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Comparison of efficacy of subhypnotic dose of midazolam and propofol in decreasing nausea and vomiting in caesarean section under spinal anaesthesia

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Abstract

Background: Midazolam and propofol by virtue of their antiemetic effect were found individually to reduce the incidence of intraoperative nausea and vomiting. This study compares the effects of midazolam and propofol in decreasing the incidence of nausea and vomiting in pregnant women undergoing lower segment caesarean section (LSCS) under spinal anaesthesia. It also assesses maternal sedation, neonatal outcome and other side effects.
Aim: To compare the effects of subhypnotic dose of midazolam and propofol in prevention of intraoperative nausea and vomiting in lower segment caesarean section under subarachnoid block.
Methods: With ethical committee permission the 60 pregnant women were randomly allocated into 2 groups after taking informed consent. Group M received 0.03mg/kg midazolam immediately after cord is clamped, Group P received 10 mg propofol immediately after cord is clamped. Incidence of nausea and vomiting was not according to Bellville scoring system (0-novomiting, 1-Nausea, 2-Retching, 3_vomiting). The degree of sedation, hemodynamic changes were noted baseline, after induction, after drug administration, 30 mins after drug administration, 60 mins after drug administration, neonatal out come and side effects were recorded.
Results: Statistically significant decrease in intraoperative nausea and vomiting in patients undergoing LSCS under spinal anaesthesia with 10 mg propofol compared to 0.03 mg midazolam is observed. Degree of sedation, respiratory rate, mean mephentermine consumption were comparable between two groups and no difference found.
Conclusion: Propofol significantly decreases incidence of intraoperative nausea and vomiting inches are in section under spinal anaesthesia as compared to midazolam.

Keywords: Midazolam, propofol, caesarean section, nausea, spinal anaesthesia

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Introduction

The most common and distressing symptoms which follow anaesthesia and surgery are pain, nausea and vomiting. Nausea and vomiting remain as major concern in caesarean section under spinal anaesthesia [1]. The causes of nausea and vomiting are multi-factorial and can largely be categorized as patient risk factors, anaesthetic technique, and surgical procedure. The incidence of nausea and vomiting during and immediately after surgery in spinal anaesthesia is high and is an annoying problem to all concerned [2].

IONV (intra operative nausea and vomiting) occurs more frequently in parturients than non-pregnant women who undergo caesarean section under regional anaesthesia [3]. Physiological changes of pregnancy are considered as an important factor for IONV during caesarean section. These changes composed of high level of progesterone and its subsequent smooth muscle relaxation, increased gastrin secretion, decreased gastrointestinal motility and lower esophageal sphincter tone [4].

Hypotension during spinal anaesthesia, especially in pregnant women is also an important factor responsible for IONV in caesarean section under spinal anaesthesia [5]. Intraoperative nausea and vomiting is seen in as many as 66% of caesarean deliveries performed under regional anaesthesia [6]. Midazolam induce its effect on nausea and vomiting via anxiolysis following lower dopaminergic influx to chemoreceptor trigger zone and decrease in adenosine reuptake [7]. Therefore, this study is taken up to compare the efficacy of midazolam and propofol in preventing nausea and vomiting in caesarean section under spinal anaesthesia.

Aims

1. To compare the efficacy of subhypnotic dose of midazolam and propofol in preventing nausea and vomiting during caesarean section under spinal anaesthesia.
2. Monitoring of sedation.
3. Hemodynamic monitoring

Methodology

After approval from institutional ethics committee, this prospective randomized double blind trial was conducted from 2019 to 2020. Those parturients undergoing elective caesarean section under spinal anesthesia who gave written informed consent, aged 18-35 years with ASA physical status of I and II were included in the study. Patient who refused the procedure, Pregnant women with comorbidities, Pregnant women who had received antiemetic prior to surgery, morbidly obese (BMI>40) and short stature pregnant women (<145cms) and those patients who had contraindication to spinal anesthesia like kyphoscoliosis or allergic to drugs used in the study were excluded from the study.

Preoperative evaluation of the patient was done on the day before surgery. After explaining the procedure, written and informed consent was obtained. Patient was advised overnight fasting and were premedicated with tablet Alprazolam 0.5 mg the night before and on the day of surgery. In the operating room, intravenous line was secured with 18G cannula and patients were preloaded with ringer's lactate solution at 15ml/kg. Monitors including pulse oximeter, noninvasive arterial blood pressure, electro cardio graph were connected to the patient and baseline vitals recorded.

After obtaining informed written consent, pregnant women were selected and divided with the help of computer generated random number tables into two groups

Group 'M': Receives 0.03mg/kg midazolam immediately after cord is clamped.

Group 'P': Receives 10mg prop of immediately after cord clamped.

Each parturient was hydrated with 500 mL of Ringer lactate solution IV and placed in the left lateral position. No other premedications were given. Electrocardiogram, pulse oximetry and non-invasive blood pressure were monitored.

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Spinal anaesthesia was performed by using a 27 gauge needle at the L2-3 toL3-4 intervertebral space. Immediately after the intrathecal injection the pregnant woman was

placed supine with left uterine displacement.Oxygen5 L/min was given via face mask during the surgery. The degree of a term and sensory were noted.

Intraoperative blood pressure (measured by a noninvasive blood pressure monitor), saturation, heart rate, respiratoryrate, oxygen saturation, degree of sedation were recorded after induction, after drug administration, 30 mins after drug administration, 60 mins after drug administration. Whenever systolic blood pressure (SBP) was less than 100 mm Hg or 20% below the pre-induction level (defined as hypotension), me phentermine 5mg was administered IV. If HR<50/min, Inj. Atropine 0.6mg IV was given. All patients were supple mented with oxygen.

The occurrence of the side effects like respiratory depression (RD) were assessed at the same times. Vomiting was treated with IV 4mg Ondansetron. Study variables were assessed by an observer blinded to treatment group assignment at baseline, after induction, after drug administration, 30 mins after drug administration, 60 mind after drug administration. At each interval, an observer questioned the patient about the presence or absence of nausea, observed for the presence of retching or vomiting. Sedation was rated by the observer using a Ramsay sedation scale [RSS] (1=anxious, 2=cooperative, 3=responding to commands, 4= briskers pounds to stimulus, 5=slug gishres ponsetostimulus, 6= noresponse to stimulus).

Following delivery fetal heart rate (FHR) was monitored and FHR of 120-160bpm was considered normal and baseline variability of ≥6bpm was considered normal. The Apgar scores of the infant was assessed. All the above parameters were recorded using a preset proforma and need fortescue antiemetics was also noted.

Parameters measured

- Presence of nausea, retching, vomiting.
- Ramsay Sedation Scale (RSS).
- Vitals-HR, BP (including systolic [SBP], diastolic [DBP] and respiratory rate (RR) and SpO_2 at induction, at drug administration, 30 mins after drugad ministration, 60 mins after drug administration.
- Apgar score of the neonate.

Primary outcome

- Satisfactory antiemetic outcome.

Secondary outcome

- Occurrenceofadversesideeffects/assessthesafetyofthestudymedication.
- Effect on the neonates.

Statistical analysis

With reference to previous study considering the incidence of nausea and vomiting as 68% and 35% in each group and taking alpha error of 5% and power of 80% sample size was calculated to be total of 60 with 30each group. Summary statistics was done by means of proportions for categorical/binary variables and mean, median, Standard deviation, Inter Quartile Range (IQR) for continuous variables. Inferential statistics was done by using independent t test and chi squaretest/Fischer exact test. All the statistical methods were done using SPSS 21.0 version for windows. P<0.05 was considered statistically significant. Chi square test/fisher exact test were used comparing two or more independent proportions.

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Results

All the patients included in the study received the assigned intervention and were followed up till the end of study. There were no exclusions or drop outs. Patient demographic characteristics were comparable in both the groups. Number of patients belonging to ASA class I and II were uniformly distributed between the groups. There was no significant difference in mean duration of surgery between the groups. (Table 1).

There was no significant change in heart rate at all intervals in both the groups (table 2), The mean value of SBP, DBP, RR and SPO2 were similar in both the groups in all intervals and was not statistically significant (table 3,4) (fig 1). Both groups did not show any maternal respiratory depression (table 5). There was decreased incidence of nausea and vomiting in group P when compared to Group M (IV).16.67% (5/30) in group M complained of nausea, 20.00% (6/30) had retching, 26.67% developed vomiting. In group P 16.67% (5/30) had nausea, 6.67% (2) had retching, 10.00% (11/60) had vomiting (table 6). When combined symptoms, statistically significant decrease in nausea, retching and vomiting was found in group p compared to group M.

The APGAR score had a mean value of 8.47±0.507 in group M and 8.40±0.498 in group P during the 1st minute, which was found to be statistically insignificant with a p-value of 0.61. The mean value of APGAR score was 9.47 in group M and 9.40 in group P during the 5th minute with p-value of 0.651 which was not statistically significant.

Table 1: Comparison of demographic parameters and duration of surgery

Parameter	Group M	Group P	P Value
AGE	26.07±3.6	25.13±3.14	0.29
BMI (KGM2)	23.97±1.60	24.19±1.63	0.59
Duration of Surgery	53.00±9.43	50.77±9.61	0.36

Table 2: Comparison of mean HR between the groups

HR	Group		P Value
	Group M	Group P	
Baseline	91.3 ± 11.911	88.7 ± 11.555	0.394
After induction	79.47 ± 10.969	82.03 ± 13.029	0.413
At Drug Administration	100.77 ± 14.801	95.13 ± 14.505	0.142
30 Mins After	94.57 ± 10.368	102.43 ± 15.229	0.023
60 Mins After	84.97 ± 9.309	85.23 ± 9.361	0.912

Table 3: Comparison of mean SBP between the groups

SBP	Group		P Value
	Group M	Group P	
Baseline	122.6 ± 6.495	123.93 ± 6.953	0.446
After induction	103.37 ± 12.453	105.93 ± 6.923	0.328
At Drug Administration	126.67 ± 17.167	124.93 ± 15.38	0.682
30 Mins After	127.6 ± 20.959	124.57 ± 18.44	0.554
60 Mins After	113.2 ± 7.439	115.8 ± 10.691	0.279

Table 4: Comparison of mean DBP between the groups

DBP	Group		P Value
	Group M	Group P	
Baseline	75.1 ± 7.174	76.43 ± 6.902	0.466
After induction	58.23 ± 10.331	60.60 ± 5.50	0.273
At Drug Administration	77 ± 14.012	77.43 ± 9.954	0.891
30Mins After	76.73 ± 10.796	73.17 ± 12.267	0.237
60Mins After	69.33 ± 5.88	72.87 ± 8.637	0.069

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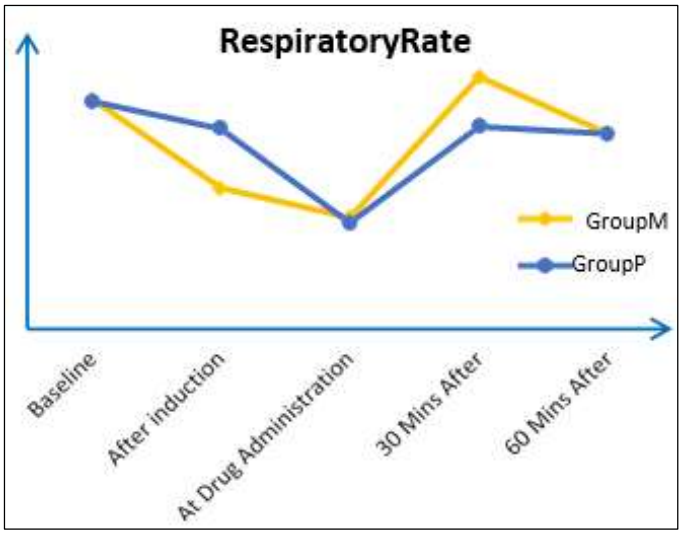

Fig 1: Line diagram showing respiratory trends between the groups

Table 5: Comparison of RSS between the groups

Sedation	Group		P Value
	Group M	Group P	
After induction	2.03 ± 0.32	1.97 ± 0.414	0.488
At Drug Administration	2 ± 0.371	2.03 ± 0.49	0.768
30 Mins After	2.23 ± 0.504	2 ± 0.455	0.065
60 Mins After	1.93 ± 0.365	2.03 ± 0.32	0.264

Table 6: Comparison of Belville nausea and vomiting scoring between the groups

Belvilla scoring	Group		Total
	Group M	Group P	
0	**11**	**20**	**31**
1	5	5	10
2	6	2	8
3	8	3	11
Total	30	30	60

Discussion

Nausea and vomiting during regional anaesthesia for caesarean section are very common and unpleasant events. They cause significant distress to the patient and also interfere with the surgical procedure. The incidence of nausea may be as high as 80% during caesarean section [3]. The cause of nausea and vomiting during caesarean section are multi-factorial. The causes of intraoperative nausea and vomiting are hypotension and increased vagal activity following subarachnoid block; surgical stimuli like exteriorization of the uterus, intra-abdominal manipulation and peritoneal traction; medications like uterotonic agents and antibiotics.

Various antiemetics are being used perioperatively do decrease the incidence of nausea and vomiting in caesarean section [8]. This study was undertaken involving 60 patients to compare the incidence of nausea and vomiting between 0.03mg/kg midazolam versus 10mg propofol and also to assess hemodynamic parameters, neonatal outcome and other side effects. Demographic data comparing age, anthropometric parameters showed statistically significant difference among the groups.

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Hemodynamic variables

In our study there was no significant heart rate alteration between the two groups. The mean value of heart rate was similar in both the group and was not statistically significant. The mean value of SBP was similar in both the groups in other intervals and was not statistically significant. The mean value of DBP was comparable between groups and was not statistically significant. There was no significant difference in mean SpO_2 and respiratory rates between the groups at all the intervals. There was no occurrence of maternal desaturation or respiratory depression at any time interval in any of the groups.

Alain Borgeat, Oliver H *et al*. [9] studied antiemetic properties of Propofol. 52 ASA physical status 1 or 2 patients received 10mg propofol and equal patients received 1 ml intralipid placebo intravenously postoperatively. Patients treated propofol experienced a larger education in nausea and vomiting (35%) the patients with placebo (81%). In our study we compared 10 mg propofol with 0.03mg/kg midazolam IV immediately after cord is clamped in LSCS cases and found propofol significantly decreases incidence of nausea and vomiting in LSCS compared to midazolam.

BipulDeka, Bharat talukdar *et al*. [10] studied effects of Midazolam during spinal anaesthesia for caesarian section. In this study one group (N=250) of women received midazolam 0.02mg/kg bolus immediately after delivery of baby and 0.01 mg/kg half hourly. Equal number of women who received placebo was taken as control group. Study concluded subhypnotic doses of midazolam are safe and significantly reduce the incidence and severity of hypotension, bradycardia, nausea and vomiting and chest pain during caesarean section under spinal anaesthesia.

Mitrajabalameli, Azim Honarmand *et al*. [11] compared the antiemetic effects of midazolam, ondansetron and combination of midazolam with ondansetron in cesarean section under spinal anaesthesia. Group M (n=44) received midazolam 30mcg/kg (0.03mg/kg) intravenously, group O (n=44) received on densitron 8mg, group MO (n=44) received iv midazolam 30mcg/kg combined with intravenous ondansetron 8mg. study showed that intravenous midazolam 30mcg/kg in combination with ondansetron was superior to administering single drug. In our study we compared0.03mg/kg of midazolam with 10mg propofol to decrease the intraoperative Nausea and vomiting in cesarean section under spinal anaesthesia and found propofol is superior to midazolam in decreasing nausea and vomiting.

Sousan Rasooli, Farnaz Moslemi [12] *et al*. studied effects of subhypnotic doses ofmidazolamandpropofolfornauseaandvomitingduringspinalanesthesiaforcesarean section. Three groups of 30 parturients were selected, one group received iv midazolam 1 mg bolus and 0.1mg/kg/hr, another group received iv propofol 20 mg bolus and 0.1 mg/kg/hr, one more group received 1 ml NS as placebo immediately after cord is clamped.

Nausea and vomiting

In our study there was decreased incidence of nausea and vomiting in group P when compared to Group M (IV).16.67% (5/30) in group M complained of nausea, 20.00% (6/30) had retching, 26.67% developed vomiting. In group P 16.67% (5/30) had nausea, 6.67% (2) had retching, 10.00% (11/60) had vomiting.

When combined symptoms, statistically significant decrease in nausea, retching and vomiting was found in group p compared to group M.

Conclusion

Our study concluded subhypnotic Dose of propofol significantly decreases intraoperative nausea and vomiting in caesarean section under spinal Anesthesia compared to subhypnotic dose of midazolam.

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