Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(11C):4082-4085 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i11.045

Original Research Article

Ondansetron and Aprepitant Vs Ondansetron alone in prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries: A comparative study

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Abstract: Recent studies have shown that aprepitant, a substance – P/ Nk 1 receptor antagonist is effective in postoperative vomiting. The present study was designed to find out whether addition of aprepitant to ondansetron would be more effective than ondansetron alone in prevention of post operative nausea and vomiting in patients undergoing laparoscopic surgeries. After obtaining informed consent, 50 patients with ASA grade I and II between 25 - 55 years of age undergoing laparoscopic surgery under general anaesthesia were randomly divided into two groups of 25 patients each. Group- I received 4 mg of ondansetron i.v and Group - II received the 4mg of ondansetron i.v with 40mg oral of aprepitant before induction. Incidence and severity of nausea, vomiting was recorded at 2, 6, 24, 48 hours post-operatively by using a standard verbal response scale ranging from 0 to 3 (0 - no nausea / vomiting; 1 - mild nausea / vomiting; 2 - moderate nausea / vomiting; 3 - severe nausea / vomiting. The data was subjected to statistical analysis by using SPSS 16.0 version software. Chi square test was employed to analyse the data and $P < 0.05$ was considered as statistically significant. The incidence of post-operative nausea and vomiting was more in group I when compare to group II at 2, 6, 24 and 48 h after surgery. The severity of post operative nausea and vomiting in group I is higher when compare to group II. The addition of aprepitant to ondansetron offered an added advantage over the usage of ondansetron alone as a single drug.
Keywords: aprepitant, ondansetron, laparoscopic surgeries

INTRODUCTION

The most common and distressing symptoms, which follow anaesthesia and surgery, are nausea and vomiting. Pathophysiology and pharmacology of postoperative nausea and vomiting is quite complex [1]. Commonly used antiemetics for postoperative nausea and vomiting include the scopolamine, promethazine, diphenhydramine, droperidol and metoclopramide. However, these antiemetics have adverse effects such as dryness of mouth, sedation, hypotension, extrapyramidal symptoms, dystonic effects and restlessness. The new class of antiemetics used for the prevention and treatment of postoperative nausea and vomiting are the serotonin receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron). These antiemetics do not have the adverse effects of the older, traditional antiemetics. Headache and dizziness are the main adverse effects of the serotonin receptor antagonists in the dosages used for postoperative nausea and vomiting. The serotonin receptor antagonists have improved antiemetic effectiveness but are not as completely efficacious for postoperative nausea and vomiting. Combination antiemetic therapy improves efficacy for postoperative nausea and vomiting prevention and treatment.

Aprepitant is an antagonist of substance – P/ Nk 1 receptor antagonist. Recently, aprepitant has shown promising results in prevention and treatment of acute and delayed chemotherapy induced nausea and vomiting. A study has shown that aprepitant is also effective in postoperative vomiting [2]. Few studies have reported that, aprepitant increases the activity of 5 - HT3 receptor antagonist like ondensetron when used in combination [3]. Recent trials have shown aprepitant to be effective in the management of brain tumors, [4]

however, mechanism involved in above effect is uncertain. It may be probably due to antagonism of substance – P. The present study was designed to find out whether addition of aprepitant to ondansetron would be more effective than ondansetron alone in prevention of post-operative nausea and vomiting in patients undergoing laparoscopic surgeries.

MATERIALS AND METHODS

After obtaining informed consent, 50 patients with ASA grade I and II between 25 - 55 years of age undergoing laparoscopic surgery under general anaesthesia were randomly divided into two groups of 25 each. Patients with gastrointestinal and renal disease, patients undergoing cancer chemotherapy, patients on antiemetic/steroid medication 24 h before surgery, pregnant patients/lactating mothers, a known allergy previously to the same drug/group, patients with no history or signs of increased intracranial pressure and history of alcohol or drug abuse were excluded from the study. All necessary medication which required in preanesthetic medication was given to the patients in a standard dosage. Group- I received 4 mg of ondansetron i.v and Group - II received 4mg of ondansetron i.v with 40mg oral of aprepitant before induction. The drug aprepitant was administered 30 min prior to ondansetron administration and ondansetron was given just before induction in the operation theatre. Patients of both the groups were induced under the same standard institutional protocol for general anesthesia. Induction of anaesthesia was done by using inj. of fentanyl (2 µg/kg/BW), inj. of thiopentone (5 mg/kg/BW) and inj. of vecuronium (0.1 mg/kg/BW). Intubation was done with an oral cuffed endotracheal tube of appropriate size. Anesthesia was maintained with air, oxygen and sevoflurane with muscle relaxant and controlled ventilation. For pain relief, injection diclofenac 75 mg intravenous (i.v.) and injection paracetamol 1 g i.v. were given to all patients intraoperatively toward the end of the surgery. Incidence and severity of nausea, vomiting was recorded at 2, 6, 24, 48 hours post-operatively by using a standard verbal response scale ranging from 0 to 3 (0 - no nausea / vomiting; 1 - mild nausea / vomiting; 2 - moderate nausea / vomiting; 3 - severe nausea / vomiting). The data was subjected to statistical analysis by using SPSS 16.0 version software. Chi square test was employed to analyse the data and $P < 0.05$ was considered as statistically significant.

RESULTS

Demographic parameters in terms of age, height, body weight and gender along with their ASA status (I or II) were comparable in both the groups and represented in Table 1. The Table 2 shows the types of laparoscopic surgeries performed in the present study. The values are presented as numbers. The patients were almost equally distributed in both the groups. The incidence and severity of post operative nausea and vomiting was compared in both the groups at 2, 6, 24 and 48 h after surgery. The incidence and severity of nausea and vomiting was statistically differed in both the groups at 2, 6, 24 and 48 h after surgery. The combination of ondansetron with aprepitant has shown less incidence and severity of nausea and vomiting when compare to ondansetron alone [Table 3].

Table-1: Demographic characteristics of patients in both groups

Parameters	Group - I	Group - II	P – Value
Age (Years)	38.61 ± 10.6	39.40 ± 11.72	0.726
Height (Cm)	68.20 ± 10.4	66.21 ± 9.11	0.652
Weight (Kg)	158.61 ± 2.81	160.52 ± 9.12	0.621
BMI	25.50 ± 3.8	24.9 ± 4.6	0.511
Duration of surgery (min)	98.28 ± 38.3	104.21 ± 19.9	0.715
Duration of Anaesthesia (min)	112.30 ± 19.8	121.8 ± 32.82	0.560

Data was expressed as Mean ± SEM, * $P < 0.05$

Table-2: Distribution of patients in various laparoscopic surgeries

Type of surgery	Group I	Group II
Diagnostic cholecystectomy	12	10
Laparoscopic cholecystectomy	8	8
Laparoscopic appendectomy	3	5
Laparoscopic ovarian cystectomy	2	2

Data are presented as number of patients.

Table-3: Incidence and severity of nausea and vomiting

Severity score	2nd h		6th h		24th h		48th h	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
0	16	20	18	21	17	24	20	25
1	2	4	0	4	2	1	0	0
2	6	1	5	0	5	0	5	0
3	1	0	2	0	1	0	0	0

Data are presented as number of patients.

DISCUSSION

The vomiting is controlled by multiple areas in the central nervous system including the medulla, vestibular apparatus and cerebral cortex. The medulla contains the area postrema (AP), the dorsal motor nucleus of the vagus and the nucleus tractussolitarius (NTS), collectively referred to as the 'emesis centre'. Additionally, the vestibular apparatus feeds auditory stimuli and positional changes into the vomiting centre, while cortical structures allow emotions, tastes, sights and smells to play a role [5].

Numerous signals must arrive at the emesis centre in an appropriate sequence to stimulate emesis [6]. When these stimuli converge, outputs activate the lower oesophageal sphincter (LES) and stomach, sympathetic ganglia, respiration, swallowing and baroreceptors. The resulting sensation of nausea is thought to originate in the cerebral cortex. Vomiting is a complex process that empties the gastrointestinal tract by retrograde phasic contractions.

The overall incidence of postoperative nausea and vomiting is around 30% and as great as 70% to 80% in high-risk individuals [7]. Although post operative nausea and vomiting is rarely fatal, it does increase morbidity by threatening wound dehiscence, hematoma formation, aspiration, oesophageal rupture, dehydration and increases in intraocular and intracranial pressures due to acute blood pressure elevations.

Substance P as a prominent neurotransmitter released from both the CNS and the peripheral nervous system (PNS) afferent neurons. Substance P interacts with NK receptors, which are rhodopsin-like structures coupled to G-proteins. This interaction of neurotransmitter and receptor is involved in many disease processes including: asthma, chronic bronchitis, inflammatory bowel disease, cystitis, migraines, seizures, pain, depression and emesis [8]. Substance P activity occurs at primary sensory neurons in the PNS and produces an inflammatory reaction referred to as neurogenic inflammation. More recent research is targeting the relationship between substance P and the CNS. Animal studies demonstrated that application of substance P to the emesis centre induced vomiting. Few human trials have proven that, NK-1 antagonists are helpful in the prevention of post operative nausea and vomiting. Of further interest, the NK-1 antagonist aprepitant may have antiemetic effects as far out from surgery as 48 h, important with post-discharge nausea and vomiting and opioid induced emesis [9]. The FDA-approved aprepitant for treatment and prevention of cancer chemotherapy induced and post operative vomiting. Post operative nausea and vomiting is a common occurrence after laparoscopic surgeries. Nowadays, 5-HT3 receptor antagonists are routinely used to prevent post operative nausea and vomiting in the patients undergoing surgeries under general anesthesia.

CONCLUSION

The present study was designed to find out whether addition of aprepitant to ondansetron would be more effective than ondansetron alone in prevention of post operative nausea and vomiting. The results of this study showed that, addition of aprepitant to ondansetron significantly reduced the incident and severity of post operative nausea and vomiting when compared to ondansetron alone. We conclude that the addition of 40mg oral aprepitant to 4mg of ondansetron i.v significantly reduces the incidence of post operative nausea and vomiting and enhance the overall comfort and satisfaction to the patients in the immediate postoperative period.

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