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Original Research Article

Carbetocin versus oxytocin in primigravida for active management of third stage of labor: a prospective study

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ABSTRACT

Background: Postpartum haemorrhage (PPH) stands as a prominent global contributor to maternal mortality. Oxytocin's short half-life and heat sensitivity pose challenges in resource-limited areas. Carbetocin, not requiring cold storage, is utilized in third-stage labor management. Consequently, this study aimed to compare the effectiveness of carbetocin with oxytocin in third-stage labor management.
Methods: In this prospective study of 200 primigravida patients, group A received heat-stable carbetocin (100 µg), while group B received oxytocin (10 IU) postpartum. Primary outcome such as mean blood loss in ml and Secondary outcomes such as proportion with blood loss >500 ml, need for uterotonic agents, blood transfusion, surgical PPH management, and drop in haemoglobin after 48 hours were recorded and compared.
Results: Groups A and B, comparable in age, blood pressure, and mild anaemia, exhibited significant gestational age differences ($p<0.0001$). Group B had higher mean blood loss (377.68 ml) than group A (345.34 ml) with a significant $p=0.0118$*. Side effects showed no differences among groups. Postpartum, group B saw a significant 7% incidence of haemorrhage compared to none in group A ($p=0.0071$).
Conclusions: Carbetocin showed superiority over oxytocin in the active management of third stage of labor, exhibiting a statistically significant reduction in PPH incidence and decreased requirement for additional uterotonic drugs.

Keywords: PPH, Active management of third stage of labor, Oxytocin, Carbetocin, Vaginal delivery, Uterotonic agents

INTRODUCTION

Postpartum hemorrhage (PPH) is a leading cause of maternal morbidity and mortality worldwide. Recognition of PPH is challenging, but once hemorrhage is recognized, management needs to focus on achieving adequate uterine tone and maintaining maternal hemodynamic stability. There have been several advances in the management of postpartum hemorrhage, many of which can be implemented at the labor and delivery unit level. PPH, occurring in 5% to 10% of deliveries, stands as a foremost contributor to maternal mortality globally.[1,2] To address this, international guidelines advocate for preventive uterotonic injections, with oxytocin and carbetocin being the most commonly used agents.[3,4] Traditionally, carbetocin finds its predominant use after cesarean deliveries, primarily due to trials conducted in high-income countries focusing on its effectiveness in such scenarios.[5] However, recent investigations have extended their scope to include carbetocin's efficacy after vaginal deliveries, especially in low- and middle-income countries. One notable study in this context is the CHAMPION (CardioMEMS heart sensor allows monitoring of pressure to improve outcomes in NYHA class III heart failure patients) randomized controlled trial.[6-8] This trial demonstrated that carbetocin was comparable to oxytocin in preventing blood loss of at least 500 mL or the need for additional uterotonic agents. Nevertheless, due to a lack of statistical power, noninferiority for blood loss exceeding 1000 mL could not be conclusively established.[7] While the use of carbetocin after vaginal deliveries has shown promise in high-income countries several studies underscore certain limitations.[8-10]

These include variability in outcomes depending on the study, inadequate assessment of severe maternal morbidity, small sample sizes, and variations in interventions within control groups, encompassing different uterotonics, doses, and routes of administration.[11] The rationale for conducting this study lies in the critical importance of addressing PPH, a leading cause of maternal mortality worldwide. Despite preventive measures advocated by international guidelines, such as uterotonic injections, variations in efficacy and limitations in the existing evidence base warrant further investigation. Specifically, the traditional use of carbetocin after cesarean deliveries and its recent exploration in low- and middle-income countries after vaginal deliveries underscore the need for a comprehensive evaluation of its effectiveness. Henceforth, we aimed to compare the effectiveness of carbetocin with oxytocin in third-stage labor management.

METHODS

This prospective study was conducted at the department of gynaecology and obstetrics, Al-Ameen medical college and hospital, Vijayapur, Karnataka, India, from January 2021 to September 2021. Ethical clearance and informed consent were obtained before enrolling 200 singleton pregnant women with a gestational age of 36 weeks or more, confirmed by both last menstrual period and ultrasound. Exclusions included individuals with placenta previa, multiple gestation, placental abruption, hypertensive disorders, preeclampsia, known cardiac, renal, liver diseases, epilepsy, moderate anaemia, and those unwilling to participate. Cases were randomly assigned sequential numbers through computer-generated randomization. During the study, 100 women received a single intravenous dose of 100 µg carbetocin, while the remaining 100 received 10 IU of oxytocin post-vaginal delivery, adhering to WHO guidelines for the third stage of labor management. Blood collection using a BRASSS-V Drape was initiated immediately after clamping and cutting the umbilical cord, with a collection period of 1 hour (extended to 2 hours if bleeding persisted beyond 1 hour). Primary outcome measurement involved quantifying blood loss in milliliters. Secondary outcome measures included the proportion of women with postpartum blood loss exceeding 500 ml, the proportion requiring additional uterotonic agents, the proportion requiring blood transfusion, the proportion requiring additional surgical management for PPH, and the drop in haemoglobin percentages estimated 48 hours after delivery.

Statistical analysis

The data obtained from the study were subjected to statistical analysis using SPSS version 20.0 for further evaluation at the significance level of p=0.05. The data were presented as mean ± standard deviation for continuous variables and frequency for categorical variables. For categorical data, Chi square statistical analysis was done, and for continuous data student's t-test and Fishers were performed.

RESULTS

The mean age in group A was 24.9±3.7 years, while in group B, it was 24.5±3.8 years. There was no statistically significant difference in age between the two groups (p=0.4516). Mild anaemia was observed in 39% of participants in group A and 45% in group B, with no significant difference (p=0.7576). No significant difference was observed among group A (113±5.9 mmHg and 77±5.0 mmHg) and group B (113±2.4 mmHg and 75±12.2 mmHg) in both Systolic and Diastolic blood pressure. The gestational age in group A was 38.02±1.5 weeks, whereas in group B, it was 39±1.8 weeks. The difference in gestational age was highly significant (p<0.0001*). (Table 1 and Figure 1). The Table 2 presents outcomes of third stage labor for two groups. Group B exhibited a higher mean blood loss of 377.68±98.57 ml compared to group A, which had a mean blood loss of 345.34±80.54 ml. This dissimilarity in blood loss was statistically significant (p=0.0118*). Additionally, the haemoglobin counts after 48 hours differed between the groups (p=0.0366*) (Figure 2). The incidence of side effects in two groups was minimal. Abdominal pain was reported by 1% of participants in both group A and group B, suggesting a comparable experience of abdominal pain between the two groups. The data implies that the incidences of side effects were rare and comparable between groups with no significant differences (Table 3) In the context of PPH, a distinct difference in outcomes was recorded. None of the participants in group A experienced PPH. In contrast, 7% of participants in group B encountered PPH (Table 4).

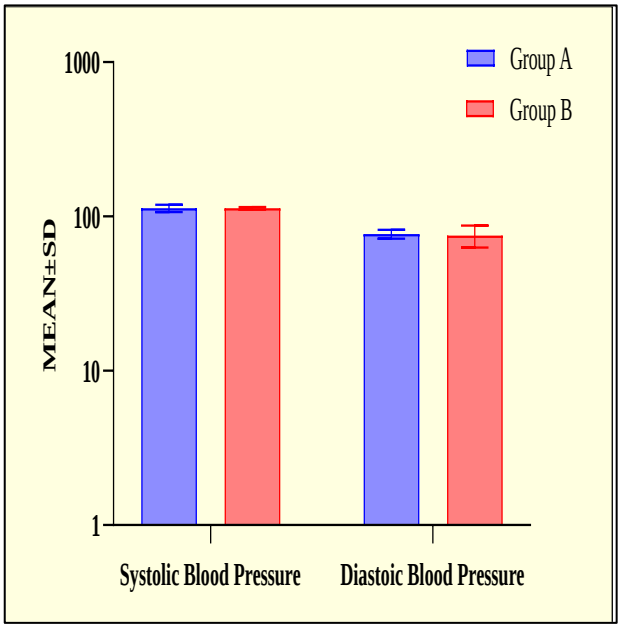

Figure 1: Blood pressure of the enrolled participants among groups.

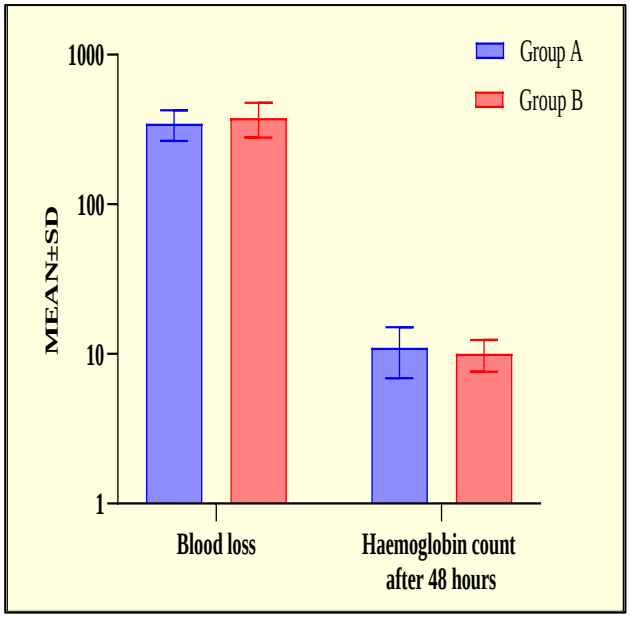

Figure 2: Blood loss and haemoglobin count of the enrolled participants among groups.

Table 1: Baseline characteristics of the enrolled participants among groups, (n=200).

Variables	Group A, (n=100) mean± SD	Group B, (n=100) mean± SD	P value
Age (In years)	24.9±3.7	24.5±3.8	t=0.7542, p=0.4516
Mild anaemia, n (%)	39 (39)	45 (45)	p=0.7576
Gestational age	38.02±1.5 weeks	39.00±1.8 weeks	t=4.183, p<0.0001*

Student's t test

Table 2: Outcomes of third stage of labour of the enrolled participants among groups.

Outcomes	Group A, (n=100) (%)	Group B, (n=100) (%)	P value
Massive blood loss (>500 ml)	0 (0)	6 (6)	0.1818
Fundal massage required	0 (0)	9 (9)	0.0294*
Blood transfusion	0 (0)	2 (2)	>0.9999
Need for additional uterotonics	8 (8)	15 (15)	0.3726
Additional surgical procedure required	0 (0)	2 (2)	>0.9999

Fisher's test

Table 3: Side effects reported by the enrolled participants among groups.

Side effects	Group A, (n=100) (%)	Group B, (n=100) (%)	P value
Abdominal pain	1 (1)	1 (1)	>0.9999
Headache	1 (1)	2 (2)	>0.9999

Fisher's test

Table 4: PPH in the enrolled participants among groups.

PPH	Group A, (n=100) (%)	Group B, (n=100) (%)	P value
Yes	0 (0)	7 (7)	X^2=7.254, p=0.0071*
No	100 (100)	93 (93)	

*Chi-square test

DISCUSSION

The Present study has showed the superior efficacy of carbetocin over oxytocin in mitigating blood loss during the active management of the third stage of labor. Additionally, carbetocin was found to decrease the requirement for supplementary uterotonics, uterine massage, and substantial blood loss in the active management of the third stage of labor following vaginal delivery. In the present study, the average age within group A was 24.9±3.7 years, compared to 24.5±3.8 years in group B. Reyes and Gonzalez et al reported mean ages of 26.5 years for participants in the carbetocin group and 26.7 years in the oxytocin group.[12] Ashraf et al documented mean ages of 23.9±3.2 years for the carbetocin group and 23.3±3.2 years for the oxytocin group, providing additional perspectives on the age distribution in these interventions.[13]

In the current study, the mean age within group A was 24.9±3.7 years, while in group B, it was 24.5±3.8 years. Notably, Reyes and Gonzalez et al found that participants in the carbetocin group had a mean age of 26.5 years, while those in the oxytocin group had a mean age of 26.7 years.[12] Ashraf et al reported mean ages of 23.9±3.2 years and 23.3±3.2 years for the carbetocin and oxytocin groups, respectively, contributing further insights into the age profiles associated with these interventions.[13]

In the current study, the gestational age emerged as a highly significant factor, with group A and group B exhibiting gestational ages of 38.02±1.5 and 39.00±1.8 weeks, respectively. Correspondingly, Maged et al found that the average gestational ages were 39.4±1.3 weeks in the carbetocin group and 39.2±1.4 weeks in the oxytocin group, closely mirroring the findings of this study.[8] Furthermore, an additional study showed comparable gestational ages of 39.01±1.1 weeks in carbetocin group and 39.09±1.7 weeks in oxytocin group.[13]

Within this study, occurrence of side effects in both groups was minimal. Specifically, abdominal pain was noted by 1% of participants in each group, while headaches reported by 1% in group A and 2% in B. Consistent with these findings, previous studies, including one by Ashraf et al have similarly indicated a lack of significant differences between study groups concerning incidence of adverse effects associated with both drugs.[8,13]

In this study, none of the patients in group A required blood transfusion, whereas in group B, 2% of patients needed blood transfusion. These findings align with others, where none of the women in the carbetocin group necessitated blood transfusion. In contrast, the oxytocin group exhibited higher rates, with 15.5% and 10.6% requiring blood transfusion in separate studies.[13,14]

In the current study, none of the patients in group A necessitated fundal massage, while in group B, 9% of patients required it. This trend is consistent with the findings of Ashraf et al.[13] Moreover, Agnes et al observed that 10% of patients in the carbetocin group and 83% in the oxytocin group required fundal massage, highlighting a notable difference in the demand for this intervention between the two drug groups.[15]

In this study, 8% of patients in group A required additional uterotonic agents, whereas in the oxytocin group, 15% of patients needed such supplementation. Correspondingly, Ortiz et al reported that only 1.5% of patients in the carbetocin group and 5.8% in the oxytocin group required additional uterotonics.[16] Additionally, El Behery et al and others reported that none of the patients in the carbetocin group needed additional uterotonics, while a substantial number of women in the oxytocin group required supplementary oxytocin to ensure adequate uterine contraction for an extended period.[14,15] Holleboom et al also highlighted the comparison between carbetocin and oxytocin, revealing that prophylactic use of carbetocin after an elective caesarean section reduced the need for additional uterotonics by more than 50% compared to the oxytocin group.[17]

In this study, PPH occurred in 7% of patients in the oxytocin group, while none of the patients in the carbetocin group developed PPH. Consistent with these findings, Ashraf et al also noted the absence of PPH cases in the carbetocin group, whereas the oxytocin group experienced a PPH incidence of 8.5%. Similarly, Maged et al reported PPH rates of 4% in the carbetocin group and 16% in the oxytocin group.[8] PPH represents a prevalent form of major obstetric bleeding, being the leading cause of maternal morbidity in developed countries and a significant contributor to global maternal mortality.[18-20] The third stage of labour is a critical period for PPH, often attributed to the sudden loss of uterine contractility. Approximately 80% of PPH cases are due to uterine atony, a condition preventable through active management of the third stage of labour.[21,22]

In this study, there was a significant difference in blood loss between group B (377.68±98.57 ml) and group A (345.34±80.54 ml), with the latter demonstrating lower blood loss. The haemoglobin counts 48 hours post-delivery was also notably lower in group B (10±2.4 gm/dl) compared to group A (11±4.1 g/dl). Similarly, Ortiz et al reported a mean blood loss of 366 ml in the carbetocin group and 400 ml in the oxytocin group when evaluating the efficacy of carbetocin versus oxytocin.[16] Maged et al found that the mean blood loss was 337 ml in the carbetocin group and 378 ml in the oxytocin group.[8] In another study, Elsafty et al observed an average blood loss of 207 ml in the oxytocin group and 87 ml in the carbetocin group.[23] Ashraf et al reported an average blood loss of 320 ml in the carbetocin group and 408 ml in the oxytocin group.[13] These collective findings highlight the consistent trend of reduced blood loss associated with carbetocin compared to oxytocin in various studies. These results indicate that carbetocin emerges as a valuable and effective option in actively managing the third stage of labour during vaginal delivery. The administration of a single 100-microgram IV dose of carbetocin proves more efficacious than oxytocin in sustaining proper uterine tone, reducing blood loss, and preventing PPH in women undergoing vaginal delivery. Carbetocin, therefore, presents itself as a viable alternative to oxytocin in the management of the third stage of labour in vaginal deliveries.

CONCLUSION

According to the result of present study, the carbetocin has showed superior efficacy in preventing PPH during vaginal delivery compared to oxytocin. These results highlight the potential of carbetocin as a more effective intervention for the active management of the third stage of labour, presenting a promising opportunity to improve maternal outcomes. The decreased need for additional uterotonics and the reduced risk of substantial blood loss underscore the clinical importance of integrating carbetocin into this context. Despite the positive outcomes, it's essential to acknowledge the limitation of potential variations in individual patient responses. Therefore, further research and larger-scale trials are recommended to validate the broader applicability of carbetocin and explore its safety profile in diverse populations.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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