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A Comparison between Ketamine and Ondansetron for Prevention of Intraoperative Nausea and Vomiting in Caesarean Section under Spinal Anaesthesia

Dr. Mohammad Mostafizur Rahman[1*], Dr. ASM Abdur Rahman[2], Dr. Jannatul Ferdous[3]

[1]Associate Professor & Head, Dept. of Anesthesiology & ICU, Ashiyan Medical College Hospital, Barua Khilkhet, Dhaka, Bangladesh
[2]Senior Consultant, Department of Anaesthesiology, Sadar Hospital, Jhenaidh, Bangladesh
[3]Associate Professor, Gynae & Obstetric, Ashiyan Medical College Hospital, Barua Khilkhet, Dhaka, Bangladesh

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***Corresponding author:** Dr. Mohammad Mostafizur Rahman

Abstract **Original Research Article**

Intraoperative nausea and vomiting (IONV) causes distress to the patient and may interfere with the surgery. Intraoperative nausea and vomiting or postoperative nausea and vomiting (PONV) affecting women undergoing regional anesthesia for cesarean section is an important clinical problem since these techniques are used widely. There are burdens of literature about IONV and several in parturient and cesarean. However, it needs more attention. The main objective of the study was to evaluate the effectiveness of ondansetron and ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia. Spinal anaesthesia is considered as gold standard for caesarean section due to its advantages of rapid and predictable onset, no airway handling, safer to mother and minimal drug exposure to fetus. But spinal anaesthesia caesarean section is associated with high incidence of IONV. Role of ondansetron as antiemetic is well established. Not many studies are there for ketamine in prevention of IONV. This comparative study was conducted in the department of *Anesthesiology* collaboratively with the department of *Obstetrics* in Ashiyan Medical College Hospital, Barua Khilkhet, Dhaka, Bangladesh during the period from January 2018 to December 2018. A total of 240 pregnant patients scheduled for CS under spinal anaesthesia were included as the total study population and divided into 2 groups. In Group I, there were 120 patients who received ketamine; in Group II there were 120 patients who received ondansetron. The patients were compared for intraoperative hemodynamic parameters, IONV, side effects like sedation and shivering. In the results we found the incidence of intraoperative nausea and vomiting (IONV) was 24% and 32% in Group I (Ketamine group) and Group II (Ondansetron group) respectively. So incidence of intraoperative nausea and vomiting (IONV) were less in Group I where we applied ketamine. Ketamine and ondansetron are both good agents for reduction of IONV during CS in pregnant patients under spinal anaesthesia without significant adverse effects. But ketamine may the better option for the patients.

Keywords: Ketamine, Ondansetron, Intraoperative nausea vomiting,Caesarean section.

INTRODUCTION

The incidence of IONV during spinal anaesthesia (SA) for Caesarean section (CS) is dependent on the anaesthesia technique used, together with preventative and therapeutic measures employed by the anaesthetist [1]. Spinal anaesthesia is the most commonly used anaesthesia for caesarean section (CS) with it being safely, quickly and easy to administer [2]. Current literature indicates a high incidence of intraoperative nausea and vomiting during caesarean section under spinal anaesthesia for which many factors may contribute like hypotension, stimulation of pharyngeal reflex noticed in abdominal surgeries, physical rupture and manipulation of abdominal viscera, due to the release of humoral 5-HT substances, which trigger the 5-HT3 receptors on vagal afferent neurons [3, 4]. During abdominal surgery under regional anesthesia, nausea may happen due to several contributing factors such as sympathetic blocks followed by parasympathetic dominance with hypotension which is the most important cause of nausea after spinal anesthesia, decreased perfusion of central nervous system, anxiety, and sudden abdominal movements during surgery and prescription of drugs [5]. Ondansetron is considered as an effective drug for

prevention and treatment of nausea and vomiting that is well tolerated by the patients [4]. It is used in surgeries which may be accompanied by nausea and vomiting without many severe adverse side effects [6]. Ketamine is a NMDA receptor antagonist that has unique central sympathomimetic, vagolytic and analgesic properties [7, 8]. These properties of ketamine are assumed to reduce the incidence of spinal induced hypotension consequently nausea and vomiting. The present study was undertaken to compare the anti-emetic efficacy of ketamine and ondansetron to decrease the incidence of IONV during CS under spinal anesthesia. The study was conducted during the year of 2018. The main objective of the study was to assess the effectiveness of ondansetron and ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia.

OBJECTIVES

a) General objective:

- To compare the effectiveness of ondansetron and ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia.

b) Specific Objectives:

- To assess the relapse rate between ondansetron and ketamine in caesarean section under spinal anaesthesia.

METHODOLOGY & MATERIALS

This comparative study was conducted in the department of *Anesthesiology* collaboratively with the department of *Obstetrics and Gynaecology* in Ashiyan Medical College Hospital, Barua Khilkhet, Dhaka, Bangladesh during the period from January 2018 to December 2018. Bangladesh. A total of 240 pregnant patients scheduled for CS under spinal anaesthesia were included as the study population and divided into 2 groups. In Group I, there were 120 patients who received ketamine; in Group II there were 120 patients who received ondansetron. The patients were compared for intraoperative hemodynamic parameters, IONV, side effects like sedation and shivering. Included patients were allocated randomly (using computer generated randomization table) into 2 equal groups. The drugs used were prepared by a separate anaesthesiologist in a syringe diluted to total volume of 5ml syringe (In the ketamine group- Ketamine 0.25 mg/ kg bodyweight diluted in 5ml saline and in the ondansetron group- Ondansetron 4mg in 5 ml saline given after clamping of umbilical artery. On the other hand, exclusion criteria included history of motion sickness, post-operative nausea and vomiting, allergy to (bupivacaine, fentanyl, ondansetron or ketamine), ASA grade 3 or more, pregnancy induced hypertension, smoking, obese patients>80 kg, epileptic patients, patients given antiemetics or corticosteroids within 24 h before CS, and patients having contraindications to spinal anaesthesia. All patients were hospitalized and kept fasting for at least 6 hours before surgery. A 18-G cannula was inserted and Ringer lactate infusion started 15 min before shifting the patient to the main operating theatre. In the operating room, patients were monitored with ECG, noninvasive arterial blood pressure and pulse oximetry. All patients were reminded to report any side effect or discomfort including nausea during surgery. Anaesthesia was standardized, by giving spinal anaesthesia in the lateral position using a 25-Guage pencil point type spinal needle, 25 microgram fentanyl and 2.2 to 2.5ml (depending on height of patient) of hyperbaric bupivacaine 0.5%, once free flow of clear CSF was obtained. All the patients were immediately returned to supine position after subarachnoid injection, table given 15- 20 degree left tilt and supplemented with oxygen 4 L min_1 via facemask. Sensory block was assessed by pinprick method and above T-6 dermatomal level was the acceptable level before surgical incision. Patients in whom the level of analgesia was insufficient were excluded from the study. Mean arterial blood pressure (MAP) was measured every 3min for the first 10 min then every 5min thereafter till end of surgery. Hypotension was treated with ephedrine 3mg and bradycardia was treated with atropine 0.6 mg. Oxytocin was given immediately after baby delivery and clamping of the umbilical cord starting by an IV bolus dose of (3 units) followed by infusion of 10 units in 500ml saline at rate 125ml/hr or according to uterine contractility and as per the obstetrician opinion. The 5 ml of the prepared drug was given just after clamping of umblical cord. Intraoperative nausea was recorded as follow (no nausea, nausea only, nausea and vomiting single episode, More than one episode of intraoperative nausea and vomiting). Nausea with retching or vomiting was managed by a rescue dose of 8mg dexamethasone, while nausea only was managed by assurance. Maternal side effects (such as desaturation, hallucinations, shivering) as well as fetal well-being (assessed with the Apgar scoring) were recorded. Maternal sedation was assessed by Ramsay Sedation Scale (RSS; 1=anxious and agitated, 2= co-operative and tranquil, 3 = drowsy but responsive to command, 4 = asleep but responsive to glabellar tap, 5= asleep with a sluggish response to tactile stimulation, 6= asleep and no response). The 2 groups were then compared with reference to patient's characteristics and intraoperative clinical data. The response within each subject group was normally distributed with standard deviation 2. Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables were presented as mean ± SD, and categorical variables as absolute numbers and percentages. Data was checked for normality before statistical analysis using Shaipro Wilk test. Normally distributed continuous variables were compared using ANOVA. Student *t*-test was used to compare between three groups of normally distributed data categorical variables were analyzed using the chi-square test. For all statistical tests, a p-

value less than 0.05 were taken to indicate a statistically significant difference.

RESULT

In the Table-1 we showed the demographic data and hemodynamic parameters of the participants of both groups. We found the mean age of 29.16±2.5 and 29.35±2.3 in Group I and Group II respectively. The mean weight was 69.75±4.1 years in Group I and 69.47±3.6 years in Group II. The mean arterial pressure (MAP- mmHg) in Group I was 79.09±8.8 and 79.23±8.2 in Group II. On the other hand the HR/min (Heart Rate/min.) was 76.4±5.2 in Group I and 76.17±5.9 in Group II. For all those data the p values were > 0.5. In the Figure-1 we showed the graph of mean arterial pressure variation of both the Groups from 0 to 75 minutes where in group I the reading were some higher than that of Group II. In total 76.67% patients of Group I and 65% patients of Group II were free from nausea and vomiting. In total 13.33% from Group I and 16.67% from Group II got nausea only where p value was 0.613. Nausea and vomiting of 1 (One) episode were occurred in Group I 7.50% and in Group II 10.83%. More than one episode was occurred 3.33% and 5.83% in Group I and Group II respectively. Rescue antiemetic dexamethasone was in needed 15% and 17.50% in Group I and Group II respectively. It was a significant variable because the p value was 0.396 which was lower than 0.5. The total intraoperative nausea & vomiting was 24.17% in Group I and 32.50% in Group II. In our study we found 76.67% patients from Group II and 65% patients from Group II who did not suffered from any kind of nausea or vomiting which was the major finding. Here the ratio of Group I is higher from Group II by 11.67%. We displayed some of our findings in figures for making those more clear. We showed 13.33% patients from Group I and 16.67% patients from Group II who had been suffered from nausea only. Besides these 7.50% patients from Group I and 10.83% from Group II suffered one episode of nausea and vomiting. On the other hand suffering from more than one episode was found 3.33% in Group I and 5.83% in Group II respectively. In Figure IV we disclosed the total frequencies of sufferings from nausea and vomiting of the patients from both the groups. We found 10.83% patients from Group I and 16.67% patients from Group II suffered one or more episodes of nausea and / or vomiting.

Table 1: Demographic data and hemodynamic parameters (n=240)

Component	Group I	Group II	P value
	n=120	n=120	
Age (years)	29.16±2.5	29.35±2.3	0.557
Weight (kg)	69.75±4.1	69.47±3.6	0.753
MAP (mmHg)	79.09±8.8	79.23±8.2	0.769
HR/min	76.4±5.2	76.17±5.9	0.656

(Here MAP=Mean arterial pressure, HR=Heart rate, SD=Standard deviation)

Table-2: Frequencies of nausea and/or vomiting in both Groups (n=240)

Symptoms	Group I		Group II		p value
	n=120		n=120		
	n	%	n	%	
No nausea or vomiting	92	76.67	78	65	0.523
Nausea only	16	13.33	20	16.67	0.613
Nausea and Vomiting 1 episode	9	7.50	13	10.83	0.574
Nausea-Vomiting more than 1 episode	4	3.33	7	5.83	0.672
Rescue antiemetic dexamethasone	18	15.00	21	17.5	0.396
Total Intraoperative nausea & vomiting	29	24.17	39	32.5	0.473

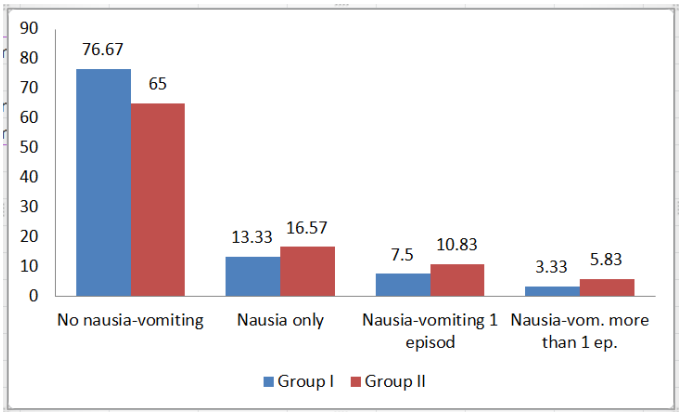

Fig-1: Frequencies of nausea and/or vomiting in both Groups (n=240)

DISCUSSION

The main objective of the study was to compare the effectiveness of ondansetron and ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia. Nausea and vomiting during spinal anaesthesia has been associated with multiple factors like sympathetic blocks followed by parasympathetic dominance, hypotension which is the most important cause of nausea after spinal anesthesia, decreased perfusion of central nervous system, psychological changes (anxiety), and sudden abdominal movements during surgery and concomitant opioid administration [9, 10]. There are many drugs used for treatment of PONV in parturients undergoing CS under spinal anaesthesia like metoclopramide, domperidone, phenothiazines, butyrophenones, anticholinergics, antihistamines and ondansetron [11]. These drugs have been used either alone or in combination and have proved effective for prevention of nausea and vomiting. Ondansetron is a selective antagonist of the 5- hydroxytryptamine (5-HT3) receptors and is a very effective agent in the prevention and treatment of nausea and vomiting. It is effective in the prevention and treatment of chemotherapy induced [12], intraoperative [13] and postoperative nausea and vomiting [14, 15]. Hypotension is probably the most important cause of IONV that occurs during CS under spinal anesthesia. Hypotension can induce the emetic symptoms by leading to cerebral hypoperfusion [16]. Prevention of hypotension is therefore important for the prevention of IONV [17]. We took the necessary measures like fluid administration at faster rate after making patient supine and using ephidrine to manage hypotension in all of our patients. We used ondansetron 4mg as at this dose it has been found to effective in the prevention of IONV during CS under spinal anaesthesia [18, 19]. Of the different agents used, droperidol 2.5 mg and 5mg has been used in controlling nausea and vomiting in CS [20, 21], dexamethasone 8mg and metachopromide 10mg also have been quiet effective in controlling nausea and vomiting during CS [22, 23], and have been compared for their effectiveness [24]. Glycopyrrolate, due to its vagolytic effect was studied in prevention of intraoperative nausea and vomiting during CS and compared with ondansetron. It was seen that effect of glycopyrrolate on nausea and vomiting during cesarean section are comparable to ondansetron, but with an increased incidence of dry mouth [25]. Ketamine is an intravenous dissociative anaesthetic agent related to phencyclidine group which works by antagonizing N-methyl D-aspartate (NMDA) receptors [7]. Because of its unique analgesic and dissociative criteria in addition to the distinct symatho-mimetic, vagolytic pharmacological properties, ketamine is used frequently in anaesthesia practice for purposes of analgesia, sedation and induction of anaesthesia many years ago. Ahmed hasnain and A M Shabana used ketamine infusion in CS and found reduction in incidence of nausea [26, 27]. The APGAR score at 1 min and 5 min in all the neonates was more than 9. Ketamine use during CS has been found safe in terms of both maternal and fetal safety, with neonatal 1 min and 5 min APGAR scores being more than 9 when used as IV inducing agent in CS [28]. Ketamine use intra the call as adjuvant to bupivacaine in CS has also shown to stabilize haemodynamics and decrease the incidence of nausea and vomiting [29]. There was statistically significant decrease in incidence of IONV in ketamine and ondansetron group as compared to control group. The antiemetic effect of ketamine and ondansetron was comparable. The ketamine group showed statistically insignificant higher HR and MAP compared to ondansetron group. This can be explained to sympathomimetic and vagolytic properties of ketamine. There were 13 patients in ketamine group with higher sedation levels (RSS =3 or more), although Ketamine neither use during spinal anaesthesia nor was it associated with increased incidence of either respiratory depression or hallucinations. The non-significant difference in the sedation level measured by RSS can be explained because of low dose of ketamine used in contrast to ketamine used for sedation in higher doses (0.5mg/kg/hr or higher) or in combination with midazolam [30]. The incidence of shivering in ketamine group was lower as compared to control group and overall shivering incidence was lower than reported due to use of intra the call fentayl. Ketamine is competitive receptor antagonist of N- methyl-D-aspartic acid (NMDA) has a role in thermoregulation in various levels. Ketamine probably controls shivering by non-shivering thermo genesis either influencing the hypothalamus or by the neither beta-adrenergic effect of nor epinephrine [31]. In our study we got some superiority of ketamine over ondansetron for prevention of intraoperative nausea and vomiting in caesarean section under anaesthesia.

Limitations of the study

This was a single centered study with comparatively small number of samples. So, the study result may not reflect the exact scenarios of the whole country.

CONCLUSION AND RECOMMENDATIONS

Ketamine and ondansetron are both good agents for reduction of intraoperative nausea and vomiting (IONV) during CS in pregnant patients under spinal anaesthesia without significant adverse effect. We find some superiority of low dose of ketamine over ondansetron for prevention of intraoperative nausea and vomiting in caesarean section under anaesthesia. We think these findings may help in further research in future. To gain more clear concept we would like to recommend for conducting more studies in several places in several times.

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