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Original Research Article

Comparative efficacy of carbetocin versus oxytocin in preventing postpartum hemorrhage during lower segment cesarean section: a prospective randomized controlled trial

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ABSTRACT

Background: This study was conducted to compare the efficacy of a single-dose carbetocin with oxytocin infusion in preventing postpartum hemorrhage (PPH) during lower segment cesarean section (LSCS).
Methods: A prospective randomized controlled trial was conducted on 120 pregnant women undergoing elective or emergency LSCS at a tertiary care hospital in the state of Maharashtra. The study participants were randomly assigned to receive either a single intravenous dose of 100 µg carbetocin (n=60) or 20 IU oxytocin infusion (n=60) after delivery of the baby. The primary outcome assessed was the incidence of PPH (blood loss ≥1000 ml) whereas the secondary outcomes included mean blood loss, need for additional uterotonics and blood transfusion requirements.
Results: The incidence of PPH was significantly lower in the carbetocin group (3.3%) compared to the oxytocin group (15.0%) (p=0.026). The mean blood loss was 435.2±152.8 ml in the carbetocin group versus 624.7±218.4 ml in the oxytocin group (p<0.001). Additional uterotonics were required in 5% of patients in the carbetocin group versus 18.3% in the oxytocin group (p=0.021). Blood transfusion was needed in 1.7% of women in the carbetocin group compared to 8.3% in the oxytocin group (p=0.048).
Conclusions: A single-dose carbetocin is more effective than oxytocin infusion in preventing PPH during LSCS, with reduced requirement for additional uterotonics and blood transfusions.

Keywords: Carbetocin, Cesarean section, Oxytocin, Postpartum hemorrhage, Uterotonic

INTRODUCTION

Postpartum hemorrhage (PPH) remains a leading cause of maternal mortality worldwide, accounting for 20% of the global maternal deaths annually.[1] In India, PPH contributes to approximately 38% of maternal mortality, with a higher incidence reported following cesarean deliveries compared to vaginal births.[2] The increasing rate of cesarean sections globally further underscores the importance of effective PPH prevention strategies.[3]

Uterine atony i.e. the failure of the uterus to contract adequately after delivery, is responsible for approximately 70-80% of PPH cases.[4] Current standard practice for preventing PPH during cesarean section involves the administration of oxytocin, a synthetic peptide that stimulates uterine contractions. However, oxytocin has a short half-life (4-10 minutes), necessitating continuous infusion to maintain uterine tone.[5] Carbetocin, a synthetic analogue of oxytocin with structural modifications, has a longer half-life

(approximately 40 minutes) and provides prolonged uterine contractions after a single dose.[6] This pharmacological advantage could potentially translate into improved clinical outcomes in terms of PPH prevention. Despite mention of this theoretical benefit of carbetocin, limited data exists comparing carbetocin with oxytocin for PPH prevention during cesarean sections in the Indian population, especially in the state of Maharashtra. The World Health Organization (WHO) has recognized the potential of carbetocin in reducing PPH and has included it in its recommendations for PPH prevention.[7] However, more evidence is needed from diverse population to establish its efficacy and cost-effectiveness compared to conventional oxytocin regimens.

This study aimed to compare the efficacy of a single dose of carbetocin with oxytocin infusion in preventing PPH during LSCS. The study findings could contribute to the development of evidence-based protocols for PPH prevention in the Indian context.

Aim and objectives

Primary objective

To compare the efficacy of a single-dose carbetocin (100 µg) with oxytocin infusion (20 IU) in preventing PPH during LSCS.

Secondary objectives

To compare the mean blood loss during LSCS between carbetocin and oxytocin study groups. To evaluate the need for additional uterotonics in both groups. To assess blood transfusion requirements in both groups. To compare the difference in pre- and post-operative hemoglobin levels between the two groups.

METHODS

Study design and setting

After obtaining ethical clearance from Institutional Ethics Review Committee, this prospective, randomized, controlled trial was conducted in the department of obstetrics and gynecology in a tertiary care hospital of Maharashtra, over the period of one year (01 June 2023 to 31 May 2024). Based on previous studies showing a PPH incidence of approximately 18% with oxytocin and an expected reduction to 5% with carbetocin with a power of 80% and significance level of 5%, the minimum sample size required for this study was calculated to be 58 study subjects per group.[8,9] Accounting for potential dropouts, we enrolled 60 participants in each study group. The inclusion criteria for study participants were- women aged 20-40 years with singleton pregnancy at ≥37 weeks of gestation undergoing elective or emergency LSCS under spinal anesthesia. The exclusion criteria were- multiple pregnancy, placenta previa, placental abruption, previous uterine surgery except cesarean section, past history of PPH, pre-eclampsia, eclampsia, coagulation disorders, anemia (Hb<8 gm/dl), intrauterine fetal death, known hypersensitivity to carbetocin or oxytocin, and contraindications to spinal anesthesia.

Randomization and blinding

Randomization was performed using computer-generated random numbers. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes containing the group assignment, which were opened by the anesthesiologist just before drug administration. The participants and the outcome assessors were blinded to the group allocation, while the anesthesiologist administering the drug was aware of the intervention.

Intervention

After obtaining written informed consent from the study participants, they were randomly assigned to one of the two groups:

Carbetocin group (n=60)

Received a single intravenous dose of 100 µg carbetocin over one minute after delivery of the baby.

Oxytocin group (n=60)

Received 20 IU oxytocin in 500 ml of Ringer's lactate solution as an intravenous infusion over 30 minutes after delivery of the baby, followed by 20 IU in 500 ml over the next 8 hours.

All cesarean sections were performed using a standardized surgical technique. The placenta was delivered by controlled cord traction in all cases. Blood loss was measured from the time of placental delivery until completion of skin closure using a calibrated under-buttocks drape and by weighing soaked sponges (1 gm = 1 ml of blood).

Outcome measures

The primary outcome was the incidence of PPH, defined as a blood loss ≥1000 ml during cesarean section. Secondary outcomes included mean blood loss, need for additional uterotonics (methylergometrine, prostaglandin F2α, or misoprostol), blood transfusion requirements, and the difference between pre-operative (within 24 hours before surgery) and post-operative (24 hours after surgery) hemoglobin levels.

Data collection

Demographic data, obstetric history, indication for cesarean section, and relevant clinical parameters were recorded using a standardized data collection form. Hemoglobin levels of study subjects were measured using

an automated analyzer within 24 hours before and 24 hours after surgery.

Statistical analysis

The study data obtained was analyzed using SPSS version 25. The categorical variables were presented as frequencies and percentages and were compared using Chi-square or Fisher's exact test as appropriate. Continuous variables were presented as mean±standard deviation and compared using Student's t-test or Mann-Whitney U test based on the normality of distribution. A p value <0.05 was considered statistically significant.

RESULTS

A total of 138 women were assessed for eligibility of this study, of whom 120 were included in the study and randomized to either the carbetocin group (n=60) or oxytocin (n=60) group. All participants completed the study protocol and were included in the final analysis.

Table 1: Demographic and baseline characteristics of study participants.

Characteristics	Carbetocin group (n=60)	Oxytocin group (n=60)	P value
Age (years)	27.4±4.2	28.1±4.5	0.384
BMI (kg/m²)	26.2±3.1	25.8±3.4	0.498
Gestational age (weeks)	38.3±1.2	38.5±1.1	0.333
Parity			
Primigravida	18 (30.0%)	16 (26.7%)	0.687
Multigravida	42 (70.0%)	44 (73.3%)	
Type of cesarean section			
Elective	38 (63.3%)	40 (66.7%)	0.699
Emergency	22 (36.7%)	20 (33.3%)	
Indication for cesarean section			
Previous CS	32 (53.3%)	35 (58.3%)	0.832
Fetal distress	10 (16.7%)	8 (13.3%)	
Cephalopelvic disproportion	8 (13.3%)	9 (15.0%)	
Breech presentation	6 (10.0%)	5 (8.3%)	
Others	4 (6.7%)	3 (5.0%)	
Pre-operative Hb (gm/dl)	11.2±1.1	11.4±1.2	0.327
Duration of surgery (minutes)	48.6±8.7	47.9±9.1	0.671

Data presented as mean±SD or number (percentage). BMI: body mass index; CS: cesarean section; Hb: hemoglobin

Table 2: Incidence of postpartum hemorrhage in study participants.

Outcome	Carbetocin group (n=60)	Oxytocin group (n=60)	P value
PPH (≥1000 ml)	2 (3.3%)	9 (15.0%)	0.026*

*Statistically significant (p<0.05)

Table 3: Secondary outcomes.

Outcomes	Carbetocin group (n=60)	Oxytocin group (n=60)	P value
Mean blood loss (ml)	435.2±152.8	624.7±218.4	<0.001*
Need for additional uterotonics	3 (5.0%)	11 (18.3%)	0.021*
Blood transfusion required	1 (1.7%)	5 (8.3%)	0.048*
Pre-operative Hb (gm/dl)	11.2±1.1	11.4±1.2	0.327
Post-operative Hb (gm/dl)	10.4±1.0	10.1±1.1	0.119
Drop in Hb (gm/dl)	0.8±0.3	1.3±0.5	<0.001*

Data presented as mean±SD or number (percentage). Hb: hemoglobin; *Statistically significant (p<0.05)

Both the study group participants were comparable in terms of their age, body mass index (BMI), gestational age, parity, and indication for cesarean section. The most common indication for cesarean section in both groups was previous cesarean section.

Primary outcome

The incidence of PPH (blood loss ≥1000 ml) was significantly lower in the carbetocin group compared to the oxytocin group (3.3% versus 15.0%, p=0.026) (Table 2).

Secondary outcomes

The mean blood loss was significantly lower in the carbetocin group (435.2±152.8 ml) compared to the oxytocin group (624.7±218.4 ml) (p<0.001) (Table 3).

The need for additional uterotonics was significantly lower in the carbetocin group (5.0%) compared to the oxytocin group (18.3%) (p=0.021). Similarly, blood transfusion requirements were significantly lower in the carbetocin group (1.7%) compared to the oxytocin group (8.3%) (p=0.048).

The drop in hemoglobin level (difference between pre-operative and post-operative values) was significantly lower in the carbetocin group (0.8±0.3 gm/dl) compared to the oxytocin group (1.3±0.5 gm/dl) (p<0.001).

DISCUSSION

Postpartum hemorrhage remains a significant cause of maternal morbidity and mortality worldwide, particularly in a developing country like India.[2] Effective pharmacological interventions for preventing PPH are essential to improve maternal outcomes, especially during cesarean deliveries where the risk of hemorrhage is higher as compared to vaginal births.[10,11] Our study demonstrated that a single dose of 100 µg carbetocin is more effective than 20 IU oxytocin infusion in preventing PPH during LSCS. The incidence of PPH was significantly lower in the carbetocin group (3.3%) compared to the oxytocin group (15.0%), representing an 11.7% absolute risk reduction and a relative risk reduction of 78%. This finding is consistent with previous studies that have reported superior efficacy of carbetocin over oxytocin in preventing PPH during cesarean section.[12,13] A study conducted in Patna by Kumari et al in 2023 has also concluded that a single injection of carbetocin is more effective than a continuous oxytocin infusion for prevention of PPH.[14] A study conducted at Government Medical College, Mahbubnagar by Priya et al in 2023 has demonstrated that carbetocin has greater efficacy in preventing PPH in high-risk women undergoing cesarean sections, as compared to oxytocin.[15]

Attilakos et al conducted a double-blind randomized controlled trial comparing carbetocin with oxytocin for prevention of PPH during cesarean section and found that women who received carbetocin had a significantly lower need for additional uterotonics (33.5% versus 45.5%, p=0.023).[16] Our study showed an even more pronounced difference, with only 5.0% of women in the carbetocin group requiring additional uterotonics as compared to 18.3% in the oxytocin group.

The mean blood loss in our study was significantly lower in the carbetocin group (435.2 ml) as compared to the oxytocin group (624.7 ml), representing a mean difference of 189.5 ml. This substantial reduction in blood loss with carbetocin is clinically relevant, especially in settings where women may have pre-existing anemia or limited access to blood transfusion services.[17] The lower mean blood loss with carbetocin could be attributed to its longer half-life and sustained uterotonic effect, which provides prolonged uterine contractions after a single dose.[18]

The drop in hemoglobin level was significantly lower in the carbetocin group as compared to the oxytocin group, which corroborates our finding of reduced blood loss with carbetocin. This is particularly important in the Indian context, where the prevalence of anemia among pregnant women is high, and even a small reduction in blood loss can have significant clinical implications.[19]

The need for blood transfusion was significantly lower in the carbetocin group (1.7%) compared to the oxytocin group (8.3%), which further supports the superior efficacy of carbetocin in preventing significant hemorrhage during cesarean section. This finding has important implications for resource-limited settings where blood products may be scarce or carry risks of transfusion-related complications.[20]

Su et al. conducted a Cochrane systematic review comparing carbetocin with other uterotonics for preventing PPH and concluded that carbetocin was associated with a reduced need for additional uterotonics compared to oxytocin (RR 0.62, 95% CI 0.44-0.88).[21] Our study findings are consistent with this review and provide additional evidence for the superior efficacy of carbetocin in the Indian population.

The WHO has included carbetocin in its recommendations for PPH prevention, particularly highlighting its potential benefits in settings where oxytocin requires cold chain storage[7]. Carbetocin's heat-stable formulation and single-dose administration make it particularly suitable for use in low- and middle-income countries like India, where logistical challenges in drug storage and administration may exist.[22]

Although not a focus of our study, it is worth noting that a single-dose administration of carbetocin offer practical advantages over the continuous infusion required for oxytocin. This simplifies drug administration, reduces the workload for healthcare providers and potentially decreases the risk of medication errors associated with infusion setup and monitoring.[23]

Our study adds to the growing body of evidence supporting the use of carbetocin for PPH prevention during cesarean section. The significant reduction in PPH incidence, mean blood loss, need for additional uterotonics, and blood transfusion requirements with carbetocin demonstrates its potential to improve maternal outcomes in the Indian setting.

Our study has certain notable limitations. This study was conducted in a single tertiary care hospital, which may

limit the generalizability of the findings to other healthcare settings. The relatively small sample size, while adequately powered for primary outcomes, restricts subgroup analysis based on patient comorbidities or cesarean section indications. Additionally, the study did not assess long-term maternal outcomes or cost-effectiveness of carbetocin versus oxytocin, which warrants further investigation in multicentric trials.

CONCLUSION

Single-dose carbetocin (100 µg) is more effective than oxytocin infusion (20 IU) in preventing PPH during LSCS. Carbetocin is associated with significantly reduced blood loss, lower requirement for additional uterotonics and decreased need for blood transfusion compared to oxytocin. These findings suggest that carbetocin should be considered as a first-line uterotonic agent for PPH prevention during cesarean deliveries, particularly in settings with a high prevalence of anemia and limited resources. There is scope for further research in terms of studies on the cost-effectiveness of carbetocin compared to oxytocin in resource-limited settings and its potential role in reducing maternal morbidity and mortality associated with PPH.

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