KETAMINE AND PETHEDINE FOR PREVENTION OF NAUSEA AND VOMITING IN CESAREAN SECTION UNDER SPINAL ANESTHESIA: COMPARATIVE STUDY

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ABSTRACT

Background: Nausea, retching and vomiting are common in cesarean section under spinal anesthesia, which is distressing for the parturient and interferes with the surgical procedure. **Objectives:** Evaluation of moderate sedation by ketamine and pethidine for prevention of intraoperative nausea and vomiting in parturient of cesarean section under spinal anesthesia in a comparative study with metoclopramide and ondansetron. **Patients and methods:** 80 patients divided into four groups; 1st group received 5ml normal saline as placebo, 2nd group received 10 mg metoclopramide diluted in 5 ml saline after clamping of the cord, 3rd group received 4 mg ondansetron diluted in 10 ml saline and the 4th group received 25 mg ketamine diluted to 5 ml saline and pethidine 25 mg diluted in another 5 ml saline by slowly intravenous injection after cord clamping. **Results:** Number of patients who suffered intraoperative nausea was less in sedation group (1, 5%) compared with 10 patients (50%) in placebo group, 7 patients (35%) in metoclopramide group and 6 patients (30%) in patients received ondansetron. **Conclusion:** Moderate sedation by ketamine and pethidine is more potent than metoclopramide and ondansetron for prevention of intraoperatie nausea and vomiting in cesarean section under spinal anesthesia.

Keywords: sedation, ketamine, pethidine, metoclopramide, ondansetron

INTRODUCTION

Cesarean delivery under regional anesthesia has become increasingly popular over the past decade, due to increased patient acceptability, improved fetal condition at birth and greater maternal safety[(1)].

Nausea, retching and vomiting during regional anesthesia for cesarean delivery are common occurrences, especially when the uterus is exteriorized[(2, 3)].

These symptoms are distressing and uncomfortable for the parturient and may interfere with the surgical procedure; patients who experience these symptoms consume more resources and require additional healthcare professional time than do those in whom these complications are avoided[(4)].

Also, postoperative nausea and vomiting are the most common complications after anesthesia and surgery[(5, 6)].

These symptoms predispose the patient to aspiration of gastric contents. Wound dehiscence, psychological distress, and delayed recovery and discharge time[(7)].

Cesarean delivery performed under regional anesthesia is associated with a relatively high incidence (50%-80%) of intraoperative, and postdelivery nausea and vomiting[(8, 9)].

Numerous antiemetics have been studied for the prevention and treatment of these emetic symptoms. These drugs include butyrophenones, benzamides, anticholinergics, corticosteroids, propofol, and serotonin antagonists, all of which have been associated with varying degree of success[(10)].

Nausea, retching, and vomiting during regional anesthesia for cesarean delivery have a complex and multifactorial etiology[(11, 12)]. These emetic symptoms are affected by maternal hypotension[(11)].

This hypotension leads to cerebral hypoperfusoin and brainstem ischemia that activates the circulatory, respiratory and vomiting centers in the medulla[(13)].

It also leads to gut ischemia and release of emetogenic substances such as serotonin from the intestine[7].

In general, a number of factors, including age, gender, smoking habit, history of motion sickness and/or previous postoperative emesis, pain, operative procedure, and anesthetic technique, are all considered to affect the occurrence of nausea, retching, and vomiting[14].

Visceral pain is a potent stimulus for emetic symptoms during regional anesthesia[15]. Handling of abdominal viscera stimulates sensory vagal fibers and induces emesis by activating the vomiting center[14].

Surgical stimuli that is responsible for nausea, retching, and vomiting during cesarean delivery performed under regional anesthesia include exteriorization of the uterus, intra-abdominal manipulation or exploration and peritoneal traction during closure(15, 16).

PATIENTS AND METHODS

The aim of our work is to evaluate the effect of conscious sedation for prevention of intra-operative and postoperative nausea, retching and vomiting in parturient with elective cesarean section under spinal anesthesia. Written informed consent is obtained before start of operation.

Patients:

80 pregnant females, full-term ASA I and II scheduled for elective cesarean section divided into four groups:

Group I: Placebo group.

Group II: Metoclopramide group.

Group III: Ondansetron group.

Group IV: Ketmaine and pethidine group.

Inclusion criteria:

Parturient scheduled for elective cesarean section with different causes, patient aged 18-35 years.

Exclusion criteria:

Patients with contraindications of spinal anesthesia, allergy to drugs used during research, patients with preoperative haemodynamic unstability like pre-eclampsia, or hypotensive patients, history of preoperative nausea and vomiting, history of motion sickness, and patients received antiemetics 24 hours before operation.

Method:

- Preoperative preparation of all patients with visit in the room, and discussion of the procedure, IV line inserted and crystalloids given as preload by 20 ml/kg with maximum fluid 1500 ml before spinal anesthesia.
- Monitoring of basal heart rate and blood pressure before spinal anesthesia.
- Spinal anesthesia with 25 G whitacre needle, in sitting position with injection of 10 mg bupivacaine 0.5% (heavy marcaine) at L_{4-5} or L_{3-4}.
- O_2 mask with 3 L/minute.
- Continuous monitoring of heart rate, blood pressure and O_2 saturation.
- Decrease of blood pressure > 20% from baseline after spinal anesthesia was treated by IV fluids and ephedrine injection to maintain the patient haemodynamically stable during the operation to avoid the effect of hypotension as a cause of nausea and vomiting. All patients received 10 IU of oxytocin after cord clamping.
- After cord clamping, patients received anti-emetic drug according to the groups:

  Group I (placebo group) received 5 ml normal saline slowly IV.

  Group II (metoclopramide group) received 10 mg metoclopramide diluted to 5 ml slowly IV.

  Group III (ondansetron group) received ondansetron 4 mg diluted in 5 ml saline slowly IV.

  Group IV (ketamine and pethidine group) received 25 mg ketamine diluted to 5 ml saline slowly IV, followed by 25 mg pethidine diluted to 5 ml saline slowly IV.

  Intraoperative and postdelivery emetic episodes (nausea, retching and vomiting) were recorded.

  Postoperative pain was recorded in the ward by blind investigator, 3 hours, 6 hours and 24 hours.

  Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.

Retching was defined as the labored, spasmodic, rhythmic contractions of the respiratory muscles without the expulsion of gastric contents.

Vomiting was defined as the forceful expulsion of gastric contents from the mouth[17].

Patients experiencing nausea evaluated its severity on a linear numeric scale ranging from 0 (no nausea) to 10 (severe nausea).

Postoperative pain was evaluated by visual analogue scale from 0 to 10.

Postoperative analgesia according to severity of pain by using diclofenac (75 mg) or pethidine 50 mg.

Collected data were analyzed using the statistical software (SPSS, ver. 13), descriptive statistics, student t-test, and Mann-Whitney test.

RESULTS

Table (1) showed the patient characteristics with no significant differences related to age by years, weight by kilogram, height by cm and gestational age by weeks.

Table (2) showed the intraoperative management of all patients in all groups in which the surgical time by minutes was shorter in sedation groups (38 ± 5 minutes) compared with placebo, metoclopramide and ondansetron groups (48 ± 17 minutes, 47 ± 10 minutes and 47 ± 14 minutes respectively). There was no changes related to the number of patients with tubal ligations. Also, the amount of intraoperative blood loss by ml had no significant differences between all groups. The dose of ephedrine (mg) used for intraoperative management had no significant changes. The number of patients who suffered intraoperative nausea were 1 (5%) in sedation group was high significant difference compared to placebo group (10, 50%) and significant changes when compared with metoclopramide (7, 35%) and ondansetron (6, 30%) respectively.

There was no patients suffering intraoperative retching in patients who received ketamine and pethidine compared with placebo (4, 20%), metoclopramide (3, 15%) and ondansetron (2, 10%).

Also, no patients had intraoperative vomiting in patients who received ketamine (25 mg IV) and pethidine (25 mg IV)with significant differences compared with patients received 5 ml normal saline (placebo) (3, 15%), metoclopramide 10 mg IV (2, 10%) and ondansetron 4 mg IV (2, 10%). Intraoperative systolic and diastolic blood pressure showed no significant changes in all groups.

Table (3) showed the postoperative evaluation of pain using VAS with significant reduction of postoperative VAS at sedation group 3 hours postoperatively (1.5, 1-2) compared to placebo (3.5, 2-5) and ondansetron group (3, 1-4). VAS after 6 hours of operations was less in patients received sedation (0.5, 0-1) compared with placebo (2.5, 2-3), metoclopramide (2, 1-3) and ondansetron (2, 1-3).

Postoperative pain evaluation after 24 hours by VAS showed significant lower VAS at sedation group (0.5, 0-1), compared with placebo group (1.5, 1-2), metoclopramide group (1, 1-2) and ondansetron group (1, 1-2).

Postoperative consumption of diclophenac was significantly lower in patients who received ketamine and pethidine during the operation (50 ± 50 mg) compared with placebo (100 ± 75), metoclopramide (100 ± 50) and ondansetron (100 ± 50) respectively.

Also, postoperative pethidine consumption was significantly lower in sedation group (25 ± 25 mg) compared with placebo, metoclopramide and ondansetron (75 ± 15, 75 ± 10 and 75 ± 75 respectively).

Table (1): Patient characteristic data expressed as mean ± SD

	Group I (placebo)	Group II (metoclopramide)	Group III (ondansetron)	Group IV (sedation)
Age (years)	24 ± 8	25 ± 5	24 ± 9	25 ± 8
Weight (kg)	65 ± 8	66 ± 6	65 ± 7	65 ± 8
Height (cm)	160 ± 5	160 ± 3	159 ± 9	160 ± 2
Gestational age (weeks)	39 ± 2	38.8 ± 1	39 ± 1	39 ± 2

Table (2): Operative management. Data expressed as mean ± SD except for tubular ligations as number and nausea, retching and vomiting as number and percentage

	Group I (placebo)	Group II (metoclopramide)	Group III (ondansetron)	Group IV (sedation)
Surgical time (minutes)	48 ± 12	47 ± 10	47 ± 14	38 ± 5
Tubal ligations	3	4	3	3
Blood loss (ml)	550 ± 100	590 ± 110	550 ± 50	550 ± 50
Ephedrine doses (mg)	30 ± 10	30 ± 10	30 ± 5	30 ± 5
Nausea	10 (50%)	7 (35%)	6 (30%)	1 (5%)
Retching	4 (20%)	3 (15%)	2 (10%)	0 (0%)
Vomiting	3 (15%)	2 (10%)	2 (10%)	0 (0%)
Systolic blood pressure	100 ± 15	100 ± 10	100 ± 8	100 ± 12
Diastolic blood pressure	60 ± 8	60 ± 10	60 ± 10	60 ± 5

Table (3): Postoperative data expressed as mean ± SD except for VAS as median and range

	Group I (placebo)	Group II (metoclopramide)	Group III (ondansetron)	Group IV (sedation)
VAS 3 hours	3.5 (2-5)	3.5 (2-5)	3 (1-4)	1.5 (1-2)
VAS 6 hours	2.5 (2-3)	2 (1-3)	2 (1-3)	0.5 (0-1)
VAS 24 hours	1.5 (1-2)	1 (1-3)	1 (1-2)	0.5 (0-1)
Total consumption of diclophenac (mg)	100 ± 75	100 ± 50	100 ± 50	50 ± 50
Total consumption of pethidine (mg)	75 ± 25	75 ± 10	75 ± 25	25 ± 25

DISCUSSION

Spinal anesthesia is considered the procedure of choice for elective or urgent cesarean section in countries such as the United States, where it is used in up to 41% of the cases in some hospitals[19].

The effects of spinal anesthesia on women on their labour period are different from those observed in non-obstetric patients. The distribution of anesthetic drug in Cerebrospinal Fluid (CSF) is less predictable in the former group. Not only because of increased spinal canal pressure[18], but also as a consequence of the changes in CSF acid-base balance and protein content[19].

Moreover, side effects, including hypotension, nausea and vomiting, and hypersensitivity to intrathecal opiates, are more common[18].

Intraoperative emetic symptoms during abdominal surgery under regional anesthesia have multifactorial origin and factors such as psychological changes (anxiety), arterial hypotension, hypoperfusion of the central nervous system, abrupt visceral movement, and concomitant opiate administration may have influence on them[19].

Surgical stimuli that is responsible for nausea, retching and vomiting during cesarean delivery performed under regional anesthesia include exteriorization of the uterus, intra-abdominal manipulation or exploration and peritoneal traction during closure[15, 16].

In our study, we used crystalloid fluids and ephedrine by IV injection in need to control the blood pressure intraoperatively and to avoid the effect of hypotension to induce nausea and vomiting.

Also, patient age, body weight, height and gestational age were nearly the same with no effect on the results, to evaluate the effect of moderate sedation (conscious sedation) to block the surgical stimulation, exteriorization of uterus and peritoneal traction with vagal stimulation and vomiting, due to release of humoral substances including 5-HT which may stimulate 5-HT_3 receptors on the afferent vagus nerves, triggering the emetic reflex especially awake patients[18]. We found that conscious sedation by ketamine 25 mg IV with pethidine 25 mg IV after clamping of the umbilical cord was effective for prevention of intraoperative nausea (one patient only, 5%) compared with 10 patients (50%), 7 patients (35%) and 6 patients (30%) in placebo, metoclopramide and ondansetron groups respectively.

Also, the incidence of intraoperative retching and vomiting were statistically significantly lower in patients received ketamine and pethidine compared with others received metoclopramide and ondansetron, and were statistically highly significant compared with placebo group. All patients were haemodynamically stable during the operation with no statistically significant changes between all groups. The surgical time was statistically lower (38 ± 5 minutes) in patients received sedation than other three groups; placebo (48 ± 12 minutes), metoclopramide (47 ± 10 minutes) and ondansetron (47 ± 14 minutes). Postoperative pain evaluation using VAS was lower after 3 hours, 6 hours and 24 hours in patients received ketamine and pethidine compared with the other three groups. Postoperative consumption of diclophenac was significantly less in sedation group (50 ± 50 mg) compared with 100 ± 75 mg in placebo, 100 ± 50 mg in metoclopramide and ondansetron groups.

Postoperative pethidine consumption was 25 ± 25 mg in sedation group which was less compared with 75 ± 15 mg in placebo, 75 ± 10 mg in metoclopramide group and 75 ± 25 mg in patients who received ondansetron.

Pan et al.[20] reported that ondansetron is as effective as droperidol in preventing intraoperative nausea and vomiting during cesarean section under epidural anesthesia.

Borgeal et al.[21] evaluated the direct therapeutic antiemetic effect of subhypnotic doses of propofol after minor gynaecological, digestive and orthopedic surgical procedures. Nevertheless, later studies have shown that this drug does not prevent the emetic complications in elective cesarean section under spinal anesthesia[22].

Garcia et al.[18] found that the IV administration of a bolus of either 4 mg of ondansetron or 10 mg of metoclopramide, immediately after clamping of the cord were equally effective in preventing intraoperative emetic symptoms in parturients undergoing cesarean section under spinal anesthesia.

CONCLUSION

Moderate sedation (conscious sedation) by ketamine 25 mg IV and pethidine 25 mg IV injection after clamping of umbilical cord is a potent method for prevention of intraoperative nausea, retching and vomiting in parturients undergoing cesarean section under spinal anesthesia, also effective in reduction of postoperative pain and the consumption of analgesics.

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الكيتامين مع البيتيدين لمنع القئ والغسيان اثناء عملية الولادة القيصرية تحت تخدير نصفي. دراسة مقارنة

الخلفية:يعتبر القئ والغسيان من الاعراض الشائعة اثناء عملية الولادة القيصرية تحت تخدير نصفي وهي اعراض تعوق الاجراءات الجراحية.
الاهداف:تقييم استخدام التسكين المعتدل عن طريق الكيتامين والبيتيدين في منع القئ والغسيان اثناء الولادة القيصرية تحت التخدير النصفي في دراسة مقارنة مع الميتوكلوبروميد والاوندانسيترون.
المرضي والطرق:٨٠ مريض مقسمة الي اربعة مجموعات: تلقي الفريق الاول ٥مللي سالين والمجموعة الثانية تلقت ١٠ مجم من الميتوكلوبروميد في ٥ مللي سالين والمجموعة الثالثة تلقت ٤مجم انانسيترون في ٥مللي سالين اما المجموعة الرابعة فتلقت٢٥مجم كيتامين في ٥مللي سالين مع ٢٥ مجم بيتيدين في ٥ مللي سالين بالحقن الوريدي ببطء بعد مصادرة الحبل السريز
النتائج: عدد المرضى الذين يعانون من الغثيان كان أقل في المجموعة الكيتامين والبيتيدين (١، ٥%) بالمقارنة مع ١٠ مرضى (٥٠%) في مجموعة المقارنة، و ٧ مرضي (٣٥ في المائة) في فريق الميتوكلوبروميد وعدد المرضى ٦ (٣٠ في المائة) في مجموعة أوندانسيترون.
الخلاصة: التسكين المعتدل باستخدام الكيتامين والبيتيدين افضل من ميتوكلوبروميد واندانسيترون في الوقاية من القئ والغثيان في الولادة القيصرية تحت التخدير النصفي..