

Effectiveness of Intravenous Metoclopramide Prophylaxis on the Reduction of Intraoperative and Early Postoperative Nausea and Vomiting after Emergency Caesarean Section under Spinal Anaesthesia

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Abstract

Background: Nausea and vomiting is a common problem after spinal anaesthesia after cesarean section. Metoclopramide is reported to be effective in reducing the incidence and severity of nausea and vomiting (NV). However, its effectiveness as monotherapy remains unexplored.

Aims: We aimed to assess the effectiveness of metoclopramide prophylaxis on the prevention of nausea and vomiting after emergency cesarean section under spinal anaesthesia.

Methods and material: A prospective non-controlled study was conducted at a referral hospital. Patients classified as metoclopramide group who received 10 mg IV prophylaxis versus no prophylaxis group. Pre-tested checklist and patient interview were employed to collect the data during operation, at 2 h, 4 h and 6 h after cesarean section. Student's t-test or Mann-Whitney U tests were used to compare the incidence and severity of nausea and vomiting between the groups. Chi-square and Fisher exact tests were used to compare the proportion of categorical variables between the groups.

Results: The overall incidence of intraoperative and early postoperative nausea and vomiting were 25.8% and 48.5% in the treatment (n=66) group and non-treatment (n=66) group respectively. Prophylactic metoclopramide significantly reduced the overall incidence of intraoperative and early postoperative nausea and vomiting (25.8% vs. 48.5%, p=0.012) compared with non-treatment group. The median score for nausea on numeric rating scale was also reduced in the prophylaxis at the end of CS, 2 h and at 4 h after CS.

Conclusion: The incidences of nausea and vomiting were high. The administration of prophylactic metoclopramide remarkably reduced the incidence and severity of intraoperative and early postoperative nausea and vomiting compared to the non-treatment group. We recommend metoclopramide prophylaxis for parturients undergoing emergency cesarean section under spinal anaesthesia. In addition, preoperative risk stratification strategies and perioperative nausea and vomiting management protocols need to be established in the hospital.

Keywords: Emergency caesarean section; Spinal anaesthesia; Nausea; Vomiting; Metoclopramide prophylaxis; Effectiveness

Introduction

Nausea and vomiting (NV) is a common anaesthetic complication during and after cesarean section under spinal anaesthesia which may cause distress to the patient, interfere with surgical procedure, aspiration of vomitus, postoperative bleeding and wound dehiscence [1]. Without prophylaxis antiemetic, the incidence is reported to be as high as 80% [2,3]. Moreover, the hormonal and anatomic changes attributed by impaired motility of the esophagus, stomach and small bowel made pregnant mothers more liable to nausea and vomiting [4,5].

Nausea and vomiting (PONV) have multifactorial causes including anaesthetic, surgical and patient factors such as hypotension, surgical stimuli, uterotonic agents, history of PONV/motion sickness, female gender, none smoking status, younger age [6,7]. PONV can be tackled by employing preventive anaesthetic and surgical techniques such as strict control offending anaesthetic and surgical factors by adequate preloading/co-loading with fluids, administration prophylactic vasopressors after spinal anaesthesia and 15 degree left uterine displacement [8-11]. Furthermore, use of optimal neuraxial opioids and limited use of systemic opioids and slow administration of uterotonic agents are believed to be preventive measures to reduce nausea and vomiting [3,8,9,11-16].

Studies revealed that prophylactic metoclopramide (10 mg) is effective to prevent intraoperative and postoperative nausea and

vomiting [13,17-19]. On the other hand, some studies found contradictory results [20,21].

Spinal anaesthesia induced hypotension which could also be aggravated by uterotonic drugs is reported to be the commonest cause for intraoperative and postoperative nausea and vomiting in parturients undergoing cesarean [2,22]. The severity of hypotension caused by uterotonic drugs depends on the dose, route and rate of administration [23] yet could also be affected by type and dose of local anaesthetic drugs [24]. Metoclopramide acts by increasing the tone of the lower oesophageal sphincter [25,26].

Nausea and/or vomiting are expected to be worse after emergency cesarean section due to the presence of potential multiple anaesthetic and surgical risks of nausea and vomiting and shortage of time for preoperative optimization. Evidences revealed that, in addition to antiemetic prophylaxis; measures to reduce the risks of nausea and vomiting due to hypotension such as rapid rehydration, use of effective prophylactic vasopressors, left lateral uterine displacement and intrathecal administration of short acting opioids and adjuvant with local anaesthetics are employed. However; there is shortage of vasopressors, short acting opioids and adjuvant local anaesthetics in low resource settings like our hospital. Metoclopramide is a generic inexpensive drug with multiple sites of action which is reported to be effective and safe for elective cesarean section by some studies [5,17,26]. Recently, metoclopramide prophylaxis is introduced for the prevention of nausea and vomiting in our hospital. However, its efficacy on the reduction of intraoperative and early postoperative nausea and vomiting as monotherapy remains unexplored. We aimed to assess the effectiveness of intravenous prophylactic metoclopramide for the prevention of nausea and vomiting among parturients undergoing emergency cesarean section under spinal anaesthesia.

Subjects and Methods

Hospital based prospective observational study was conducted in our university hospital from March 8 to May 8, 2017. On average about 100-200 emergency cesarean sections are performed per month (retrospective audit from operation logbook). Spinal anaesthesia is a preferable anaesthetic technique in this hospital unless contraindicated. Perioperative patient management (anaesthetic, PONV treatment choices etc) was up to the decision of the responsible anaesthetist. Group allocation was performed based on their exposure status for metoclopramide (metoclopramide prophylaxis groups and no metoclopramide prophylaxis group) treatment after cesarean section. The researchers did not do any intervention.

Study population: All parturients who delivered by emergency cesarean section under spinal anaesthesia during the study period were included in the study.

American Society of Anaesthesiologist Physical Status (ASA) Classes I- II, term pregnancy mothers who had emergency cesarean section under spinal anaesthesia was included in the study.

Exclusion criteria: Mothers who had history of acute or chronic medical illness associated with nausea and vomiting such as acid peptic disease, pregnancy induced hypertension within 24 h or mothers who received antiemetic medication within 24 h before surgery indicated or mothers who were given propofol, ketamine, atropine in the intra operative period were excluded. And mothers who had an additional dose metoclopramide concurrent use of an alternative multimodal anti-emetic regimen in the study period were

excluded. In addition, mothers who had complicated surgery diagnosis of APH and PPH during the study period were excluded.

Operational definitions

Intraoperative and early postoperative nausea and vomiting following cesarean section under spinal anaesthesia-a patient must have at least one episode of nausea, vomiting or both (retching considered as vomiting) in the intraoperative and early (0-6 h) postoperative period. Severity of nausea was described with 10-mc linear numeric scale (0=without nausea or vomiting, 10=very severe nausea) [26]. The decrease in systolic blood pressure >20% of baseline values and/or less than 100 mm/Hg immediately after spinal injection will be considered as hypotension.

Number of vomiting episode: defined as total number of vomiting episodes experienced in during intraoperative and early postoperative period.

Duration of uterus exteriorized: the time when the uterus lifted out of the abdominal cavity during uterine repair.

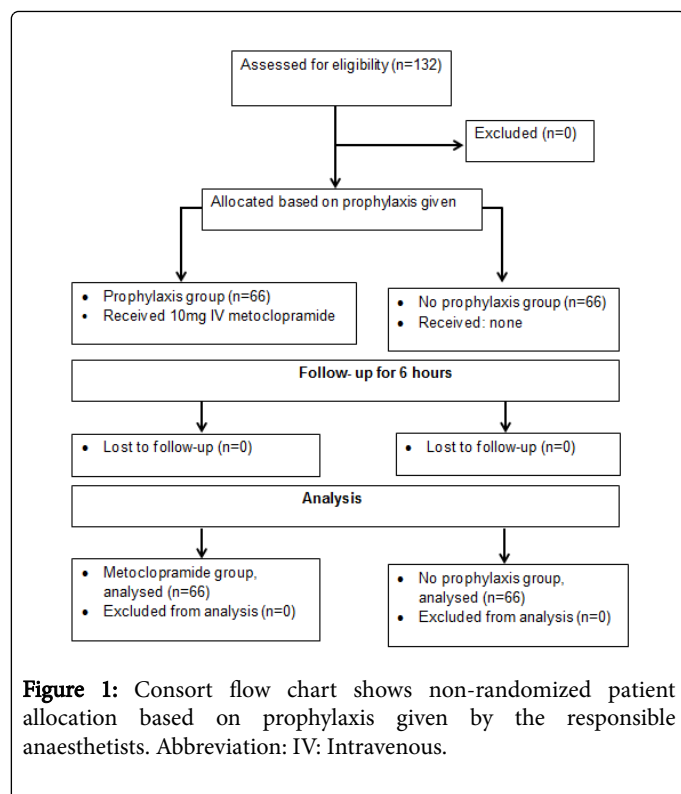
Sever post anaesthesia shivering: refers to patient experiencing more than 3 score of shivering or that manifested with body movement.

There was no documented study that shows the incidence of nausea and vomiting (NV) after spinal anaesthesia for cesarean section in the study area. However; from recent studies in abroad over all 24 h incidence of nausea and or vomiting after spinal anaesthesia for cesarean section ranges from 40% to 80% when no prophylactic antiemetic was given [27]. On the other hand based on Apfel simplified risk score and rule of thumb including patients with at least two risk factors assumed to result an average 50% predicted incidence of postoperative nausea and or vomiting [28]. Using two sample proportion sample size calculation formula, sample of 66 candidate parturients in each group were calculated to detect 25% difference between the groups with 5% alpha error at a power of 80%.

Subject recruitment and data collection

Ethical approval was obtained from College of Medicine and Health Sciences, Academic, Research and Community Services Vice Dean. Written informed consent was obtained from each study participant before the commencement of the study. The data were collected prospectively using pretested structured standardized checklist and interview-based questionnaire. All consecutive parturients who underwent cesarean section during the study period were included. Participants were Parturients were identified and coded by principal investigator based on no prophylaxis given or administration of 10 mg metoclopramide by the responsible anaesthetist within 30 min before spinal anaesthesia for cesarean section (Figure 1).

The preoperative and intraoperative anaesthetic and operative managements were continuously observed by one data collector. Oxygen saturation, pulse rate and systolic blood pressure of each woman was monitored and recorded every 5 min during the surgery and every one hour post-operatively during the study period. Another trained nurse data collector interviews each parturients for the occurrence of nausea and vomiting every 2 h interval up to 6 h postoperatively. Severity of nausea was evaluated on a linear numeric rating scale which ranged from 0 to 10 (no nausea: 0; mild nausea: 1-3; moderate nausea: 4-7; severe nausea: 8-10). The type of analgesics given to postoperative pain management was identified by the data collector.



Data analysis

Data was checked for completeness, accuracy and clarity on the day of collection before entered in to database by the Principal Investigator. Data clean up and cross-checking was done before analysis. Continuous supervision was also done by principal investigator. Data analysis done using SPSS version 20. The data were tested for normality using the Shapiro-Wilk normality test and homogeneity of variance as assessed by Levene's Test for equality of variances. Baseline demographic characteristics, anaesthetic and surgical management and measures of effectiveness were compared between the study groups using independent t-test for normally distributed data and Mann Whitney U test for non-normally distributed data and chi square or fisher's exact test for categorical variables. For none normally distributed data (numeric rating scale for nausea), between group comparisons at each interval were made by using Mann. Whitney U test and presented as median (IQR). Normally distributed data presented as mean ± SD. Significance level <0.05 considered statistically significant. Demographic characteristics, operative management and risk levels were checked for comparability in distribution across groups.

Results

Socio-demographic characteristics of study participants

In this prospective observational study, one hundred and thirty two emergency cesarean section mothers included with a response rate of 100%. All cesarean sections were performed for varieties of indications (cephalopelvic disproportion, fetal distress and failed induction, prolonged rupture of membrane, malpresentation, previous scare and me conium stain). Of these, 66 were mothers who got 10 mg

metoclopramide prophylaxis before cesarean section (Group A) and the rest 66 who were not given the prophylaxis (Group B). None of mothers had history of smoking. The socio-demographic characteristics (age, weight, height, ASA status, fasting hours and history of PONV/motion sickness and duration of surgery and uterus exteriorized) were comparable in both groups (Table 1).

Characteristics	Group A (n=66)	Group B (n=66)	p-value
Age (yr)	26.71 ± 4.61	27.33 ± 5.81	0.498
Weight (kg)	60.03 ± 7.03	58.03 ± 6.63	0.095
Height (cm)	161.77 ± 4.69	161.07 ± 4.77	0.399
ASA (I/II)	62/4	65/1	0.365
Gravidity -Primi-gravida	29 (43.9%)	34 (51.5%)	0.384
-Multi-gravida	37 (56.1%)	32 (48.5%)	
History of PONV/motion sickness	17 (25.8%)	21 (31.8%)	0.442
Duration of surgery (min)	51.97 ± 10.51	50.59 ± 11.15	0.466
Fasting hours before cesarean section			0.315
shorter than 6 h	19 (28.8%)	14 (21.2%)	
longer than 6 h	47 (71.2%)	52 (78.8)	

Table 1: Socio-demographic characteristics of mothers who underwent emergency cesarean section, 2014. Values are given as mean ± SD, (%), student t-test and chi-square by 2 × 2 tables, α<0.05 significant.

Perioperative anaesthetic and operative characteristics of study participants

The perioperative anaesthetic and operative characteristics of the parturients were observed in both groups (Table 2).

None of anaesthetists used 15 degree left lateral tilt as the operating table was not flexible and no patient was observed to have pulse rate less than 50 during surgery in both groups. More than half of the study participants (54.5%) experienced more than three grade of shivering during cesarean section and supplemental oxygen were given for 42% of the total study participants. The only antibiotic prophylactic given during the study period was ceftriaxone. All baseline perioperative anaesthetic and operative characteristics were comparable between the two groups.

The incidence of intraoperative and early postoperative (0-6 h) nausea and vomiting

In this observational study, the incidence of intraoperative nausea in the metoclopramide group was significantly lowered when compared to none metoclopramide group (10.6% vs. 39.4%, p=0.037). Of the 26 parturients who experienced nausea during the intraoperative period in none treatment group; 18 were experienced vomiting. On the other hand, from 14 parturients who experienced nausea in treatment group: seven were experienced vomiting. There were statically significant differences between groups: experiencing nausea and vomiting during the intraoperative period.

Characteristics	Group A (n=66)	Group B (n=66)	P-value
Type of local anesthetics given for block			0.302
0.5% isobaric bupivacaine	29 (43.9%)	30 (45.53%)	
0.5% heavy bupivacaine	26 (39.4%)	19 (28.8%)	
2% Lidocaine with adrenaline	11 (16.7%)	17 (25.8%)	
Level of sensory block before incision	T6 (T7-T6)	T6 (T8-T6)	
pain complain during surgery	18 (27.3%)	25 (37.9%)	0.194
Uterotonic drugs given after delivery			0.98
oxytocin bolus (5 IU) + infusion (20 IU)	20	22	
oxytocin infusion (20 IU)	23	23	
Ergometrine(0.2 mg IM)	12	11	
Oxytocin infusion (20 IU) + Ergometrine (0.2 mgIM)	11	10	
Amount of crystalloid pre-loaded(ml)	1000 (512.5)	1000 (670)	0.261
Amount of fluid co-loaded (ml)	1200 (300)	1200 (400)	0.085
Total fluid during surgery (ml)	1874.24 ± 501.08	1867.27 ± 725.76	0.932
Estimated blood loss during surgery	1050 (420)	920 (400)	0.078
Fall in SBP >20% from the baseline	36 (54.5%)	26 (39.4%)	0.081
supplemental oxygen during operation	26 (39.4%)	29 (43.9%)	0.724
Analgesic drugs during surgery			0.151
Tramadol 50 mg	18 (27.3%)	26 (39.4%)	
Diclofenac 75 mg (im)	0	1	
postoperative analgesic drugs			0.134
Tramadol 50 mg (im)	46 (69.7%)	35 (53%)	
Diclofenac 75 mg (im)	17 (25.8%)	25 (37.9%)	
Tramadol and diclofenac	3 (4.5%)	6 (9.1%)	

Table 2: Perioperative anaesthetic and operative characteristics of each group of mothers who undergo emergency cesarean section, 2014. Values are given as mean ± SD, median (IQR), n (%), student t-test/MUT and chi-square or fisher exact.

In the early postoperative period; 19 patients were experienced one or more episodes of nausea in none treatment group. Of these, 13 were experienced nausea in the intraoperative period. Likewise, six of parturients who experienced nausea during early postoperative period in group treatment group; three of them were experienced intraoperative nausea in the intraoperative period. There were statically significant differences between groups experiencing nausea in early postoperative period. However; the difference in the incidence of early postoperative vomiting was statically insignificant (Table 3).

However, the overall number of vomiting episodes were also significantly lowered in treatment group compared to none treatment group during intraoperative and early postoperative period as shown in Table 3. No patient was experienced vomiting without nausea.

In this study, the overall incidence of intraoperative and early postoperative nausea and vomiting was observed lower in parturients

received metoclopramide(group A) as compared to those who were not given prophylaxes metoclopramide (25.8% vs. 48.5%, p=0.012).

In this study, the median nausea NRS score experienced by patients during and after CS in each time interval were analyzed. The median nausea for group A. (metoclopramide group) was significantly lowers than group B at the end of CS, 2 h and 4 h after surgery. However, there was no significant differences severity of nausea at 6 h after CS (Table 4).

	parameters	Group A (n=66)	Group B (n=66)	p-value
Intraoperative	nausea	14 (21.2%)	26 (39.4%)	0.037
	vomiting	7 (10.6%)	18 (27.3%)	0.026

Early postoperative (0-6 h)	nausea	6 (9.1%)	19 (28.8%)	0.008
	vomiting	1 (1.5%)	7 (10.6%)	0.062*
Overall (intraop-6 h) nausea and or vomiting		17 (25.8%)	32 (48.5%)	0.012
Number of vomiting episodes (intraop-6 h)				0.004
none		58 (87.9%)	41 (62.1%)	
one		6 (9.1%)	14 (21.2%)	
two		2 (3%)	7 (10.6%)	
three or more episodes		0	4 (6.1%)	

Table 3: The incidence of intraoperative and postoperative (0-6 h) nausea and or vomiting in group of patients who underwent emergency cesarean section, 2014. Values refer numbers (%), chi-square with continuity correction/fisher's exact test. significant, * = not significant.

Time	Prophylaxis group A (n=66)	Non-prophylaxis group B (n=66)	P-value
At the end of surgery	0 (0-7)	0 (0-9)	0.006
At 2 h	0 (0-6)	0 (0-9)	0.002
At 4 h	0 (0-6)	0 (0-8)	0.031
At 6 h	0 (0)	0 (0-3)	NS

Table 4: The comparison of severity of nausea using numerical rating scale between groups. Values are presented as median (interquartile range).

Discussion

Spinal anesthesia is the preferred method for cesarean section in most setups. However, its adverse effects such as hypotension, headache, nausea and vomiting remain the main challenge. The causes of nausea and vomiting during cesarean section under spinal anaesthesia include patient, anaesthetic and surgical factors [2]. Spinal anaesthesia induced hypotension, which is the commonest cause of PONV, can be tackled by rapid fluid infusion, left uterine displacement, prophylactic vasopressors such as ephedrine and phenylephrine, and uterotonic drugs such as slow administration of oxytocin [9,14,29,30].

In this observational study, the overall incidence of intraoperative and early postoperative nausea and vomiting were 25.8% and 48.5% in the treatment group and non-treatment group respectively. This could affect negatively anaesthetic experience of the mother and possibly increase perioperative patient morbidity and mortality.

Moreover, the incidence of intraoperative nausea was significantly lowered in metoclopramide group compared with non-prophylaxis groups (21.2% vs. 39.4%, p=0.008). And the incidence of vomiting was significantly lowered in the treatment groups compared with non-prophylaxis group (10.6% vs. 27.3%, p=0.026). These findings were comparable with a study conducted in Japan [21]. On the other hand, our finding was low compared with a study conducted in USA (14% vs. 81%, p<0.0001) [5]. This could attribute to adequate rehydration of all patients (preloaded 1500 ml warm lactate ringer solution), intravenous

administration of ephedrine to prevent and or treat hypotension, supplemental oxygen was given *via* face mask before induction of spinal anaesthesia, and addition of fentanyl with bupivacaine which might have high, dense conduction block which could limit severe visceral pain and reduce the need for intraoperative intravenous opioids which may predispose nausea and vomiting.

However, in our study, the median crystalloid fluid used to preload before spinal was 1200 ml, only 41% of mothers were given supplemental oxygen *via* face mask, none of parturients were given prophylactic vasopressors. In addition, the reasons for higher incidence in control group in the previous study might be due to parturients were interviewed many times during surgery whereas we only interviewed once at the end of surgery which might result in under reporting of the incidence of PONV in the current study.

In this study, the administration of 10 mg metoclopramide before spinal anaesthesia significantly lowered the total incidence of intraoperative and early postoperative nausea and or vomiting compared with none prophylaxis group (25.8% vs. 48.5%, p=0.012). This result was in line with a recent RCT and meta-analysis conducted in Iran (26) and USA (17) with a comparable observation period. The similarity in the incidence of nausea and vomiting in our study regardless of limited standardized preoperative and intraoperative anaesthetic and operative managements might be inability to differentiate nausea from other discomforts due to the presence of pre-existing painful labor and anxious condition.

In contrast to the current study and the above studies; a previous randomized control trail conducted in India showed that there was statically insignificant reduction in the total incidence of nausea and vomiting during surgery and up to 4 h post-delivery between metoclopramide and placebo [20]. This discrepancy could be due to small sample size and shorter follow up period to detect the effect of the drug in incidence of nausea and vomiting compared with our study and other studies.

In this study, the median severity of nausea experienced during cesarean section, at 2 h and 4 h postoperative was significantly lowered in the metoclopramide group compared with none metoclopramide group, but it was comparable at 6 h postoperative time. A randomized controlled trail conducted in Iran found that the mean nausea score at 30 min, 60 min, 90 min, 120 min, 2 h, 4 h and 6 h after surgery in elective cesarean section under spinal anesthesia was significantly reduced compared with the placebo. This discrepancy might be due to the fact that NRS scores of nausea in 4-6 h postoperative were zero in most of our patients; only two patients were experiencing nausea in no prophylactic groups in this study; which made insufficient to compare.

Previous studies have reported that metoclopramide had dual role for parturients. Its central antiemetic action on chemoreceptor trigger zone tends synergistic with its peripheral action to enhance the lower esophageal sphincter tone and shortens gastric emptying [2,5,17,31]. In this study, we observed that more than 22% reduction in the overall intraoperative early postoperative incidence of nausea and vomiting which depicts the advantage of metoclopramide for the prevention of PONV.

Limitation and Strength of the Study

This study is not a randomized controlled trial as RCT study was not allowed in our hospital. As a result of this, we could not control variations in the anaesthetic and surgical techniques and the use of

different drugs which could affect our finding. This is the first study in our hospital and country in emergency cesarean section with different indications for cesarean delivery which could help anaesthetist and other caregivers in the hospital to treat PONV using metoclopramide.

Conclusion

The incidences of nausea and vomiting were high after emergency cesarean section operated upon under spinal anesthesia. The administration of prophylactic 10 mg metoclopramide remarkably reduced the incidence and severity of intraoperative and early postoperative nausea and vomiting compared to the non-treatment group. We recommend metoclopramide prophylaxis for parturients undergoing emergency cesarean section under spinal anaesthesia. Moreover, preoperative risk stratification strategies and perioperative nausea and vomiting management protocols need to be established in our hospital. Furthermore, RCT study should be conducted in large cohort of patients both in our hospital and other similar settings in the country to strengthen our finding.

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