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Compare the Efficacy of Prochlorperazine and Granisetron in Patients Undergoing Total Abdominal Hysterectomy

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Abstract

Aim: To compare the effectiveness of mouth dissolving antiemeticsprochlorperazine and granisetron in the prevention of postoperative nausea and vomiting in patients undergoing abdominal hysterectomy under spinal anaesthesia *Materials and Methods:* A total number of 50 cases of ASA Gr.I and Gr. II were taken into a double blind randomized study and divided into two groups. 25 of them received Granisetron 1mg mouth dissolving tablet and the other 25 patients received Prochlorperazine 5mg mouth dissolving tablet for preventing postoperative nausea and vomiting and observed for a period of 24 hours. *Results:* There were no statistically significant differences between the groups with respect to patient characteristics, type of surgery and duration of anesthesia. Administration of Prochlorperazine and Granisetron 60min before surgery, effectively controlled nausea and vomiting during early postoperative period i.e., within 6 hours after surgery. Postoperative nausea and vomiting in the 6 – 24 hours postoperative period was significantly lower with Granisetron when compared to Prochlorperazine. (p value <0.01) *Conclusion:* Administration of Granisetron 1hr before surgery was superior to Prochlorperazine in long term prevention of postoperative nausea and vomiting following Total abdominal hysterectomy under spinal anesthesia.

Keywords: Prochlorperazine; Granisetron; Abdominal Hysterectomy; Spinal Anesthesia.

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Introduction

Postoperative nausea and vomiting is one of the most common and distressing side effect encountered by patients following anesthetic and surgical procedures. In the present scenario, it is estimated that 22 to 30% of adult patients develop postoperative emesis, which is consistently lower when compared to 75 to 80% reported during the ether era [1,2].

As per the literature, incidence of postoperative nausea and vomiting ranges from 25 to 55% following inpatient surgery and 8 to 47% for outpatient surgery. When questioned before surgery, it was observed that patients were concerned about postoperative nausea and vomiting apart from pain. Severe and persistent postoperative nausea and vomiting can cause tension on suture lines, bleeding at operative sites and wound dehiscence, venous hypertension, oesophageal tears and rupture, rib fractures, gastric herniation and muscular fatigue. In neurosurgical cases, postoperative nausea and vomiting can cause increased intracranial tension. It can also increase the risk of pulmonary aspiration. It may result in dehydration and electrolyte imbalance in pediatric population [3].

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Postoperative nausea and vomiting is a major contributor to burgeoning healthcare costs for both the hospital and the patient [4]. These costs may result from longer recovery, extended stay in the hospital, added attention required from nurses and physicians, additional drug supplies as well as unanticipated admissions following outpatient procedures. Most of the currently used antiemetic drugs like anti-histaminics, anticholinergics and dopamine receptor antagonists possess clinically significant side effects.

Mouth dissolving tablets are novel and advanced oral drug delivery systems used in the management of postoperative nausea and vomiting to achieve better patient compliance. The present study was intended to compare the efficacy of mouth dissolving tablets prochlorperazine and granisetron in prevention of postoperative nausea and vomiting in patients undergoing total abdominal hysterectomy.

Material and Methods

It is a comparative study done in patients undergoing abdominal hysterectomy under spinal anesthesia in Government maternity hospital, Sultan bazar, Government maternity hospital, Petlaburz and Niloufer hospital attached to Osmania medical college Koti, Hyderabad. A total number of 50 patients in the age group of 26 to 52 years belonging to ASA Grade I and ASA Grade II were randomly divided into two groups, Group A and Group B, each consisting of 25 patients. Group A received 1 mg of Granisetron mouth dissolving tablet and group B received 5 mg of prochlorperazine mouth dissolving tablet one hour before starting of surgery. The study was approved by the hospital ethics committee and written informed consent was obtained from patients.

Inclusion Criteria

Patients of ASA Grades I, and II, age group of 26 to 52 years.

Exclusion Criteria

Patients belonging to ASA Grade III, IV and V, below the age of 26years, above the age of 52 years, H/o acid peptic disease, migraine , motion sickness, Patients with clinically significant cardiovascular, pulmonary, renal, hepatic, neurological and endocrinological abnormalities.

Preoperative visit was conducted on the previous day of surgery and a detailed history and present complaints were noted. General and systemic examinations of cardiovascular, respiratory and central nervous system were done. Routine laboratory investigations like complete haemogram, blood urea, serum creatinine, and blood sugar, ECG, bleeding time and clotting time were done. Preoperative data collected included age, weight, heart rate, blood pressure, history of motion sickness, previous surgery and PONV.

After the patient arrived in the operation theatre, ECG pulse-oximeter and NIBP were attached and an intravenous line with 18 G intracath was established. All the women in two groups were hydrated with Ringer's lactate solution 20 ml/kg, before the procedure.

Lumbar Spinal Anaesthesia

After keeping the operating table horizontal, the patient was shifted onto the table. The patient was positioned in left lateral position, with the help of an assistant standing in front of the patient. Strict aseptic precautions were taken. The hands a were scrubbed to elbows with soap and water, after application of spirit the sterile gown and gloves were put on. The patient's back was cleaned with betadine solution (contact time – 3 minutes) followed with surgical spirit from the angle of scapulae the coccyx in a cephalad to caudal direction, from the centre to the periphery. Then the patient's back was draped with sterile spinal hole towel.

A 25 G disposable Quincke's needle was inserted in the middle of the interspace parallel to the table and angled about 100 Cephalad since the inter-laminal space is slightly Cephalad to the interspace. The bevel was positioned laterally so that the longitudinal fibres are separated rather than cut. As the needle pierces the ligamentum flavum and the dura, arachnoid distinct changes in resistance and characteristic loss of resistance will be felt. The stylet was removed and observed for free flow of cerebrospinal fluid (CSF).

After obtaining the clear and free flow of CSF, the bupivacaine 0.5% 3-4 ml was injected intrathecally. The spinal needle was withdrawn and patent was positioned supine. Throughout the procedure the patient received Oxygen (4 liters/ minute) through Hudson's mask continuously. The level of sensory blockade was tested every 2 minutes after intrathecal injection of local anesthetic agent. The level of work was maintained around T4. Monitoring was done continuously.

Bradycardia was treated with atropine and Hypotension with 100% oxygen, Vasopressors and IV fluids promptly. The incidences of PONV were

recorded within the first 24 hours after surgery at intervals of 0-6 hours, and 6-24 hours. Episodes of PONV were identified by spontaneous complaints by the patients or by direct questioning. Incidence of nausea and vomiting occurring in first six hours is considered as early nausea and vomiting and incidence of PONV after six hours was considered as late emetic episode.

"Complete response" was defined as the absence of nausea, retching or vomiting and no need for rescue antiemetic during the 24-hour observation period. Rescue antiemetic was provided with Inj. Metoclopramide 10mg i.v in the event of 1 or more episodes of vomiting depending on the observer's discretion. We made no distinction between vomiting and retching (i.e., retching event was considered a vomiting event). Nausea and vomiting were evaluated on three point ordinal scale. 0=none, 1=nausea, 2=retching or vomiting.

Data was entered in Microsoft excel and analysis was done using SPSS version 20. Descriptive statistical analysis was done. Results on continuous measurements are presented as Mean & Standard Deviation.Results on categorical measurements are presented as Percentages. Significance is assessed at 5% level of significance. Student t test (independent, two tailed) has been used to find out the significance of study parameters on a continuous scale between two groups. Chi square test is used to find out the significance of study parameters on a categorical scale between two groups.

Results

A total number of 50 cases were taken into study. 25 of them received Granisetron 1mg mouth dissolving tablet, and the other 25 patients received Prochlorperazine 5mg mouth dissolving tablet for preventing postoperative nausea and vomiting through a period of 24 hours.

There were no statistically significant differences between the two groups with respect to patient characteristics age and weight, duration of surgery and anesthesia (Table 1).

The incidence of nausea in first 24 hours of postoperative period was 12% and 48% in Granisetron and Prochlorperazine respectively ($p<0.01$). incidence of vomiting in first 24 hours of postoperative period There were no emetic episodes in Group A. Incidence of emetic episodes in Group B is 32%. Incidence of emetic episodes in 24 hours of postoperative period is significantly high in group B compared to group A ($p <0.01$) (Table 2).

Incidence of early nausea (0-6 hours) in Granisetron and Prochlorperazine were 4% and 20%. Incidence of early nausea (0-6 hours) in Granisetron group and Prochlorperazine groups did not show any statistically significant difference. (p value >0.05). Incidence of late nausea was 12% and 40% in Prochlorperazine and Granisetron groups respectively, which was statistically significant difference (Table 3).

Table 1: Demographic Details

Patient characteristics	Mean±SD Group A	Mean±SD Group B	P value
Age	40.52±8.7	39.84±7.44	0.2968 NS
Weight	50.36±5.81	48.16 ±6.71	1.2379 NS
Duration of anesthesia (min)	100.00±26.61	89.00±23.62	1.5454 NS
Duration of surgery (min)	91.20±17.39	99.20±25.15	1.3079 NS

Table 2: Incidence of postoperative nausea and vomiting in first 24 hours

Postoperative nausea and Vomiting	Group A (Granisetron) (N=25)	Group B (Prochlorperazine) N=25)	Chi Square	P- Value
Nausea in first 24 hours				
Present	3(12%)	12(48%)	7.8095	0.01
Absent	22(88%)	13(52%)		
Vomiting in first 24 hours				
Present	0	8 (32%)	9.6726	0.01*
Absent	25 (100%)	17 (68%)		

Table 3: Incidence of postoperative nausea

Postoperative nausea	Group A (Granisetron) (N=25)	Group B (Prochlorperazine) N=25)	Chi Square	P- Value
Incidence of early nausea (0-6 hours)				
Present	1 (4%)	5 (20%)	3.219	0.05*
Absent	24 (96%)	20 (80%)		
Incidence of late nausea (6 – 24 hours)				
Present	3 (12%)	10 (40%)	5.1975,	0.05*
Absent	22 (88%)	15 (60%)		

Table 4: Incidence of postoperative vomiting

Vomiting	Group A (Granisetron) (N=25)	Group B (Prochlorperazine) N=25)	Chi Square	P- Value
Incidence of early vomiting (0-6 hours)				
Present	0	2 (8%)	**2.**602	0.05
Absent	25(100%)	23 (92%)		
Incidence of late vomiting (6- 24hours)				
Present	0	8 (32%)	**9.**6726	0.05
Absent	25 (100%)	17 (68%)		

Two patients in Prochlorperazine and none in Granisetron had vomiting during first 6 hours of postoperative period. Both Granisetron and Prochlorperazine were equally efficacious in preventing vomiting during early postoperative period after recovering from anesthesia (p value >0.05). There were no emetic episodes during 6–24 hours postoperative period in Granisetron group whereas 32% of patients in Prochlorperazine group developed emesis during this late postoperative period, which showed statistically significant difference. (Table 4).

Discussion

Nausea and vomiting following anaesthesia has been a distressing problem for the patients and is frequently listed among the most important preoperative concerns apart from pain. With the change in emphasis from inpatient to outpatient office based medical/surgical environment, there has been an increasing interest in the big little problem of postoperative nausea and vomiting.

Inspite of so many advances in the management of postoperative nausea and vomiting with the invention of new drugs, multimodal approaches of management like administering multiple different antiemetic medication, less emetogenicanesthetic techniques, adequate intravenous hydration, adequate pain control, etc., the incidence of postoperative nausea and vomiting remains still high ranging from 25%-55% following inpatient surgery and 8%-47% following outpatient surgery.

An effective antiemetic that could be used to treat nausea and vomiting without extending recovery time and that remains effective for 24 hours following treatment would be a significant asset to the anesthesiologists armamentarium, especially in settings like office based anesthesia where the patient is admitted for day care surgery and discharged on the same day. Drugs acting for longer duration also have an advantage in surgeries where the incidence of postoperative nausea and vomiting is very high like laparoscopic surgery, middle ear surgery, tonsillectomy, laparotomy, strabismus surgery, orchipexy, etc.

Unfortunately, commonly used medications like antihistamines, anticholinergics, gastro-prokinetics, butyrophenones, cause undesirable side effects like sedation, dysphoria, restlessness and extrapyramidal symptoms. To overcome these serotonin antagonists like Ondansetron, Tropisetron, Dolasetron, Ramosetron, Palonosetron and Granisetron were introduced for treatment of nausea and vomiting. They were primarily used in treating chemotherapy induced vomiting with minimal and clinically acceptable side effects. The most distressing and intolerable emesis induced by anti-malignant medications was better controlled with these 5HT3 antagonists and they proved to have a promising role in the field of oncology. Abundant research in the field of oncology demonstrates the efficacy of these drugs. However, there were anecdotal reports in the

literature about their role in the prevention of postoperative nausea and vomiting [4,5].

To overcome the difficulties associated with conventional tablets i.e. difficulty in swallowing which leads to poor patient compliance, scientists have developed innovative drug delivery system known as fast dissolving tablets. The benefits in terms of patient compliance, rapid onset of action, increased bioavailability and good stability make these tablets popular as a dosage form of choice in the current market. These tablets disintegrate instantaneously when put on tongue, releasing the drug which dissolves or disperses in the saliva. Some drugs are absorbed in mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailabilty of the drug significantly greater than those observed from conventional tablet dosage form.

In the present study, the antiemetic efficacy of Prochlorperazine and Granisetron were assessed in postoperative nausea and vomiting for a period of 24 hours. The postoperative period was again divided into two groups of assessment period (0-6 hrs, early postoperative period and 6-24 hours, late postoperative period) to assess the efficacy of both the drugs during different time intervals. We have selected similar groups of patients in respect of age, weight, duration of surgery and duration of anesthesia to compare the efficacy of the drugs. Analgesia for postoperative pain was standardized and patients of both groups were observed for a period of 24 hours postoperatively. Hence we believe that the difference in postoperative nausea and vomiting is attributed exclusively to the study drugs.

The present study was conducted only in elective surgeries in patients with no obvious causes for nausea and vomiting. Patients with risk factors of PONV like motion sickness, migraine, gastro-oesophageal reflux disease etc. were excluded from the present study.

In our study, there were no significant differences in the incidence of PONV between the Granisetron and Prochlorperazine groups during first 6hrs of surgery. 22 out of 25 patients receiving Granisetron had no symptoms of nausea and vomiting, while only 13 out of 25 patients receiving Prochlorperazine had no symptoms of nausea and vomiting.So it was concluded that Granisetron was superior to Prochlorperazine in the long term prevention of PONV (6-24 hrs).

Burris H et al. [6] conducted a double blind randomised parallel group study in 230 adult cancer patients who received moderately emitogenic chemotherapy to compare the efficacy and safety of oral granisetron vs oral prochlorperazine in preventing nausea and emesis. The results were granisetron was significantly more effective than prochlorperazine in achieving the complete response (74% vs 41%) respectively and total control of nausea and vomiting (58% vs 33%) respectively. They concluded that oral granisetron 1mg twice a day was significantly more effective than oral prochlorperazine sustained release capsule 10mg twice a day in complete response and total control of nausea vomiting at 24hrs after chemotherapy.

A G Wilson et al. [7] conducted a randomised double blind placebo controlled dose ranging study compared three doses (0.1mg, 1mg and 3mg) of the 5HT3 receptor antagonist, granisetron as prophylactic therapy for prevention of PONV. The aims were to determine the optimum dose of granisetron. They studied 527 adult patients undergoing elective open abdominal surgery or vaginal hysterectomy during general anaesthesia. They concluded that granisetron was well tolerated and the optimum dose was 1mg.

Lowen P S et al. [8] in 2000 conducted a randomised double blind controlled study to compare efficacy of 5HT3 receptor antagonist (Ondansetron, Granisetron, Dolasetron and Tropisetron) vs traditional agents (Metaclopramide, Prochlorperazine, Cyclizine and Droperidol). Results in the 32 studies examining PONV indicated a 46% reduction in the odds of PONV in the 5HT3 treated group (0.54 [95% Cl 0.42-0.71], $p<0.001$). They concluded that 5HT3 receptor antagonists are superior to traditional antiemetic agents for prevention of PONV.

D Angelo et al. [9] conducted a randomised, double blind, placebo study, pilot study of PONV prevention in patients undergoing elective open abdominal hysterectomy requiring general anaesthesia received a single dose of Granisetron 0.1mg, 0.2mg, 0.3mg or placebo administered approximately 15 minutes prior to end of surgery. The results were the proportion of patients with no vomiting episode in 0-6 hr interval after administration of study medication was higher in each Granisetron treatment group (>90%) than in the placebo group (77%). Proportion of patient with no vomiting episode in 0-24 hr interval were similar across treatment groups. They concluded that Granisetron doses 0.1mg, 0.2mg, 0.3mg administered just prior to end of surgery suggested a trend of improved efficacy compared to placebo in prevention of PONV in first 6hrs after total abdominal hysterectomy.

Dasgupta M et al. [10] in 2012 conducted randomised placebo controlled trial to evaluate the

efficacy and safety of Granisetron on incidence of nausea and vomiting in caesarean deliveries under spinal anaesthesia. 80 parturients received Granisetron 40mcg/kg or placebo (n=40) intravenously immediately after clamping of fetal umbilical cord. Nausea and vomiting and adverse events were observed for 24 hrs after administration of spinal anaesthesia. The results were complete response 0-4 hr after administration of spinal anaesthesia was achieved in 80% patients with Granisetron and in 45% of patients with placebo. The corresponding incidences during (4-24hrs) were 82.5 and 55% (p value <0.05).

Our study agrees with and confirms the various aspects of the above studies. We found that Granisetron has definite advantage over Prochlorperazine in prevention and treatment of PONV in female patients undergoing abdominal hysterectomy under spinal anaesthesia. There was absolutely negligible need for rescue antiemetic medication in granisetron group whereas some patients in prochlorperazine group needed rescue medication in the form of metaclopramide.

Mouth dissolving tablets of Granisetron available freely in India 1mg strength by the trade name Graniforce-MD (Mankind) and Prochlorperazine 5mg tablet by the trade name of Emikind-MD (Mankind).

Conclusion

The administration of Granisetron 1hr before surgery was superior to Prochlorperazine in long term prevention of postoperative nausea and vomiting following total abdominal hysterectomy under spinal anesthesia.

The postoperative sequelae, side effects and behaviour of the patients , though not a part of our study were comparable in both the groups and both the drugs are safe for routine clinical use during Total abdominal hysterectomy under spinal anesthesia.

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