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Original Research

To study 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: Postpartum hemorrhage (PPH), with an estimated fatality rate of 140 000 per year, is the leading cause of maternal death globally. "Active management of the third stage of labor" can stop the majority of them. An artificial, long-acting oxytocin counterpart, carbetocin was initially described in 1987. The purpose of this retrospective observational study was to evaluate the effectiveness of carbetocin in preventing blood loss and primary postpartum hemorrhage (PPH) following cesarean births in a tertiary hospital. **Methods:** Both prophylactic treatments with and without carbetocin were applied to eligible gravid women (27–41 weeks gestation) for whom data were available. The main outcome was blood loss, which was determined by intrapartum/intraoperative, postpartum (recovery room), and primary PPH incidence rates. **Results:** 529 deliveries were assessed in total. Maternal age (29 years), BMI (26 kg/m2), and parity (1.4) were comparable between those treated with and without carbetocin for cesarean deliveries. Between cesarean deliveries with and without carbetocin prophylaxis, there was a significant reduction in intraoperative and total blood loss (< 0.001). PPH was considerably lower in cesarean deliveries with [23 (6.7%)] than those without [67 (19.7%); p= 0.006]. Prophylactic carbetocin administration. **Conclusion:** Compared to the conventional oxytocin regime, a single bolus dosage of carbetocin is more effective at preventing PPH after caesarean surgery and is hemodynamically stable.
Keywords: Carbetocin, Elective caesarean, postpartum haemorrhage, oxytocic drugs, spinal anaesthesia.

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INTRODUCTION

Postpartum hemorrhage (PPH) is the loss of more than 500 ml of blood following a vaginal delivery or more than 1000 ml following a cesarean section, according to the World Health Organization.[1] Despite the advancement and application of fetal-maternal care in contemporary obstetrics, PPH continues to be the world's leading cause of maternal death.[2, 3]. A woman dies worldwide from PPH every eight minutes, according to estimates that it causes 68,000 maternal fatalities each year.[2] Although some studies suggest that it can complicate up to 15% of deliveries, the incidence of PPH is higher than 5% in developed countries[4-7]. In addition, alarming increases have been reported in some nations, including Canada,[8] the United States[9], Australia[10], and Ireland [11], which cannot entirely be attributed to increases in very well-known risk factors like pregnancies following assisted reproductive technologies, advanced maternal age, multiple pregnancies, or cesarean sections. PPH is primarily caused by uterine atony, which can be reduced by up to 60% with uterotonic medications (oxytocin and misoprostol in the first line, followed by ergot alkaloids and prostaglandins in the second line) [12, 13]. The review of these medications and the search for new uterotonics that have the same safety profile

as the more widely used oxytocin and are more or equally effective at preventing PPH and reducing the need for therapeutic uterotonics have received special attention over the past 20 years because of this. A carba-1-deamino alkylated oxytocin analog is carbetocin. Similar to oxytocin, it has the same receptor [14]. The molecule has a half-life of up to 42 9 min, which is 4–10 times longer than that of oxytocin [15,16] thanks to the N-terminal region's deamination, which shields it from aminopeptidase activity and the change of the bridge 1-6 disulfide by a methylene group of the disulfidases [14,15].A single dosage of carbetocin has been proposed to function as a 16-hour intravenous oxytocin infusion in the case of elective caesarean section (CS), boosting uterine tone and reducing the risk of PPH.[17] According to some study, carbetocin may be a good substitute for oxytocin when it comes to preventing postpartum hemorrhage. The first step in primary prevention [18–20] is to identify recognized PPH risk factors. The current study sought to ascertain the effectiveness of carbetocin in lowering blood loss and primary PPH during cesarean deliveries in a tertiary hospital in light of the aforementioned context.

MATERIALS AND PROCEDURES

STUDY DESIGN

In this retrospective observational study, women who were given carbetocin (Duratocin, Ferring Pharmaceuticals, Inc., SaintPrex, Switzerland) or any other uterotonic medication as a preventative measure for active management of third-stage labor (AMTSL) during cesarean delivery were assessed for blood loss and the prevalence of primary PPH. Data from a tertiary hospital were examined. For eligible gravid women who underwent a CS, the hospital database was checked. They were divided into two groups: those who got prophylactic carbetocin for PPH prophylaxis and those who did not. By evaluating the intra- and postoperative blood loss during CS, either with or without carbetocin prophylaxis, the primary outcome was to ascertain the blood loss and incidence of primary PPH.

PARTICIPANTS

The analysis covered all women who underwent CS and had gestations longer than 27 weeks (27-41 weeks). Complete information about their age, gestational week number, height, weight, intrapartum period, postpartum period, and follow-up examination four to six weeks after delivery had to be available. Heart disease, hypertension, and preeclampsia in women were prohibited. After the baby was successfully delivered by CS, carbetocin was given intravenously (IV) in the form of a 100 mg (1 mL) bolus over the course of one minute. Before or after placenta delivery, carbetocin may be injected. According to hospital protocol, women who weren't given prophylactic carbetocin received an appropriate level of care with a single dosage of oxytocin (5 U). Following that, the attending nurses estimated intrapartum blood loss and measured it every half-hour during the postpartum observation period, including two hours in the recovery room. This was done by weighing the absorbency of the gauze and pads. 500 mL of blood were lost after vaginal deliveries and 1000 mL with cesarean sections as signs of PPH. Repeat carbetocin, oxytocin, or intramuscular ergonovine were used to treat women with PPH.

STATISTICAL ANALYSIS

Utilizing SPSS Statistics for Windows, version 25.0 (SPSS Inc., Chicago, IL, USA), statistical analysis was carried out. Chi-square tests (with continuity corrections in the case of 2× 2 tables) and Student t tests for categorical and continuous variables were used to compare groups.

RESULTS

Based on the eligibility requirements, 340 out of a total 529 deliveries were evaluated and included in the study. Between the groups treated with and without prophylactic carbetocin for cesarean deliveries, maternal characteristics like the mean age (29 years), mean body mass index (26 kg/m2), and mean parity (1.4) were generally comparable (Table 1). Women treated with [612.9 mL] versus [853.4 (371.96) mL; p <0.0001] carbetocin prophylaxis experienced significantly decreased mean (SD) blood loss during CS. Similar amounts of blood were lost in the postoperative recovery area whether patients were given carbetocin prophylaxis or not. Women who received carbetocin prophylaxis compared to those who did not experienced significantly less overall blood loss (p <0.001).(Figure 1) The data showed that the incidence of PPH was significantly lower for women treated with carbetocin prophylaxis compared with that in women without (23 [6.7%] vs. 67 [19.7%], Pearson Chi-square with continuity correction, (p = 0.006) (Table 2)). As a result, carbetocin prophylaxis demonstrated considerable benefits in lowering the risk of PPH.

Table 1: Characteristics of the study population

Characteristic	With carbetocin (n =120)	Without carbetocin (n =220)	P value
Maternal age (y)	30.39 (3.63)	29.48 (3.31)	0.039
BMI (kg/m2)	25.75 (3.9)	26.58 (4.5)	0.499
Parity	1.36 (0.54)	1.49 (0.65)	0.121

Figure 1: Postpartum blood loss with and without use of prophylactic carbetocin during cesarean delivery.

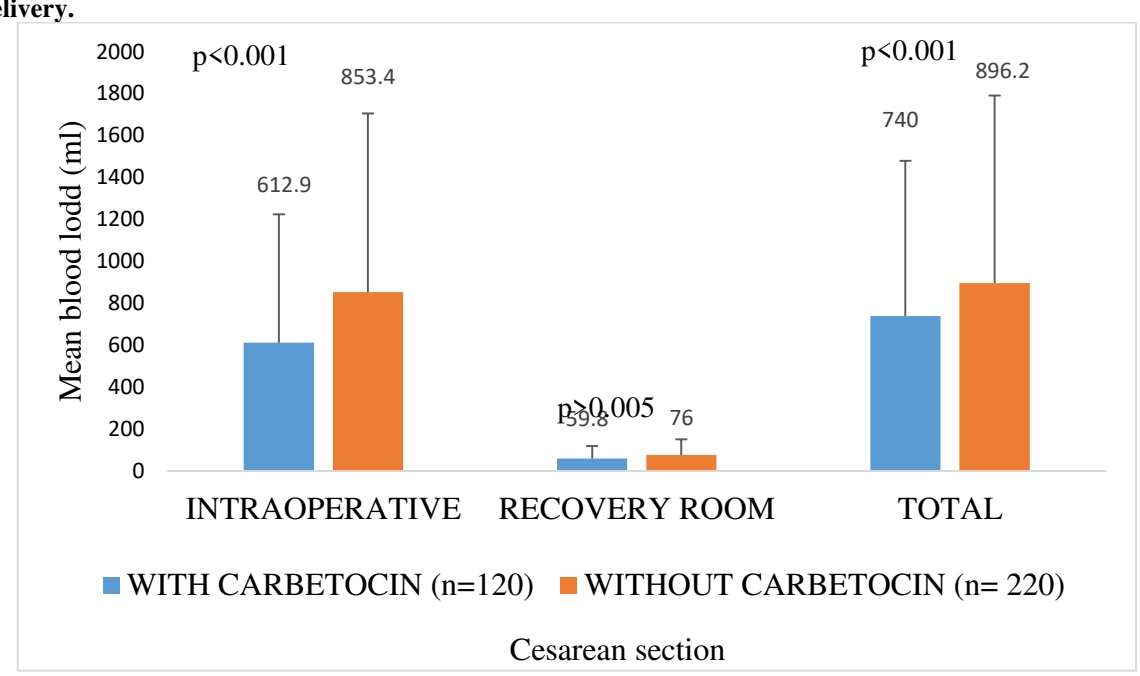

Table 2: Incidence of primary postpartum hemorrhage (PPH) with and without prophylactic carbetocin: cross-tabulation for cesarean deliveries.

Cesarean delivery	No PPH	PPH	Total
With carbetocin	97 (28.5)	23(6.7)	120(35.2)
Without carbetocin	153(45)	67(19.7)	220(64.8)
Total n (%)	250 (73.5)	90 (26.4)	340(100.0)

Pearson Chi-square, p= 0.004.
Pearson Chi-square with continuity correction, p=0.006.

DISCUSSION

Oxytocin and uterine massage are typically given to pregnant patients to treat and prevent PPH. OTRs are found in the heart, major arteries, and uterus. The effects of oxytocin include an increase in tachycardia, stroke volume, and cardiac output (CO). Patients with insufficient cardiovascular reserve may experience stronger effects from oxytocin boluses [21–23]. Myocardial ischemia may be brought on by hemodynamic side effects, particularly in cardiac or hypovolemic individuals.[24] Oxytocin and carbetocin bolus doses were prohibited by the American College of Obstetricians and Gynecologists (ACOG). The FOGSI suggests administering 5 IU of diluted oxytocin in a 1-minute bolus.[25] In a tertiary hospital in Taiwan, this retrospective observational study assessed the actual effectiveness of carbetocin in lowering blood loss and the incidence of primary PPH during vaginal and cesarean deliveries. The group studied had a mean maternal age of 29.9 years. The findings were in line with the literature that is currently available for AMTSL in combination with carbetocin for cesarean deliveries[18,19,20,21,26,27]. Prophylactic carbetocin administration greatly reduced CS blood loss, which was reflected in the large reduction in overall blood loss. The Society of Gynecologists and Obstetricians of Canada (SOGC)[28].The SOGC advises using carbetocin as a 100-mg IV bolus administered over 1 minute rather than a continuous oxytocin infusion during elective CS to prevent PPH.[6] Additionally, despite the crucial policies and programs, a PPH and preeclampsia/eclampsia survey from 37 countries revealed that despite potential gaps in the programs' implementation[29] .Examining the specific third-stage management components is crucial, according to a review of seven studies contrasting the efficiency of active vs expectant management of the third stage of labor. A significant multicenter experiment conducted by the World Health Organization in 2012 underscored the significance of an effective uterotonic agent and emphasized that uterotonics continue to be the major intervention. Controlled cord traction and uterine massage may give a negligible or no benefit to the prevention of PPH in women who have had a uterotonic, respectively.[30] Although the amount of blood loss is a clear indication of effectiveness, the need for additional uterotonic medications is also a crucial indicator of uterine tone and blood loss. Using prophylactic carbetocin instead of prophylactic oxytocin (5 IU) for cesarean deliveries was related with a lesser requirement for further oxytocic medications in a double-blind, randomized, single-center research in the United Kingdom.[19] Similar to this, in a small, prospective, controlled trial of

cesarean deliveries with at least one risk factor for PPH, carbetocin was found to be equally safe and effective in maintaining uterine tone, with the added benefit of reducing postoperative pain perception.[26] With a similar hemodynamic profile and a little antidiuretic impact, carbetocin was also found in a prospective case-control study of cesarean deliveries to be more efficient in reducing extra uterotonic needs than a continuous infusion of oxytocin.[18] In a double-blind, randomized study of cesarean deliveries, carbetocin was equally as effective as, and more dependable than, a continuous infusion of oxytocin in preserving enough uterine tone and preventing excessive intraoperative blood loss following placenta release.[17] Despite the fact that the findings of this observational study are consistent with the literature on cesarean deliveries, we list a number of potential limitations, including the retrospective study design and data from a single center in ---------. Limitations include the absence of segmentation based on maternal risk factors, age, and the use of assisted delivery (forceps or vacuum). Although cesarean deliveries are on the rise globally and continue to be a major risk factor for PPH, the results of this observational study are encouraging and show that carbetocin is effective in reducing blood loss and PPH.[31]

CONCLUSION

According to the current study, using carbetocin as a preventative measure after cesarean deliveries resulted in a notable reduction in blood loss. Therefore, the incidence of PPH during caesarean deliveries was significantly reduced by the prophylactic use of carbetocin.

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