side effects depend on the type of anaesthesia–general, regional or local. The two most common complications occurring after surgery and anaesthesia are pain and vomiting. The seemingly harmless nausea and vomiting can be so distressing that it may increase perioperative costs, perioperative morbidity, postanesthesia care stay, prolong hospital stays, length of stay/delay discharge, delay the time that the patient can go back to work, and lead to readmissions.[1]

From the homely aspirin to the most sophisticated prescription medicine, all drugs come with side effects. Perhaps the most common set of side effects for drugs taken internally involves the gastrointestinal system. Nearly any drug can cause nausea and vomiting. About 20-30% of the population undergoing surgery experience

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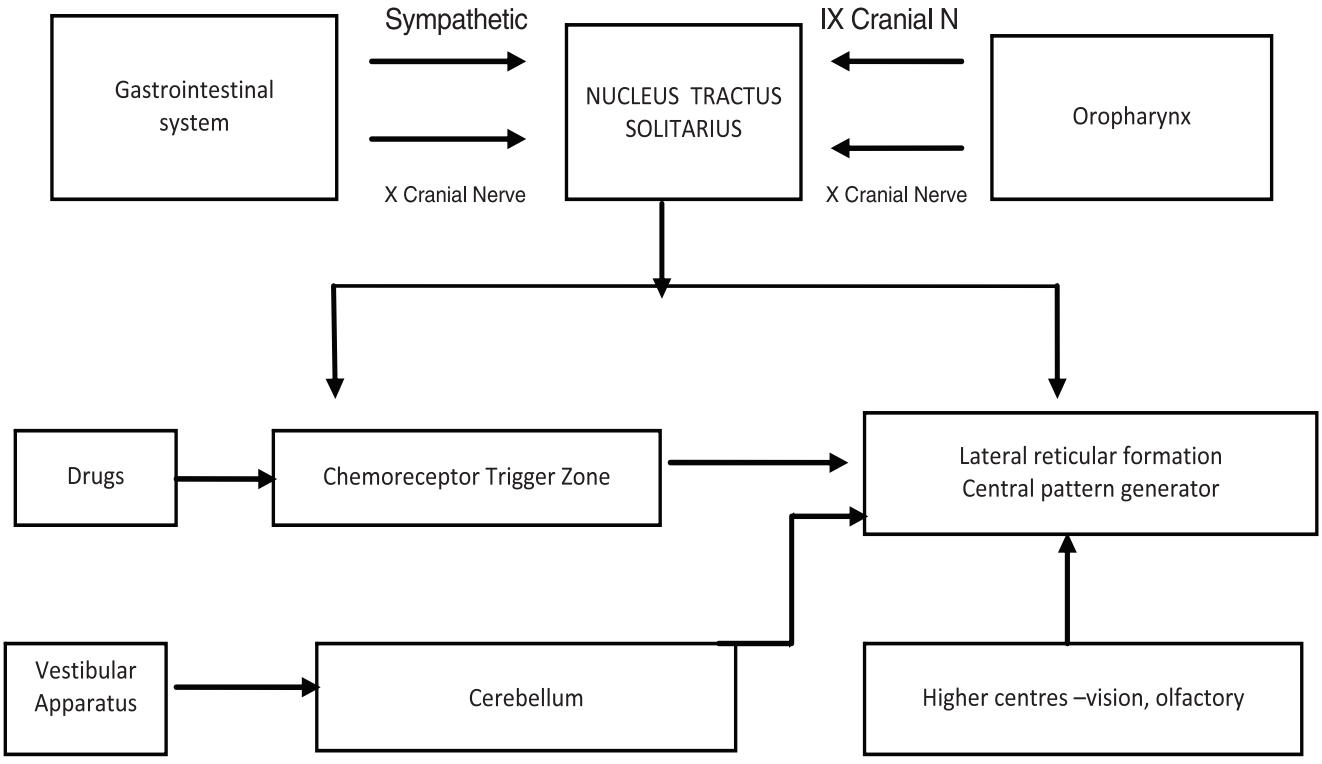
Postoperative nausea and vomiting (PONV) and this percentage increases to 70 in high risk patients within 24 hrs of surgery [2–4]. The mechanism of nausea and vomiting can be explained by the chart below:

Triggers of vomiting arise from various sites like pharynx, gut and ear. Pharyngeal stimulation may trigger an emetic reflex. Vestibular apparatus, mechanoreceptors of the urinary bladder, gallbladder and the gastric chemoreceptor's may all trigger an emetic reflex. From the gut, vagus nerve transmits signals to the cholinergic receptors in the nucleus tractus solitarius and other centers in the area postrema. The afferent stimuli detect the need to vomit and stimulate the vomiting centre located in the lateral reticular formation of the brain stem close to the fourth ventricle which is in close proximity to other visceral centres like the respiratory and vasomotor centres. Cholinergic, dopaminergic, histaminic and serotonergic receptors are the four types of receptors involved. The motor component of vomiting reflex is mediated by both autonomic and somatic senses. The vagal motor neurons supplying the gut and the heart originate in dorsal motor vagal nucleus and nucleus ambiguous. The output of these nuclei is coordinated to produce the physiological pattern associated with vomiting [5]. The independent predictors for PONV include among the many factors, female gender, past history of PONV and motion sickness, use of opioids, nitrous oxide and non-smoking history. With the increasing understanding of the pathophysiology of acute pain, especially the occurrence of peripheral and central hypersensitization, it is unlikely that a single drug or intervention is sufficiently broad in its action to be adequately effective, especially with moderate or greater pain [6].

Various drugs have been used over the years for the treatment of PONV. Antiemetics are the mainstay of the management. The traditional anti emetics include antihistamines, anticholinergics and dopamine-receptor antagonists [7]. Serotonin Receptor Antagonists (SRA)are the newer class of drugs which provides better efficacy and safety as compared to the traditional drugs. Ondansetron, a prototype of this group is widely used drug of this group [8]. It binds to the 5-Hydroxytryptamine subtype 3 (5HT3) receptors, selectively blocking the emetogenic stimuli during anesthesia and surgery. The drug has a proven efficacy and is recommended as a prophylactic antiemetic at the time of induction of anesthesia.

Prokinetic drugs like Metoclopramide, Domperidone and Cisapride have also been used preoperatively [10]. Metoclopramide causes reduction of nausea and vomiting by two methods. It increases the smooth muscle tension of the lower oesophagus and stomach, increases gastrointestinal motility and relaxes the pylorus and duodenum. The second mechanism is by antagonism of the dopamine receptors of the CTZ. Dexamethasone is the



commonest corticosteroid which has been used for the treatment of nausea and vomiting [11]. It acts by inhibiting prostaglandin synthesis and prevent the inflammatory response of the serotonin on the gut.It also enhances the effects of other antiemetic drugs.Thus there are a large number of drugs available for management of Post operative nausea and vomiting.The aim of this study was to assess which of the three drugs;ondansetron, metoclopromide and dexamethasone was better in managing postoperative nausea and vomiting in patients undergoing laparoscopic surgery.

Material and Methods

The study protocol was approved by the Ethical Committee of the hospital. The study was conducted in the Operation Theatre (OT), MH Jhansi from May 2014 to Oct 2016. A written/informed consent was obtained from all the patients.

Study Design

This was a prospective, randomized, placebo-controlled, double blind study.

Inclusion Criteria: We included 135 adult ASA I or II female patients, aged 20-50 years, undergoing elective laparoscopic surgery under GA.

Exclusion Criteria: Patients with ASA grade III and IV, BMI >30 kg/m^2, history of motion sickness were excluded from the study. Patients with upper gastrointestinal pathology like acid peptic disease, reflux esophagitis, pyloric stenosis and patients taking anti-emetic were also excluded. No patients with known allergy or with psychiatric diseases were included. All patients were admitted 24 hours before surgery. All preoperative investigations were carried out and patients with any condition mentioned above were excluded. Pre-anaesthesia assessment was carried out by a Anaesthesiologist who was blind to the study. Patients were kept nil orally for 12 hours as per the hospital protocol. Preoperatively no opioid analgesics were given. On arrival in the OT, an 18 gauge I/V cannula was passed in the non-dominant hand. Perioperative monitoring included pulse-oximetry, non-invasive blood pressure every 3 min, capnography and continuous ECG. Normal saline solution was given as a fluid therapy during the perioperative period.

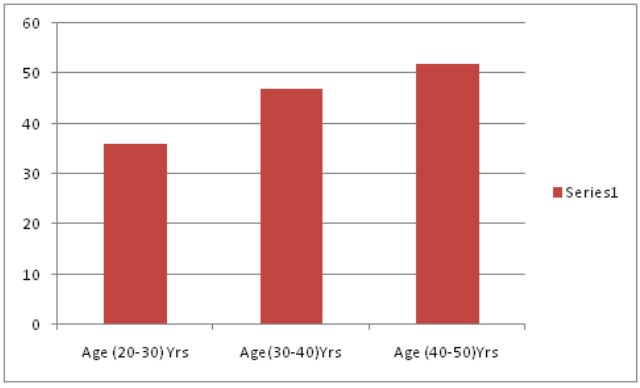
Statistical analyses were performed using SPSS (Statistical Package for Social Sciences) version 20. Student t-test was used for analyzing age, weight, duration of surgery and duration of anesthesia while chi-square test was utilized for the gender, ASA physical status, and frequency of nausea and vomiting and use of rescue antiemetic. P-value less than 0.05 were considered statistically significant.

Results

All the 135 patients, 45 in each group were included in the study. There were no significant differences between the two groups with regard to regards to age ($p>0.05$), weight ($p>0.05$), height ($p>0.05$), ASA physical status ($p>0.05$), duration of surgery ($p>0.05$), and duration of anesthesia ($p>0.05$) as shown in the various graphs (1-4). The frequency of nausea and vomiting was lower in the ondansetron group as compared to the metoclopramide group and the dexamethasone group and the results were statistically significant ($p<0.05$). In group A, 95.6.% patients did not have nausea or vomiting postoperatively, while 4.4% experienced nausea. In group B, 66.6% had nausea, 40% had vomiting, while 33.4 % of patents did not complain of either nausea or vomiting (graph 6.). In group C, 40% had nausea, 11.6 % had vomiting, while 60 % of patents did not complain of either nausea or vomiting (graph 5 shows use of rescue antiemetics shown in table was significantly higher in metoclopromide and dexamethasone group ($p<0.05$). None of the patients experienced headache, flushing or other side effects. Dizziness and extrapyramidal symptoms were noted in the metoclopromide group.

Age of patients

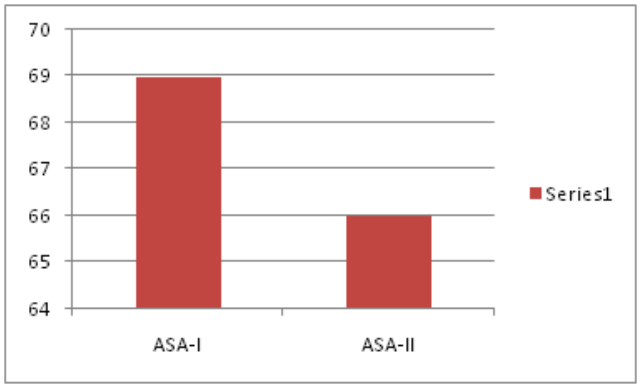
Age (Yrs)	No.
20-30	36
30-40	47
40-50	52



Graph-1

Physical Status of Patients

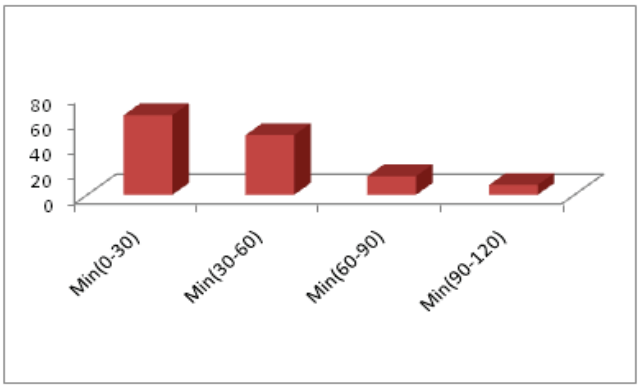
	Nos.
ASA-I	69
ASA-II	66



Graph-2

Duration of Surgery

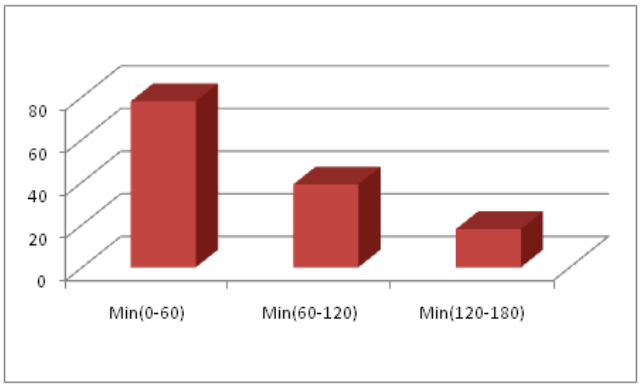
Minutes	Nos.
0-30	64
30-60	48
60-90	15
90-120	08



Graph-3

Duration of Anaesthesia

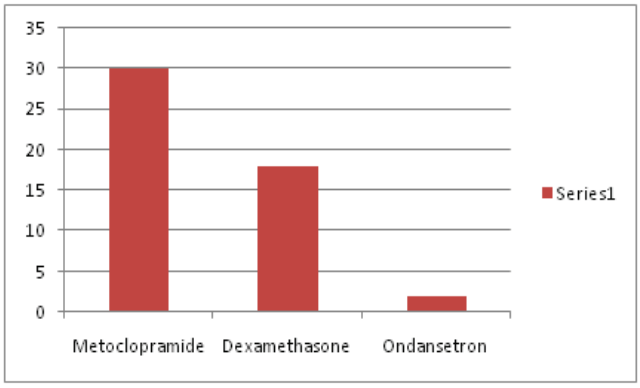
Minutes	Nos.
00-60	78
60-120	39
120-180	18



Graph-4

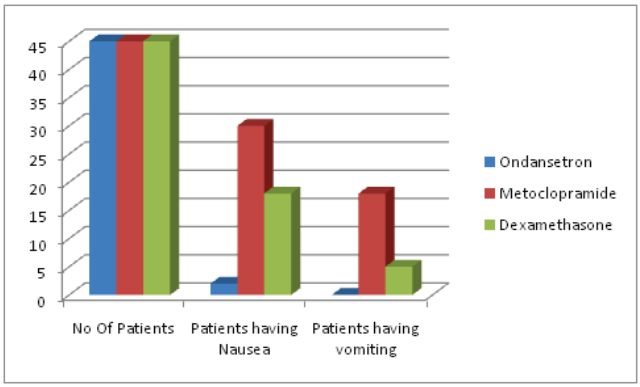
Requirement of Rescue Emetics

Rescue Emetics	Nos.
Metoclopramide	30
Dexamethasone	18
Ondansetron	02



Graph-5

Drugs	No. of Patients	Patients having Nausea	Patients having vomiting
Ondansetron	45	2	0
Metoclopramide	45	30	18
Dexamethasone	45	18	5



Graph-6

Discussion

Nausea and vomiting create a significant predicament that can result in wound dehiscence, aspiration, impaired wound healing and increased bleeding. The various causes of vomiting including pharyngeal stimulation, gastrointestinal distension, abdominal surgery, anaesthetic agents, pain, opioid medication, hypoxia, hypertension and various psychological factors. The etiology of emesis is multifactorial. The factors could be classified in the appropriate temporal sequence in which the patient is exposed- Patient factors, preoperative factors. Intraoperative factors could be further divided into anaesthetic factors, anaesthesia techniques and surgical factors. Post operative factors include pain and ambulation [12].

The number of variables was kept constant for all the three study groups. All patients received laparoscopic surgery, and anesthesia was induced by the same team of anesthetists. All the drugs and techniques were standardized, including postoperative analgesics. Duration of anesthesia and surgery was comparable and there was no difference in age, gender, weight, in all the three groups. All patients with a previous history of motion sickness or PONV were excluded. The study tried to ensure that the difference in the incidence of PONV among the groups could only be attributed to the difference in drugs tested for their efficacy in preventing PONV. Metoclopromide and Dexamethasone were used in comparison with ondansetron since they are the most commonly used antiemetic agents [13].

Three drugs

Metoclopromide, ondansetron and dexamethasone were compared with each other in three different groups. This study showed that ondansetron 4 mg was compared with metoclopromide 10mg and Dexamethasone 8mg administered in adult patients undergoing elective laparoscopic surgery under GA significantly decreases the frequency of PONV. Ondansetron as a prophylaxis has shown a variable incidence of PONV. Fujii Y. in 2008 found that the antiserotonins were highly effective after middle ear surgery in controlling PONV [14]. Pawar et al in 2008 compared Ondansetron and Dexamethasone in gynaecological laparoscopic surgery and found ondansetron to be better in controlling PONV [15]. Polati et al in 1997 compared Ondansetron with Metoclopromide and found ondansetron to be superior [16]. Krobbuaban also published similar results in 2008 when he compared ondansetron and metoclopromide [17]. Our conclusions were in agreement with Pawar et al, Polati et al, Fujiii et al and Krobbuaban et al. Efficacy of ondansetron as a standalone antiemetic could not be checked as there was no placebo group. Nevertheless, a complete response (no nausea/vomiting) was observed in 95.6% of patients in ondansetron group in our investigation. In contrast to our study Steinbrook et al. found out that metoclopramide is more effective in preventing PONV than ondansetron [18] but they had added droperidol along with it. Corticosteroids provide antiemetic efficacy but the potential of toxic effects may impede its acceptance as a therapeutic drug. Hence these drugs may be reserved for high risk cases.

Conclusion

Our study showed that prophylactic use of ondansetron is more effective and associated with fewer side effects than metoclopromide and Dexamethasone in the prevention of PONV during laparoscopic surgeries in adult patients.

Furthermore, metoclopramide was associated with more adverse effects, major being dizziness and extrapyramidal symptoms.

Conflict of interest:	All authors declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
Funding:	No external funding
Guarantor:	Lt. Col. Dheeraj Kumar will act as guarantor of this article on behalf of all co-authors.

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