Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: www.saspublishers.com

OPEN ACCESS

Anaesthesiology

Efficacy of Ketamine on Intraoperative Nausea and Vomiting during Caesarean Section under Spinal Anaesthesia

ASM Abdur Rahman[1*], Md Monirul Islam[2], Md Nurul Amin[3], Naznin-Ara Khanom[4]

[1]Senior Consultant, Department of Anaesthesiology, Sadar Hospital, Jhenaidh, Bangladesh
[2]Assistant Professor, Department of Anaesthesiology, Pabna Medical College Hospital, Pabna, Bangladesh
[3]Associate Professor, Department of Anaesthesiology, Women's Medical College Hospital, Sylhet, Bangladesh
[4]General Practitioner, Doctors Clinic, Jhenaidh, Bangladesh

DOI: 10.36347/sjams.2019.v07i07.040 | **Received:** 16.07.2019 | **Accepted:** 24.05.2019 | **Published:** 30.07.2019

***Corresponding author:** Dr. ASM Abdur Rahman

Abstract **Original Research Article**

Background: Intraoperative nausea and vomiting 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 intraoperative nausea and vomiting (IONV) and several in parturient and cesarean. However, it needs more attention. Ketamine is a potential drug in this procedure. ***Objective:*** The main objective of the study was to evaluate the efficacy of ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia. ***Introduction:*** 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. In Bangladesh there are not many studies on the efficacy of Ketamine in prevention of IONV. ***Methods:*** This comparative study was conducted in Department of Obstetrics and Gynaecology collaboratively with the Department of Anaesthesiology of Sadar Hospital, Jhenaidah, Bangladesh during the period from January 2018 to December 2018. In total 120 patients were randomly allocated into two equal groups: the ketamine group; in which 0.5 mg/kg was infused intravenously in 20 min and the placebo group; in which normal saline was infused. The two groups were given subarachnoid block with local anaesthetic hyperbaric 0.5% bupivacaine and intrathecal fentanyl. ***Results:*** The incidence of intraoperative nausea was 20% and episodes were 38 in total in the ketamine group compared with 38.33% and episodes were 76 in total in the placebo group, which was statistically significant (P value 0.176). Both vomiting episodes and number of patients who required rescue anti-emetics in the ketamine group compared with placebo one (3.33% vs 6.67% and 2 vs 5 respectively) were not statistically significant P values 0.682 and 0.593. ***Conclusion:*** In our study, we found the satisfactory efficacy and better compliance from the patient's front. Ketamine may be used without hesitation for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia.

Keywords: Ketamine, Nausea & Vomiting, Caesarean Section, N- methyl D-aspartate (NMDA).

INTRODUCTION

Spinal anaesthesia is the most commonly used anaesthesia for caesarean section (CS) with it being safely, quickly and easy to administer [1]. 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[2]. Ketamine is a NMDA receptor antagonist that has unique central sympathomimetic, vagolytic and analgesic properties [3]. These properties of ketamine are assumed to reduce the incidence of spinal induced hypotension consequently nausea and vomiting. The present study was undertaken to evaluate the anti-emetic efficacy ketamine to decrease the incidence of IONV during CS under spinal anesthesia. Intraoperative nausea and vomiting (IONV) during caesarean section (CS) under spinal anaesthesia is a common complication with an incidence ranging from 40% to 60% [4]. Many factors may contribute to this high rate of IONV during CS; sympathetic block and the resultant hypotension secondary to spinal anaesthesia, visceral pain and vagal stimulation during CS are probably the most important

factors[5]. Ketamine has unique central sympathomimetic, vagolytic and analgesic properties [6]. These properties of ketamine are assumed to reduce the incidence of spinal induced hypotension. In this study, we hypothesized that an IV infusion of ketamine would lower the incidence of intraoperative nausea and vomiting secondary to spinal-induced hypotension. This placebo-controlled prospective randomized double-blinded study was designed to evaluate the impact of ketamine on prevention of intraoperative nausea and vomiting as a primary outcome in parturients subjected to elective CS under spinal anaesthesia. Maternal and fetal side effects were considered as a secondary outcome. The main objective of the study was to evaluate the efficacy of ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia.

Objectives

General objective

- To evaluate the efficacy of ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia.

Specific Objectives

- To assess the relapse rate of ketamine in caesarean section under spinal anaesthesia.

METHODOLOGY & MATERIALS

Taking approval by an ethical committee obtaining a written informed consent from eligible parturients scheduled for elective caesarean section under spinal anaesthesia, ASA1 and 2 parturients having pregnancy were included as study population. Exclusion criteria included history of motion sickness, post-operative nausea and vomiting, gastrointestinal disease, allergy, pregnancy induced hypertension, history of non-gestational diabetes and history of smoking. Besides this obese patients, epileptic patients, patients given anti-emetics or corticosteroids within 24 h before CS, patients who was heavy sedated and patients having any absolute contraindications to spinal anaesthesia were excluded. Included patients were randomly, using computer generated randomization table allocated into two equal groups: the ketamine group, Group I (n = 60) and the control group, Group II (n = 60). In Group-I, ketamine was diluted to a total volume of 20 ml via normal saline. Using an infusion pump (Graseby 3100-waltford, Herts-UK), ketamine was given at a dose of 0.5 mg kg—1 over 20 min started while patient back was being cleaned and scrubbed for spinal anaesthesia before intrathecal injection. In the control group, a similar volume of normal saline was given using the same technique used in the ketamine group. In order to achieve blindness of the study, one researcher was involved only in drug preparation according to patient's randomization and group assignment. The other anaesthesia provider gave spinal block, managed the patient according to the study protocol and recorded the intraoperative data. Patients started NPO midnight of the surgery, Ringer lactate infusion in a rate of 1.5 ml/kg—1 h—1 commenced at 6 am on the day of surgery through an 18-G peripheral IV cannula, a 20 ml of 0.3 M sodium citrate given orally 15 min before shifting the patient to the main operating theatre. In the waiting area of the operating room, patients were monitored with ECG, automated noninvasive arterial blood pressure and pulse oximetry. An average of two readings of the mean arterial blood pressure (MABP) and heart rate (HR) were taken 5 min apart and considered the basal readings. Preloading with 10 ml Kg—1 of hydoxyethyl starch solution (6% HES 200/0.5 Braun Melsungen AG-Germany) was completed within 15–20 min, after which patient was shifted to the operating room (OR) where the standard monitoring of ECG, HR, BP and SpO2 was extended. In the OR, we performed spinal anaesthesia in the sitting position under complete aseptic technique and skin infiltration with 0.5 ml of 1% lidocaine at site (L3-4 or L4-5) of spinal needle insertion. We used a spinal needle 25-G pencil point type, once free flow of clear CSF was obtained a 15 lg fentanyl loaded in 2 ml syringe was injected intrathecally followed by a hyperbaric bupivacaine 0.5%. The dose of bupivacaine was adjusted according to parturients height, 2 ml (10 mg) was given to those having a height <155 cm and 2.2 ml (12 mg) was given if the height was P155 cm. After intrathecal injection, patients were immediately returned supine with left uterine dis- placement and supplemented with oxygen 4 L min—1 via clear facemask. Dermatomal level of sensory block was assessed by pinprick method; T5 was the minimum acceptable level before surgical incision. Both groups were given the same anaesthetic management by well-trained anaesthetists having an experience more than 10 years in the anaesthesia practice. Mean arterial blood pressure (MABP) was measured every 1 min for the first 10 min then every 2 min until the end of ketamine or placebo infusion. Intraoperative hypotension-defined by MABP less than 20% of the basal reading-was managed by increasing the infusion rate of Ringer lactate solution concomitant with administration increments of 3 mg ephedrine hydro- chloride. Arterial blood pressure was measured 1 min after ephedrine injection and if hypotension persists another ephedrine bolus was given, atropine sulphate (0.5 mg) was given when hypotension was associated with bradycardia (HR <50 beats min—1). At the end of CS the incidence of hypotension (percentage per each group), hypotensive episodes (number of hypotensive episodes per each group) and increments of ephedrine hydrochloride in mg. were recorded. 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). It was used to measure sedation level at 5, 10, 15, 20, 25, and 30 min after surgical incision,

patients having RSS 4 or more were rejected. Oxytocin was given immediately after baby delivery and clamping of the umbilical cord. Using a 10 ml syringe, a 10 units of oxytocin diluted into 10 ml of normal saline was given incrementally starting by an IV bolus dose of 2 ml (2 units) followed by increments of 2 units according to uterine contractility as per the obstetrician opinion. At the end of surgery; the total amount of oxytocin units administered, the technique of uterine repair and duration was recorded. Patients given uterotonics other than oxytocin were rejected from the study. We replaced rejected patients from the study according to group assignment. During surgery; intraoperative pain was managed by administration of 20 lg fentanyl given as IV bolus. At time of consent and again before the administration of spinal anaesthesia, patients were reminded to report any side effect or dis- comfort including nausea. Leading questions about nausea were avoided. Intraoperative nausea was recorded as follow (no nausea = 0, nausea only = 1, nausea and retching = 2), also the timing of IONV (during infusion or after) was re- corded. Nausea with retching or vomiting were managed by a rescue dose of 10 mg metoclopramide diluted in a 10 ml of normal saline and given IV slowly, while nausea only was man- aged by assurance. Maternal side effects (such as desaturation, hallucinations) as well as fetal well-being (assessed with the Apgar scoring) were recorded. Upon completion of the CS, parturients were transported to the post-anaesthesia care unit (PACU) where routine monitoring of BP, ECG, and SpO2 in addition to oxygen supple- mentation were applied to all patients under the care of PACU nurses then all patients were discharged and shifted uneventfully to the ward. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 17). Based on previous investigations which reported an incidence between 40% and 60% of intraoperative nausea of parturients operated for CS under neuraxial anaesthesia, assuming 30% is the predicted incidence in the control group, to achieve 50% reduction in the incidence of intraoperative nausea (the primary outcome) at two-sided significance level 0.050% and 80% power, it was calculated that a minimum of 110 patients were required in each group. Normally distributed numerical data were presented by its mean and standard deviation (SD), while in-between group differences were compared parametrically using the independent-samples Student t test. Non-normally distributed numerical data were presented as absolute number (percent or range), while inter-group differences were compared non-parametrically using the Mann–Whitney U test. Significance level was set at $P < 0.50$ as usual.

RESULT

Only 120 patients continued till the finishing period of the study was finally defined as the total population. In Ketamine Group, Group I there were 60 patients and in controlled group, Group II there were 60 patients. Before this selection, 6 patients were rejected, 3 patients required general anaesthesia 2 because of failed block and the 2 because of inadequate block, 5 patients given methyl-ergometrine according to the obstetrician opinion, 1 patient had RSS = 4, and 1 patient was given midazoalm immediately after delivery as she was very anxious were rejected. There was neither maternal, fetal mortality, nor serious regional complications in the form of total spinal, paraplegia, epidural abscess, haematoma. There was no significant difference except weight in patient's data including age, weight, height, basal MABP and basal heart rate with *P* values 0.572, 0.327, 0.568, 0.719, and 0.413 respectively. Obstetric data including sensory block, bupivacaine dose, uterine exteriorization, number of parturients underwent bilateral tubal ligation (BTL), duration from skin incision to uterine repair, operative time, oxytocin requirements showed no significant statistical difference between the two groups: *P* values 0.574, 0.647, 0.827, 0.741, 0.643, 0.578, and 0.365 respectively Besides these, Apgar scores at 1 and 5 min did not show significant changes with *P* values 0.506 and 0.573 respectively. The lower incidence of intraoperative hypotension (31.67% vs 46.67%) was significant (P value 0.214), however the number of hypotensive episodes and ephedrine requirements increased significantly in the placebo group compared with ketamine group P values 0.418 and 0.174 respectively. Five patients (4 in the placebo group and 1 in the ketamine group) recorded concomitant hypotension and bradycardia and were given IV bolus 0.5 mg atropine sulphate. The incidence of intraoperative nausea was in 18 (20%) in the ketamine group compared with in 23 (38.33%) in the placebo group, which was statistically significant (P value 0.176). Both vomiting episodes and number of patients who required rescue anti-emetics in the ketamine group compared with placebo one (3.33% vs 6.67% and 2 vs 5 respectively) were not statistically significant P values 0.682 and 0.593. The majority of hypotensive episodes occurred during first 20 min of operation (infusion period) in both ketamine and placebo groups, similarly incidence of nausea during infusion period in both ketamine and placebo groups was 11 and 23 respectively.

Table-I: Demographic and Haemodynamic data of Participants (N=120)

Component	Group I	Group II	P value
Age (yrs.)	30.36 ± 4.16	30.61 ± 4.62	0.572
Weight (Kg)	76.38 ± 8.14	77.48 ± 8.04	0.327
Height (cm)	161 ± 4.11	161 ± 3.91	0.568
Basal MABP mmHg	86.13 ± 8.23	86.19 ± 7.24	0.719
Basal HR; bpm	75.33 ± 10.24	75.61 ± 10.47	0.413

Table-II: Anaesthetic and obstetric data of participants (N=120)

Component	Group I	Group II	P value
Sensory block	T4(T2–T6)	T4(T2–T5)	0.574
Bupivacaine dose	11.82 ± 0.76	11.56 ± 0.78	0.647
Exteriorization of uterus; n	19 (31.67)	21(35)	0.827
BTL; n	4 (6.67)	7 (8.33)	0.741
Time from skin incision to closure	17.72 ± 4.67	17.43 ± 4.68	0.643
Operative time; min	52.36 ± 8.17	52.13 ± 8.13	0.578
Oxytocin dose; U	12.65 ± 3.52	12.9 ± 3.86	0.565
Apgar score 1st min	7.87 ± 0.89	7.81 ± 0.96	0.506
Apgar score 5th min	8.62 ± 0.74	8.72 ± 0.69	0.473

Table-III: Several episodes, dosage and symptoms of participants (N=120)

Component	Frequency	Group I	Group II	P value
Intraoperative hypotension		19 (31.67)	28 (46.67)	0.314
hypotensive episodes	Total number	38	76	0.418
	during 1st 20 min	33	66	–
	After 1st 20 min	5	10	–
Intraoperative nausea	Total number	11	23	0.174
	during 1st 20 min	8	18	–
	After the 1st 20 min	3	5	–
Intraoperative vomiting		2 (3.33)	4 (6.67)	0.682
Rescue anti-emetics		2 (3.33)	5 (8.33)	0.593
pain		2 (3.33)	3 (5)	0.456
Hallucinations		1 (1.67	1 (1.67	0.426

DISCUSSION

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[7]. The use of ketamine in the current study was associated with significant reduction in the incidence of intra-operative nausea and hypotensive episodes in parturients subjected to elective CS under spinal anaesthesia; however, the reduction in the incidence of intraoperative vomiting and rescue antiemetic requirements was not statistically significant. The well-documented maternal and fetal safety of spinal anaesthesia compared to general anaesthesia encouraged anaesthetists to use it as the gold standard for the anaesthetic management of parturient subjected to CS. Unfortunately intraoperative hypotension, and IONV are significant and irritating drawback of spinal anaesthesia [2]. In our study the incidence of hypotension in the control group was less compared to previous reports [8]. This can be explained by the use of prehydration with colloid fluid that was reported by Ngan Kee *et al*. found that colloid in the form of gelfusine or heastril preloading was associated with less incidence and severity of hypotension during CS under regional anaesthesia[9]. Titrating bupivacaine dose according to the patient height and maintaining left uterine displacement are other factors. The use of ketamine as IV induction agent in haemodynamically compromised patients subjected to emergent surgical interventions was shown to increase mean arterial blood pressure by a mean of 10% when compared to basal readings as reported by White PF [10]. In our study, the frequency of hypotensive episodes during infusion period was nearly twice in the placebo group compared with ketamine group (55 vs 24) with significant statistical difference in the total hypotensive episodes between the two groups; this could be explained by the sympathomimetic effect as well as vagolytic effect of ketamine. Low dose of IV ketamine was shown to reduce the incidence of postoperative nausea/vomiting score in other types of surgeries as reported by Yamauchi *et al*. [11]. They found that administration of a low-dose ketamine infusion at skin incision and continues post-operatively not only improved the analgesic effects, but also it reduced postoperative nausea and vomiting. This finding is agreed with the result of our study despite different explanation. Both maternal and fetal safety of ketamine in CS is documented; Ngan Kee *et al*.[12] compared the effect of ketamine induction vs thiopental induction on postoperative analgesia in elective CS, they found that patients in the ketamine group required less analgesic drugs in the first 24 h compared with thiopental group and the neonatal apgar score was comparable without inter-group significant changes In another study Nielsen and Holasek [13] studied ketamine as an induction agent in CS and found an excellent Apgar scores (mean 9.1 at 1 min and 9.9 at 5 min) associated with ketamine induction. These studies agree with our results that did not detect any significant changes in the apgar scores between the two groups at both 1 and 5 min Apgar scores. The non-significant difference in the sedation level measured by RSS between the two groups disagrees with the result of Saricalouge *et al*. study [14] which investigated the impact of intravenous ketamine on ischaemia-reperfusion in- jury in patients subjected

to knee arthroscopy under spinal anaesthesia and found significantly higher RSS in the ketamine group. This difference could be explained by the higher ketamine dose and the use of midazoalm in their study[14], although a higher sedation score was reported in their study [14], it was not associated with increased incidence of either respiratory depression or hallucinations in the ketamine group which agrees with the result of the our study. We speculate that; despite the reduction in the incidence of hypotension was insignificant however the frequency of hypotensive episodes was significantly less in the ketamine group, hence the ephedrine requirements, compared with placebo group could explain the statistically significant reduction in the incidence of intraoperative nausea in ketamine group com- pared to the placebo one.

CONCLUSION

According to the findings of our study we would recommend to use ketamine for prevention of intraoperative nausea and vomiting in caesarean section under spinal anaesthesia widely. This was a single centered study with smaller size sample. So the findings may not reflect the exact scenario of the whole country.

REFERENCES

1. Juhani TP, Hannele H. Complications during spinal anesthesia for cesarean delivery: a clinical report of one year's experience. Reg Anesth Pain Med. 1993 Mar 1;18(2):128-31.
2. Kestin IG. Spinal anesthesia in obstetrics. Br J Anaesth. 2004;66:596–607.
3. Morgan GE, Mikhail MS, Murray MJ, Larson CP. Clinical anesthesiology. New York: Lange Medical Books/McGraw-Hill; 2006 Sep 20.
4. Balki M, Kasodekar S, Dhumne S, Carvalho JC. The prophylactic granisetron does not prevent postdelivery nausea and vomiting during elective cesarean delivery under spinal anesthesia. Anesthesia & Analgesia. 2007 Mar 1;104(3):679-83.
5. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology. 1992 Jul;77(1):162-84.
6. Morgan GE, Mikhail MS, Murray MJ, Larson CP. Clinical anesthesiology. New York: Lange Medical Books/McGraw-Hill; 2006 Sep 20.
7. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology. 1992 Jul;77(1):162-84.
8. Kee WD, Khaw KS, Tan PE, Ng FF, Karmakar MK. Placental transfer and fetal metabolic effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2009 Sep 1;111(3):506-12.
9. Kee WN, Khaw KS, Lee BB, Ng FF, Wong MM. Randomized controlled study of colloid preload before spinal anaesthesia for caesarean section. British Journal of Anaesthesia. 2001 Nov 1;87(5):772-4.
10. White PF. Comparative evaluation of intravenous agents for rapid sequence induction--thiopental, ketamine, and midazolam. Anesthesiology. 1982 Oct;57(4):279-84.
11. Yamauchi M, Asano M, Watanabe M, Iwasaki S, Furuse S, Namiki A. Continuous low-dose ketamine improves the analgesic effects of fentanyl patient-controlled analgesia after cervical spine surgery. Anesthesia & Analgesia. 2008 Sep 1;107(3):1041-4.
12. Kee WD, Khaw KS, Ma ML, Mainland PA, Gin T. Postoperative analgesic requirement after cesarean section: a comparison of anesthetic induction with ketamine or thiopental. Anesthesia & Analgesia. 1997 Dec 1;85(6):1294-8.
13. Nielsen JD, Holasek J. Ketamine as induction agent for caesarean section. Acta Anaesthesiologica Scandinavica. 1982 Apr;26(2):139-42.
14. Saricaoglu F, Dal D, Salman AE, Doral MN, Klnç K, Aypar Ü. Ketamine sedation during spinal anesthesia for arthroscopic knee surgery reduced the ischemia-reperfusion injury markers. Anesthesia & Analgesia. 2005 Sep 1;101(3):904-9.