A Randomized placebo controlled study to compare Propofol and Ondansetron for Control of Emetic Episodes during Caesarean Delivery under Spinal Anesthesia

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Abstract

Background: Caesarean deliveries done under spinal anesthesia are associated with higher incidence of post-operative nausea and vomiting (PONV).

Aims and Objectives: Present study was performed to find the efficacy of subhypnotic dose of propofol compared to ondansetron and placebo in controlling nausea and vomiting during caesarean delivery under spinal anesthesia.

Material and Methods: A randomized placebo controlled study was done on 90 parturient patients at GMC and Hamidia Hospital, Bhopal between May 2013 and December 2013. All the study patients were randomly divided into three groups: Group I (Placebo treated), Group II (1 mg/kg/hr infusion of propofol) and Group III (4 mg of Ondansetron). Emetic episodes (nausea and vomiting) were evaluated using linear numerical scale ranging from 0 (No nausea and vomiting) to 2 (Vomiting).

Results: In present study we found that on administration of study drugs incidence of PONV was low (13.33%) in propofol group as compared to ondansetron group (16.66%) ($p > 0.05$). Incidence of PONV was significantly more in placebo treated group (53.33%).

Conclusion: Propofol and ondansetron, both were highly effective as compared to placebo in preventing the emetic episodes during caesarean delivery under spinal anesthesia. Moreover subhypnotic dose of propofol was more effective than ondansetron in the prevention of PONV.

Keys words: Post-operative nausea and vomiting, Propofol, Caesarean deliveries

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Introduction

For the parturient patients, nausea and vomiting are the common side effects of caesarean section done under spinal anesthesia (SA).[1] Incidence of nausea and vomiting after caesarean section varies from 50% to 80% when no prophylactic antiemetic is given.[1] Therefore, some authors recommend giving prophylactic antiemetics during caesarean delivery.[2]

Different treatment options are available to reduce post operative nausea and vomiting (PONV), such as 5-HT3 antagonists like ondansetron and granisetron, antihistamine drugs and dopamine receptor antagonists.[3] But these treatment options are associated with many limiting factors, such as cost with 5- HT3 antagonists, extrapyramidal symptoms with dopamine receptor antagonists, excessive sedation and tachycardia with antihistamine drugs.[3]

Propofol is a short acting non-opioid sedative–hypnotic agent. It is believed to work by enhancing the binding of c-amino butyric acid to receptor sites in the central nervous system. [4] Propofol is reported to be an antiemetic also and therefore it is useful to decrease the incidence of post-operative nausea and vomiting when used at subhypnotic doses.[5]

The present study was done to evaluate the efficacy and side effects of propofol at subhypnotic dose and compare it with ondansetron and placebo for reducing emetic symptoms.

Materials and Methods

A randomized placebo controlled study was done on 90 parturients (undergoing elective or emergency LSCS) of age group between 18-35 years belonging to American Society of anesthesiologist grade I and II in Department of Anesthesiology, GMC and Hamidia Hospital, Bhopal.

A written informed consent from all the patients and Ethical Committee approval was obtained before starting the study. All the patients were assessed before the surgery and judged for fitness. The study was conducted between May, 2013 and Dec., 2013.

The patients with contraindication for regional anesthesia and/ or with a history of sensitivity to the drugs used in the study, patients who had gastro-intestinal disease, renal, hepatic, cardiac diseases, hyper-emesis gravidarum and those who had received drugs with anti-emetic properties within last 24 hours before surgery were excluded from the study.

All patients received ranitidine 150 mg orally, the night before the surgery as a premedication. Baseline measurement of blood pressure, pulse rate, respiratory rate and arterial oxygen saturation were taken. After

obtaining proper informed consent and confirming 'nil orally' status, pre operatively all patients were administered 20ml/kg of Ringer lactate solution before spinal anesthesia.

Dural puncture was performed at the L3 – L4 interspaces with a 25G-26G lumbar puncture needle in the right lateral decubitus position. After the free flow of CSF, 2.2 ml of 0.5% heavy hyperbaric bupivacaine was injected intrathecally. The decrease in systolic blood pressure (non invasive blood pressure) was recorded every 10 min after injection and more than 20% from base line values and/ or less than 90mm Hg) after spinal anesthesia (SA), was treated by increasing the rate of IV fluid administration, by exaggerating the uterine tilt and by administering 5-10 mg of ephedrine intravenously until hypotension was resolved. Oxytocin (10 units) was given after umbilical cord clamping via IV infusion over 10 min.

Patients were randomly divided into 3 groups of 30 patients each, using computer generated random numbers ; Group I (2ml normal saline), Group II (1 mg/kg/hr infusion of propofol) and Group III (2 ml containing 4 mg of ondansetron I.V. bolus).

Emetic episodes (occurrence of nausea, vomiting and retching) experienced by the patients were recorded by the anesthesiologists every 30 min (intra-operative) and till 4.5 hrs post delivery. In present study vomiting is defined as the ejection of matter from the stomach in retrograde fashion through the esophagus and mouth. In present study retching is defined as gastric and esophageal movements without expulsion of vomitus.[6]

Episodes were identified by direct questioning or by spontaneous complaints by patients.

Also post-operative adverse effects were noted in all the patients by direct questioning or by spontaneous complaints by patients.

All the data were analyzed using IBM SPSS Statistics 20. Demographic data were analysed for variance. Unpaired t-test and chi-square test were used where appropriate. Sample size of 90 with 30 parturient in each group was determined with power of study of 80%. Data were expressed as mean±standard deviation (SD); standard tests of significance were applied to determine the p value. $P < 0.05$ was considered as significant.

Results

In present study, demographic variables and other patients characteristics were comparable in both the groups ($p>0.05$) (Table 1).

Out of 30 patients in each Group, 4 (13.33%) patients in Group II complained of PONV. Five (16.66%) patient in Group III complained of PONV and in Group I 16 (53.33%) patients complained of PONV. The incidence of PONV in Group I, Group II and Group III was 53.33%, 13.33% and 16.66% respectively ($p<0.05$))(Table 2).

Table 1: Characteristics of patients in present study

Parameters	Group I	Group II	Group III
Age(years)	25.27±45.59	24.37±3.56	25.10±4.76
Gestational age (weeks)	39.17±1.94	36.07±2.34	36.73±2.16
Weight (Kg)	53.00±8.82	55.20±10.63	59.60±14.49
Pulse rate (preoperative)	91.87±13.59	89.57±14.13	92.30±14.14
SBP (mm Hg)*	125.13±16.78	123±17.66	126.40±14.57
DBP (mm Hg)*	81.60±10.88	78.40±10.83	81.97±10.07
RR (min)*	20.93±2.71	20.53±2.46	19.73±2.33

Data are expressed as mean±SD, all parameters between groups were statistically non-significant ($p>0.05$). *Basal value is measured. Systolic Blood Pressure; SBP, Diastolic blood Pressure; DBP, RR; Respiratory rate

Incidences of post operative adverse events were also noted in the groups.

In Group I incidence of headache, dizziness and abdominal distress was 3.33%, 6.33% and 16.66% respectively. Incidence of both hypotension and sedation was 3.33% in Group II. Incidence of hypotension, headache, dizziness, abdominal distress and facial flushing was 6.6%, 10%, 3.33%, 3.33% and 3.33% respectively in Group III. All the complications were statistically significant between groups with $p <0.05$.

Table 2: Incidence of Emetic episodes in Groups

Interval (min)	Group I		Group II		Group III	
	Present*	Absent#	Present*	Absent#	Present*	Absent#
0-30	16(53.3)	14(46.7)	4(13.3)	26(86.7)	5(16.7)	25(83.3)
30-60	14(46.7)	16(53.3)	4(13.3)	26(86.7)	6(20.0)	24(80.0)
60-90	11(36.7)	19(63.3)	3(10.0)	27(90.0)	5(16.7)	25(83.3)
90-120	6(20.0)	24(80.0)	1(3.3)	29(96.7)	0(0)	30(100.0)
120-150	1(3.3)	29(96.7)	4(13.3)	26(86.7)	1(3.3)	29(96.7)
150-180	4(13.3)	26(86.7)	4(13.3)	26(86.7)	0(0)	30(100)
180-210	0(0)	30(100)	2(6.7)	28(93.3)	0(0)	30(100)
210-240	0(0)	30(100)	2(6.7)	28(93.3)	0(0)	30(100)
240-270	0(0)	30(100)	2(6.7)	28(93.3)	0(0)	30(100)

All the data are expressed as no of patients (%), * nausea and vomiting was present, #nausea and vomiting was absent

Discussion

Spinal blockade is considered the procedure of choice for elective or emergency LSCS in many developed and developing countries.[7]

If preoperative antiemetic is not given to patients undergoing caesarean section in spinal anesthesia, risk of PONV is high.[8]

The possible reasons for PONV in parturient undergoing caesarean delivery may be due to stimulation of uterus and broad ligament. It has been reported that catecholamine level increases due to surgical pain which may also cause PONV.[5]

Propofol is reported to be used for the treatment of chemotherapy induced emesis and postoperative nausea, vomiting without any side effects at subhypnotic doses.[8] Ondansetron has also reported as an effective agent for the prevention and treatment of PONV.[7]

In present study, all the treatment groups were similar with regard to maternal characteristics and operative management.

The study included 90 patients who were scheduled to undergo LSCS under spinal anesthesia. The patients selected were in age group 18-35 years belonging to ASA 1 and ASA 2. Thus they were all healthy females not suffering from systemic disorder.

All three groups were comparable and identical in respect to age, weight, pulse rate, blood pressure and respiratory rate ($p>0.05$). Studies done by Rasooli et al and Swati et al have also reported similar results. [5,9] In our study each patient received 20ml/kg of ringer lactate solution as recommended by Rudra et al before administration of spinal anaesthesia.[8]

All three groups were given spinal anesthesia with identical technique. We used hyperbaric bupivacaine 0.5% heavy 2.2 ml to achieve the T 6 level of analgesia. It has a longer duration of action (90 – 120 min). The T6 was the upper level of sensory block and it was same in all the groups. The duration of analgesia was adequate for caesarean section and none of patient required general anesthesia.

In present study incidence of PONV was higher in Group I (53.33%) which was a placebo group followed by ondansetron group (16.66%). The lowest incidence was observed in propofol group (13.33%). A study done by Rudra et al has reported the incidence of 14% in patients who received propofol at a subhypnotic dose (1 mg kg^{-1} hr^{-1}).[8] Also, the subhypnotic dose of propofol used in present study was not only superior compared to placebo to control the incidence of emesis, but also without unwanted respiratory or cardiovascular side effects. Rasooli et al in their study reported almost similar results.[9] Swati et al has done a similar study on 60 patients and reported that in propofol group only 20.3% and 6% patients experienced nausea and vomiting compared to control group (49.8% nausea and 20.1% vomiting).[5]

The antiemetic mechanism by which propofol prevents emesis is not known. But many studies have postulated that the effect may be due to antagonistic action at the 5-HT3 receptor.[10] But, Borgeat et al suggested modulation of subcortical pathways as a possible mechanism for antiemetic action of propofol.[11]

Our study has few limitations such as small sample size, absence of blinding and pain score was not measured which may also lead to vomiting. Large randomized trials are required to confirm the findings.

Conclusion

Our findings suggest that both propofol and ondansetron are effective as compared to placebo in preventing the emetic episodes during caesarean delivery under spinal anesthesia. Moreover subhypnotic dose of propofol is more effective than ondansetron in preventing PONV during and in the early hours after caesarean section performed under spinal anaesthesia.

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