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Original Research

Efficacy of Granisetron for prevention of nausea and vomiting in patients undergoing cesarean section under spinal anesthesia: A randomized double blind placebo-controlled study

Sanju Sharma[1], Mamta Singh[2]

[1]Assistant Professor, Department of Anaesthesiology, M.G.M. Medical College, Kishanganj, Bihar, India;
[2]Associate Professor, Department of Gynae. & Obstetrics, Nalanda Medical College, Patna, Bihar, India

ABSTRACT

Background: Nausea and vomiting are common and unpleasant complications for cesarean section during and after spinal anesthesia. During regional anesthesia, granisetron has been shown to be effective in the prevention of emetic symptoms. **Objective**: The objective of our study was to assess the efficacy and safety of granisetron ($5HT_3$ receptor antagonist) for preventing PONV in patients undergoing cesarean delivery under spinal anesthesia. **Methods**: In our randomized, double-blind study, 100 ASA grade I and II women undergoing cesarean section under spinal anaesthesia were studied. Patients in group D (n=50) received injection granisetron 40 µg/kg and group P (n=50) 0.9% saline intravenously. Main outcome measures were occurrence of nausea, vomiting and adverse events in the postoperative period. The response of patient to therapy and side effects were evaluated in both groups for 24 hrs after administration of spinal anesthesia. **Results**: Demographic characteristics of both groups were comparable patients in granisetron (82%) had more complete response as compared to placebo (48%). No clinically important adverse events were observed in both the groups. **Conclusion**: Granisetron is effective for preventing nausea and vomiting during spinal anaesthesia for caesarean section.

Key words: Granisetron, caesarean section, spinal anaesthesia.

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Corresponding Author: Dr. Mamta Singh, D.G.O., M.D., Associate Professor, Department of Gynae. & Obstetrics, Nalanda Medical College, Patna, Bihar, India

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INTRODUCTION

Postoperative nausea and vomiting (PONV) remains one of the most common complications related to surgery and anaesthesia. Referred to as the "big little problem", its complications range from minor discomfort to gastric aspiration.[1] PONV are common sequel of general as well as regional anaesthesia and a leading cause of delayed procedure.[2] An overall estimate of PONV is approximately 20-30% of all adult surgical patients. There is higher incidence of nausea and vomiting after surgery in female adults as compared to male adults. The incidence of PONV after day care and laparoscopic surgeries varies from 36-82% during immediate postoperative recovery and can be as high as 73% in certain gynaecological procedures.[3]

Nausea and vomiting in cesarean delivery under spinal anesthesia are a common problem and have been reported in more than 66 % cases.[4] Furthermore, this can complicate postoperative recovery in several ways like aspiration of vomitus, reactionary haemorrhage, electrolyte disturbance, dehydration, delay of nutrition, fluid intake, oral drug therapy, and wound dehiscence.[5]

The introduction of 5-hydroxytryptamine type 3 ($5\text{-}HT_3$) receptor antagonist in 1990s was heralded as a major advance in the treatment of PONV because of the absence of adverse effects that were observed with commonly used traditional antiemetics.[6] Among the antiemetics used

currently, 5-HT_3 antagonists such as ondansetron and granisetron are gaining popularity. Granisetron is a selective 5-HT_3 receptor antagonist and has more potent and longer-acting properties than ondansetron for the treatment of cisplatin-induced emesis. Recently, granisetron has been found to have a prophylactic antiemetic effect on PONV in patients undergoing surgery under general anesthesia.[7]

There is paucity of data on use of granisetron for preventing PONV in cesarean delivery in association with spinal anesthesia in our region. So, we conducted this randomized, double-blind, placebo-controlled study to assess the efficacy and safety of granisetron ($5HT_3$ receptor antagonist) for preventing PONV in patients undergoing cesarean delivery under spinal anesthesia.

METHOD

The study was carried out in a teaching hospital of Bihar. After approval of institutional ethical committee and obtaining written informed consents, hundred American Society of Anesthesiologists (ASA) physical Status I and II, 20–35 years old women, scheduled for elective Caesarean Section surgery under spinal anesthesia were included for the study. All participants were explained the procedure and were randomly allocated into two groups (Group D and Group P) using a computer generated random number table. Women who had previous history of emesis in post-delivery period, history of acid peptic disease, body weight >85 kg, cardiopulmonary disease, any chronic medical or surgical disorders complicating the pregnancy, and conditions contraindicating spinal anesthesia, were excluded from this study.

On arrival to the operating room, standardized monitoring was done throughout the perioperative period for all patients. Heart rate (HR), ECG, SBP, respiratory rate, and SpO_2 were recorded. All participants received injection Ranitidine 40 mg intravenously before procedure and intravenous hydration with 20 ml/kg of Ringer's lactate solution before induction of spinal anesthesia. Under overall aseptic precaution, spinal anesthesia was administered in the right lateral decubitus position through L_{3-4} intervertebral space using 25 gauge Quincke's spinal needle with 0.5 % hyperbaric bupivacaine 2.5ml (12.5 mg). Patients were continuously monitored during the procedure. The decrease in systolic blood pressure >20 % of baseline values and/or less than 80 mmHg immediately after spinal injection was treated with additional intravenous fluids and/ or phenylephrine 50-100 mcg intravenously, as indicated. After due confirmation of spinal block at $T_{4–5}$ level, surgery was started. Lower segment Cesarean section was performed in all the cases. Patients in each group were allowed to receive fentanyl 1 mcg/kg intravenously if required for pain relief after delivery of the baby due to uterus exteriorization and/or peritoneum manipulation. Syntocinon (10 Units) was administered through intravenous infusion at the time of umbilical cord clamping.

Study drugs were prepared, according to the randomization, by one of anesthesia staff who was not involved in the study. The prepared solution (Granisetron 40 µg /kg or 0.9% Saline) was given in 5ml syringes to the blinded anesthesiologist who injected drug intravenously after clamping of the umbilical cord. Patients and anesthesiologist who collected post-delivery data were blinded to the study drug administered. Intraoperative and postoperative emetic episodes (nausea, retching, and vomiting) were recorded by direct questioning or by spontaneous complaint by the patients at any time by the attending anaesthesiologist blinded to which type of treatment the patients had received.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. *Retching* was defined as the laboured, spasmodic, and rhythmic contraction of the respiratory muscles without the expulsion of gastric contents. *Vomiting* was defined as the forceful expulsion of gastric contents from mouth.[8]

If two or more episodes of emesis occurred in each observation period, another rescue antiemetic (ondansetron 4 mg) was given intravenously. We have made no distinction between vomiting and retching in our study. The details of adverse effects were recorded during study period by the attending anesthesiologist. Postoperative analgesia was provided with tramadol 2 mg/kg administered intravenously.

All quantitative variables were expressed as mean ± standard deviation and qualitative as percentage. Statistical differences between two groups in discrete and continuous variables were tested using Chi-sqaure (χ^2) test and Student's *t* test, respectively. A *p* value of <0.05 was considered significant.

RESULTS

A total of 100 full-term pregnant women who were posted for elective cesarean section under spinal anesthesia were included in the study and were equally distributed in two groups. The pre-operative and intraoperative details of the participants are summarized in Table 1 & Table 2.

The demographic characteristics such as age, weight, ASA grade, and gestational age were comparable in both the groups ($P > 0.05$). There was no significant difference in baseline vital signs (HR, SBP, and SpO_2). [Table 1]

Duration of surgery was 46.8±8.3 min in Group D and 48.2±7.6 min in Group P and was comparable in both groups.($P = 0.78$). Other parameters were also not statistically significant. [Table 2]

In the early (0-6 hrs) postoperative period after administration of spinal anesthesia, PONV occurred in 9 (18.0%) of patients who had received granisetron and in 28 (56.0%) of patients who had received placebo.

Table 1: Pre-operative details of the Participants

Pre-operative Variables	Group D Granisetron (n=50)	Group P Placebo (n=50)	p Value
Age (Years)	26.2±4.2	26.5±4.0	0.67
Primigravida	34	32	0.63
Multigravida	16	18	0.38
Gestational Age (Weeks)	38.4±1.2	38.2±1.5	0.27
Weight (kg)	56.6±8.1	57.1±7.8	0.72
ASA Grade I	38	40	0.54
ASA Grade II	12	10	0.21
Heart Rate (bpm)	92.1±20.2	93.5±19.6	0.42
Systolic Blood Pressure (mmHg)	124.1±7.5	124.8±6.8	0.54
SpO_2 (%)	99.7±1.7	99.7±1.6	0.97

The frequency of nausea and/or vomiting during late (6-24 hrs) postoperative period was less in granisetron group as compared to placebo.

Table 2: Intraoperative details of the Participants

Clinical Parameters	Group D Granisetron (n=50)	Group P Placebo (n=50)	p Value
Sensory Block Level (median)	T6(T4-T11)	T6(T4-T11)	
Duration of Surgery (mins)	46.8±8.3	48.2±7.6	0.78
Uterus exteriorized (n)	32	34	0.66
Duration of Uterus exteriorized (mins)	14.2±5.1	14.6±5.7	0.82
Estimated Blood loss (ml)	540±110	550±130	0.89

The overall cumulative incidences (0–24 h) of PONV were 12 (24.0 %) with granisetron and 33 (66.0 %) with placebo. The difference between the two groups was statistically significant ($p< 0.05$). [Table 3]

Table 3: Frequency of PONV in the two groups during Postoperative period

Postoperative period	Group D Granisetron (n=50)	Group P Placebo (n=50)	P Value
Early PONV (0-6 hrs)	9 (18.0%)	28 (56.0%)	0.001
Late PONV (6-24 hrs)	7 (14.0%)	24 (48.0%)	0.001
Total PONV (0-24hrs)	12 (24.0%)	33 (66.0%)	0.001

We observed headache, dizziness, dry mouth, and constipation in both the groups but it was not clinically serious and there was no difference in the incidence of adverse effects between the two groups.

DISCUSSION

Nausea and Vomiting are the most commonly encountered symptoms after anaesthesia and incidence following cesarean section is relatively high without prophylactic antiemetics.[4] PONV depends on factors like maternal demographics, operative procedure, perioperative hypotension, postoperative pain, use of perioperative opioids, anesthetic techniques, peritoneal traction, and exteriorization of uterus.[1,8,9]

The dopaminergic, histaminic (H1), cholinergic, muscarinic, and 5HT3. neuro-transmitter systems appear to play an important role in mediating the emetic response. The drugs for PONV management are thus generally antihistaminic, anticholinergics, phenothiazine derivatives, and dopamine receptor antagonists with untoward side effects like sedation, restlessness, tachycardia, extrapyramidal symptoms, and dry mouth, and have interactions with other anaesthetic medications. Recently introduced 5HT3 receptor antagonists which include ondansetron, granisetron, dolasetron, and tropisetron are devoid of such side effects and highly effective in prevention and treatment of PONV.

We have therefore studied the effects of granisetron in nausea and vomiting in Cesarean deliveries under spinal anaesthesia. The results of this randomized, double-blinded, placebo-controlled study demonstrate that granisetron is an effective method for prevention of spinal anesthesia induced Nausea and Vomiting during cesarean section compared to saline control group. In our study we matched the groups for their demographic and pre-operative characteristics.

It has been reported that nausea and vomiting develops in more than 66 % cases of spinal anaesthesia patients undergoing caesarean section; which was similar to the control group of our study (66.0%). Recent studies demonstrated that granisetron was effective for

prevention of nausea and vomiting during and after spinal anesthesia for cesarean section when compared with placebo ($P < 0.01$) and this correlated with our results.[10,11] On the basis of the findings of the present study, we concluded that prophylactic therapy with granisetron is effective and safe for the prevention of post operative nausea and vomiting after administration of spinal anesthesia in elective cesarean section.

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