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Original Research Article

Evaluation of the Efficacy of a Single Bolus Dose of Carbetocin for Prevention of Postpartum Haemorrhage in Elective Caesarean Section under Spinal Anaesthesia

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Abstract:

Background: The biggest cause of maternal deaths globally is postpartum hemorrhage (PPH), which accounts for an estimated 1,40000 deaths annually. By employing "active management of the third stage of labor," most of them can be avoided. A synthetic oxytocin analogue with a longer half-life, carbetocin was first described in 1987. The current study's objectives were to assess carbetocin's effectiveness in reducing intraoperative blood loss and to track its effects on hemodynamics.

Methods: In this study, 120 individuals who underwent an elective caesarean delivery while under spinal anesthesia and had a gestation of at least 37 weeks were included. Two groups of patients (Group CT and Group C) were created. After the anterior shoulder was delivered, women in the carbetocin group (group CT) got an IV bolus of 100 mcg/ml of carbetocin whereas those in group C received an oxytocin infusion. The study's parameters included mean effective blood loss, HR and MAP, as well as side effects like headache, palpitations, and nausea and vomiting.

Results: Both groups showed no PPH occurrence. The average effective blood loss in groups CT and C, respectively, was 423.0±150.1 ml and 635.3 ±245.4 ml. Six patients in Group C required rescue oxytocin. The mean total dose of mephentermine was statistically lower in group CT (23.8±12. 0) than in group (56.8±8.6).

Conclusion: The conventional oxytocin protocol is less efficacious and hemodynamically unstable in preventing PPH during caesarean section than a single bolus dose of carbetocin.

Keywords: Carbetocin, caesarean section, PPH, spinal anaesthesia.

Introduction

The caesarean section is currently the procedure that is carried out most frequently on women worldwide. The number of caesarean sections performed has increased as a result of enhanced local anesthesia, better anesthesiologists, more medical facilities, and government encouragement of institutional deliveries [1].

With an estimated 140000 deaths per year, postpartum hemorrhage (PPH) is the main cause of maternal fatalities globally. Uterine atony is the cause of about 70% of PPH cases [2]. In India, PPH was the cause of 38% of all maternal deaths. According to The Federation of Obstetric and Gynecological Societies of India (FOGSI), the majority of deaths occur within four hours of birth, indicating that they are the result of the third stage of labor [3]. Blood loss of at least 500 milliliters (mL) during vaginal delivery and blood loss of more than 1000 mL following cesarean section within 24 hours is referred to as PPH [4].

WHO recommends "active management of the third stage of labor," which includes preventative use of uterotonics in all to prevent PPH. The controlled cord traction and delayed cord clamping (preferred over early cord clamping) and uterine massage are other noteworthy recommendations. In order to avoid PPH during the third stage of labor, oxytocin 10-unit IM is advised. Other injectable uterotonics (such as ergometrine/ methylergometrine, syntometrine, or misoprostol) and miso-

prostol are recommended as alternatives to oxytocin when it is not available to prevent PPH. In their recommendations for caesarean sections, the Royal College of Obstetricians and Gynecologists (UK) 5 suggested a gradual intravenous bolus administration of 5 IU of oxytocin. The United States, in contrast, advises against using a bolus dose and instead suggests using an oxytocin infusion. This method may have been created in response to worries regarding the physiological effects of oxytocin given in bolus dosage form [2].

In the case of PPH, additional recommendations include intravenous (IV) oxytocin or alternative uterotonics if oxytocin is not available, uterine message, crystalline fluid resuscitation, injection of tranexamic acid, intrauterine balloon tapenade, bimanual uterine compression, uterine artery remobilization, and surgical interventions. [2-4,6] According to the Society of Obstetricians and Gynecologists of Canada (SOGC) [7], to prevent PPH and lessen the need for therapeutic uterotonics during elective caesarean sections, 100 mcg/ml of carbetocin should be administered as a slow IV bolus over a period of one minute. The synthetic oxytocin analogue carbetocin, also known as 1-deamino-1-monocarbo-(2-O-Methyltyrosine)-oxytocin, was first identified in 1987.

Its half-life is 40 minutes, which is 4 to 10 times longer than that of oxytocin, and uterine contractions start to happen less than two minutes after an IV injection of the recommended dosage of 100 mcg/ml [8]. It has been proposed that a single dosage of carbetocin acts as a 16-hour intravenous oxytocin infusion after elective caesarean sections to increase uterine tone and reduce the incidence of PPH [9]. According to some literature, prophylactic carbetocin injection may be a good substitute for oxytocin in the prevention of postpartum hemorrhage.

The initial stage in primary prevention is the identification of identified PPH risk factors [10–12]. The objective of the current study was to assess carbetocin's effectiveness in reducing intraoperative blood loss and to look at its hemodynamic consequences.

Material and Methods

From March 2022 to February 2023, the study was carried out in the Department of Obstetrics and Gynecology, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar. 120 women who underwent an elective caesarean section under spinal anesthesia and had physical status I and II according to the American Society of Anaesthesiologists (ASA) and were between the ages of 18 to 35 were included in the study.

All women who underwent CS and had gestations longer than 27 weeks (27-41 weeks) were included in the analysis. It was necessary to have access to complete information on each participant's age, gestational week number, height, weight, intrapartum period, postpartum period, and follow-up check-up four to six weeks following delivery.

Women with heart problems, hypertension, and preeclampsia were not allowed. Carbetocin was administered intravenously (IV) in the form of a 100 mcg (1ml) bolus over the course of one minute after the infant was safely delivered via CS. Carbetocin injections can be given either before or after placenta birth. Women who weren't administered prophylactic carbetocin received an appropriate level of care with a 10 units of oxytocin IM in accordance with hospital procedure. Following that, during the postpartum observation period, including the two hours spent in the recovery room, the attending nurses calculated intrapartum blood loss and took measurements every half-hour. Weighing the absorbency of the pads and gauze was used to do this. PPH definition included blood loss of 500 mL following vaginal births and 1000 mL following cesarean sections. Women with PPH were given injectable ergonovine, carbetocin, or oxytocin repeatedly. Statistical analysis was completed using SPSS Statistics for Windows, version 20 (SPSS Inc., Chicago, IL, USA). To compare groups, categorical and continuous variables were subjected to Student t tests and chi-square tests (with continuity corrections in the case of 2×2 tables).

Results

In Microsoft Excel 10, data given as mean±SD or patient counts were tabulated and evaluated. 60 participants were eliminated from the study out of a total of 180 patients who had their eligibility evaluated. Due to not fitting the inclusion criteria, 45 patients were excluded from preoperative visits (n=45). 6 patients (n = 6) either had an insufficient block or were sent to general anesthesia. Nine individuals (n = 9) who got mephentermine for prenatal hypotension were disqualified from the trial.

The number of patients who participated in our study was 120, with 60 individuals in each group. Table 1 lists the patient characteristics. Demographic information showed no statistically significant difference between the two groups. The initial HR, MAP, and time of operation did not differ statistically either. PPH was not present in either group (blood loss was less than 100 ml). In group CT, the mean effective blood loss was 423.0 ±150.1 ml, while in group C, it was 635.3 ±245.4 ml. The total amount of blood lost between group C and group - was significantly different (P value<0.05) (Table 2).

Table 1: Demographic Variables

Variables	Group CT (n=60)	Group C (n=60)	p-value
Age in years	23.8±3.1	23.3±4.9	0.721
Height in cm	151.1±6.3	153.3±4.3	0.469
Weight in kg	71.0±12.5	66.3±12.3	0.291
ASA I/II	58/2	57/3	0.93
Body mass index in kg/m^2	27.7±3.9	26.4±4.5	0.390
Initial Heart Rate (beats/min)	89.6±12.3	86.4±11.0	0.832
Mean Atrial Pressure (mg/Hg)	101.2±12.9	97.6±13.5	0.67
Mephentermine dose (mg)	23.8±12.0	56.8±8.6	<0.005
Operation time (min)	45.9±13.5	41.4±14.1	0.354

While no patients in group CT required additional oxytocin as uterotonics, six patients in group C required rescue oxytocin. Between group CT and group C, there was a significant difference in the additional uterotonics required (p value<0.05) (Table 2).

Table 2: Estimation of Blood Loss, Rescue Uterotonics and Complication

Variables	Group CT (n=60)	Group C (n=60)	p-value
Estimated Blood Loss (ml)	423.0±150.1	635.3±245.4	<0.05
No. of patients needed rescue oxytocin (IM)	0	6	<0.05
Complications	6	2	<0.05

The mean HR at T0 was the same in both groups. However, there was a significantly higher HR in group CT than in group C at time points T30, T1, and T2, respectively (P -value <0.05). At T0, there was no discernible difference in the MAPs of the two groups. There was no hypotension as defined, despite a significant reduction in MAP in group CT at T30 and T1 (p value <0.05). There was a statistically decrease in the mean total dose of mephentermine in group CT (23.8 ±12.0) than in the group (56.8 ± 8.60).

By employing a Likert scale to question the concerned obstetrician, uterine tonicity was objectively assessed. The Likert scale in group CT (2.3±0.11) was significantly higher than in group C (3.54±0.21). Both groups did not have chest discomfort or ECG abnormalities. Compared to two patients in group C, six patients in group CT complained of headaches and nausea.

Discussion

Most obstetric patients receive oxytocin prophylactically along with a uterine massage for the prevention and management of PPH. In addition to the uterus, oxytocin receptors (OTRs) are also present in the heart and main arteries. Vasodilation brought on by oxytocin results in tachycardia, an increase in stroke volume, and an increase in cardiac output (CO). Patients with reduced circulatory reserve may have negative effects from oxytocin administration since these effects are more pronounced when given as a bolus [14–19]. Myocardial ischemia could result from these hemodynamic adverse effects, particularly in patients with hypovolemia or cardiac conditions [20]. The American College of Obstetricians and Gynecologists (ACOG) consequently forbade the administration of bolus dosages of oxytocin and carbetocin [2]. However, FOGSI recommends that bolus injection of oxytocin 5 IU diluted to 5ml can be given over 1 min.[3]

A long-acting synthetic agonist counterpart of human oxytocin, carbetocin has uterotonic and antihemorrhagic properties. After being administered, carbetocin binds to and activates peripheral oxytocin receptors found on the smooth uterine musculature. This results in uterine contractions and stops excessive bleeding for 16 hours after childbirth. However, myocardial and peripheral blood arteries are where carbetocin has the least affinity [8,19]. After birth, the Society of Obstetricians and Gynecologists of Canada (SOGC) suggests administering a 100 mcg/ml bolus of carbetocin intravenously as a preventative measure.[7]

To the best of our knowledge, however, there aren't many studies that have used carbetocin as a uterotonic for the prophylactic prevention of PPH in elective caesarean sections, both in terms of the haemodynamic effects and the prevention of PPH. According to a recent study by Moertl et al.[21], patients treated with carbetocin experience less haemodynamic side effects than those treated with oxytocin.

Our research focused on preventing PPH following an elective caesarean delivery that used a preventive single bolus dose of carbetocin. Our short study's findings are quite positive and satisfying. Uterine contractility and intraoperative blood loss are the study main results. The immediate haemodynamic effects and negative consequences of carbetocin administration were the secondary outcome. According to a recent study by Moertl et al.[21], patients treated with carbetocin experience less haemodynamic side effects than those treated with oxytocin.

In our study, the carbetocin group experienced a total blood loss of 423.0±150.1 ml, while the control group saw a total blood loss of 635.3± 245.4 ml. There was a 200-milliliter discrepancy. The surgeon in the carbetocin group was really delighted with uterine contractility. In a study by Borruto et al., it was discovered that the mean blood loss following carbetocin administration was 30 ml lower than that following oxytocin administration (P = 0.5). With carbetocin, more patients (81 vs. 55%; P = 0.05) had blood losses under 500 ml.[22]. Early postpartum uterine involution was boosted by carbetocin. In the carbetocin group, rescue uterotonics were required in 2 cases, compared to 5 in the oxytocin group.

In our trial, none of the patients required extra uterotonics, as opposed to the six women who received oxytocin. KY Tse et al. examined the effectiveness of carbetocin and oxytocin infusions in lowering the need for further uterotonics or procedures in women who had caesarean sections and were at higher risk of postpartum hemorrhage. In women with significant placenta praevia or multiple pregnancies, they found that taking carbetocin initially decreased the requirement for extra uterotonics or procedures, as well as the rate of postpartum hemorrhage [23].

Dansereau et al. discovered that more women in the oxytocin group than the carbetocin group 24 required more oxytocin, comparing the effects of a single 100 mcg/ml dosage of carbetocin with those of a typical 8-hour infusion of oxytocin. In a similar study, Attilakos et al. compared the amount of extra oxytocin needed to prevent PPH and discovered that carbetocin is more efficient [11].

The worried surgeon used a Likert scale to rate uterine contraction, and the group receiving carbetocin performed better than the group receiving oxytocin. Boucher et al. investigation revealed that carbetocin promoted early postpartum uterine involution. More patients who received carbetocin at 0, 2, 3, and 24 hours had the fundus below the umbilicus [9]. In our study, mean blood loss was 200 ml less overall and 41 ml less in the carbetocin group. In our investigation, blood loss was quantified and estimated.[13]

Regarding hemodynamic alterations, there was an abrupt rise in HR that persisted for 2 minutes following carbetocin injection. Contrary to the oxytocin group, there was a drop in MAP immediately after carbetocin, but hypotension was not observed over the course of the session. Mephentermine was administered to the carbetocin group as a vasopressor at a lower total dose than to the oxytocin group. This was most likely caused by the fact that carbetocin reduces blood loss and has a lower affinity for peripheral blood vessels and cardiac epithelial cells. MG In their investigation, Moertl et al. examined the hemodynamic effects of carbetocin and oxytocin bolus dosages after elective caesarean sections, however they found no negative hemodynamic effects in either group. The outcomes matched what we found in research [21].

With a similar safety profile and less blood loss for the prevention of PPH, it was determined that a single bolus dosage of carbetocin appears to be more effective than a continuous infusion of oxytocin in maintaining normal uterine tone. The absence of a single obstetrician was one of the study's weaknesses. Due to the palpation technique being employed, the attending obstetrician's measurement of the uterine tone was therefore arbitrary and perhaps changeable. Furthermore, there is no alternative readily available, accurate, objective test for uterine tone measurement. Because the haematocrit was not calculated, a precise calculation of blood loss could not be made. We used quantitative methods, which are frequently used to quantify blood loss, to measure blood loss in the suction chamber and on surgical swabs.

The smallest effective or ideal amount of carbetocin needed to produce sufficient uterine tone was not found.

Conclusion

According to our study, a single bolus of carbetocin is more effective at preventing PPH after cesarean sections than a traditional oxytocin regimen and is also more hemodynamically stable.

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