Original Article

Comparative Study of the Effectiveness of Carbetocin versus Oxytocin for the Prevention of Postpartum Hemorrhage in Women Undergoing Normal Vaginal Delivery at a Tertiary Care Centre in Bihar

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ABSTRACT

Background: Postpartum hemorrhage (PPH) is a leading cause of maternal mortality and morbidity, particularly in regions with limited healthcare resources, such as Bihar, India. Active management of the third stage of labor (AMTSL) is recommended to prevent PPH, with oxytocin being the first-line uterotonic. However, its short half-life and refrigeration requirements necessitate alternatives like carbetocin, a long-acting synthetic oxytocin analog.

Objective: This study aimed to compare the efficacy and safety of carbetocin versus oxytocin in preventing PPH in women undergoing normal vaginal delivery at a tertiary care center in Bihar, India.

Methods: A randomized controlled trial was conducted from February to November 2024, including women aged 18-45 with singleton pregnancies and low risk for postpartum hypertension. Participants were randomly assigned to receive either carbetocin (100 mcg) or oxytocin (10 IU) immediately after delivery. Primary outcomes included the volume of blood loss within 24 hours, while secondary outcomes assessed adverse effects, need for additional uterotonics, and maternal and neonatal outcomes.

Results: The study included 150 participants, with no significant differences in baseline characteristics between the two groups. The mean blood loss was significantly lower in the carbetocin group (362.53 ± 40.13 ml) compared to the oxytocin group (392.89 ± 47.34 ml, P = 0.00004). Other secondary outcomes, including the incidence of adverse effects and neonatal outcomes, showed no significant differences between the groups.

Conclusion: Carbetocin significantly reduces mean blood loss in postpartum women compared to oxytocin, indicating its potential as a more effective management option for PPH. Both medications exhibited similar safety profiles regarding maternal and neonatal outcomes, supporting the inclusion of carbetocin in clinical guidelines for PPH management.

Keywords: Postpartum Hemorrhage, Carbetocin, Oxytocin, Maternal Health, Blood Loss.

INTRODUCTION

Postpartum hemorrhage (PPH) is a prominent cause of maternal mortality and morbidity globally, especially in Bihar, India.[1,2] PPH—500 ml or greater blood loss within 24 hours of birth—has a major influence on maternal health.[3, 4] Obstetric care has improved, but PPH management and prevention remain difficult, especially in places with limited healthcare resources and qualified staff.[5]

PPH causes a large number of maternal deaths in India. Effective PPH prevention is needed, especially in places with high maternal mortality, according to the WHO. To minimize PPH, active third-stage labor management (AMTSL) is advised. AMTSL uses uterotonics, controlled cord traction, and uterine massage immediately after delivery.[6] Due to its effectiveness in uterine contractions and blood loss reduction, oxytocin is the first-line uterotonic drug in AMTSL.[7,8] Oxytocin's short half-life and need for refrigeration have compelled the search for alternatives.[9]

A possible PPH preventive approach is carbetocin, a long-acting synthetic oxytocin analog. Carbetocin mimics oxytocin but lasts longer, making it useful in situations where cold chain storage and continuous monitoring are not possible.[10] Carbatocin is proved to be as effective as oxytocin in PPH due to its efficacy and safety, according to several studies.[11]

A comprehensive literature review shows inconsistent results on carbetocin and oxytocin effectiveness. Some research shows that carbetocin reduces the need for uterotonics and severe PPH. Some studies demonstrated no difference between the agents. However, most research emphasizes carbetocin's long-lasting effect, especially in low-resource situations.[12] Due to its stability at ambient temperature and single-dose administration, carbetocin is suitable for usage in rural and distant places without access to healthcare or refrigeration.[13]

Based on evidence, the study compared carbetocin and oxytocin to determine the best uterotonic drug for PPH prevention. To improve mother health in India, an efficient and feasible intervention was needed due to high maternal

mortality rates. The study's findings had potential to influence national and local PPH preventive policies and guidelines.

This comparative study aimed to evaluate the efficacy and safety of carbetocin versus oxytocin in preventing PPH in women undergoing normal vaginal delivery at a tertiary care center in Bihar. The primary objective was to assess the reduction in postpartum blood loss with carbetocin compared to oxytocin. Secondary objectives included evaluating the incidence of adverse effects, the need for additional uterotonic agents, and maternal and neonatal outcomes.

MATERIALS AND METHODS

Study Design: This randomized controlled trial was done at a Bihar, India tertiary care hospital from February to November 2024. All participants gave informed consent, understanding the study's goal, procedures, risks, and benefits. Participants' privacy was protected during the investigation.

Inclusion Criteria: Women who were between the ages of 18 and 45, carrying a singleton pregnancy, delivering their babies vaginally, and having a low risk of postpartum hypertension were included in the study.

Exclusion Criteria: Multiple pregnancies, pre-existing medical issues, past cesarean birth, and known allergies to either carbetocin or oxytocin were among the factors that were used to exclude participants from the study process.

Randomization and Blinding: Participants were randomly assigned to one of two groups using a computer-generated randomization sequence: Group A received carbetocin, and Group B received oxytocin. The allocation was concealed from both participants and healthcare providers to ensure blinding.

Intervention: Group A received 100 mcg of carbetocin intramuscularly immediately after the delivery of the baby. Group B received 10 IU of oxytocin intramuscularly following the same protocol. Both groups received standard care for the third stage of labor, including controlled cord traction and uterine massage.

When the baby was delivered, the drugs were started immediately, and the third stage of labor was managed in accordance with the standards provided by the World Health Organization (WHO).[6] In the aftermath of the clamping and cutting of the umbilical cord, a plastic drape was placed over the woman's buttocks with the purpose of collecting blood.

Outcome Measures: The volume of blood loss that was measured within the first twenty-four hours after delivery was the primary focus of the outcome measurement. Blood loss was measured with the help of a collection bag and a drape that had been calibrated. The incidence of adverse effects, the requirement for further uterotonic drugs, maternal hemodynamic stability, and neonatal outcomes were all included in the secondary outcome measures.

Data Collection: Clinical observations, interviews with patients, and a review of medical records were the methods that were utilized to obtain data. Both immediately after delivery and twenty-four hours after delivery, the amount of blood loss was documented. Throughout the duration of the study, adverse events were tracked and documentation was obtained. Assessments and documentations were made about the hemodynamic parameters and neonatal outcomes.

Sample Size Calculation: The sample size was calculated based on previous studies comparing carbetocin and oxytocin, aiming for a power of 80% and a significance level of 5%.[11] A total of 150 participants (75 in each group) were required to detect a clinically significant difference in blood loss between the two groups.

Statistical Analysis: Data were analyzed using SPSS software. Descriptive statistics were used to summarize demographic and clinical characteristics. The primary outcome was compared between the two groups using an independent t-test. Secondary outcomes were analyzed using chi-square test or fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 demonstrates no significant differences in baseline demographic and clinical features between Group A (carbetocin) and Group B (oxytocin). Both groups average 27 years old and 39 weeks gestational age. The groups have similar numbers of primigravida women, induced labor, and enhanced labor. Both populations have similar postpartum bleeding rates.

Table 1: Comparison of baseline demographic and clinical characteristics between Group A (carbetocin) and Group B (oxytocin group)

Variables	Group A (n = 75)	Group B (n = 75)	P-Value
Age in years (Mean ± SD)	27.12 ± 2.21	27.14 ± 2.37	0.96*
Number of primi-gravida	34	32	0.87**
Gestation age in weeks (Mean ± SD)	38.96 ± 1.01	39.05 ± 1.18	0.62*
Number of women in which labour was induced	14	16	0.84**
Number of women in which labor was augmented	30	28	0.87*
Number of women with previous postpartum haemorrhage	3	2	>0.99**
*Unpaired t-test **Fisher's exact test			

Table 2: Comparison of effectiveness between Group A (carbetocin) and Group B (oxytocin group)

Outcome Measures	Group A (n = 75)	Group B (n = 75)	P-Value (Fisher's exact test)
Mean blood loss in ml ± SD	362.53 ± 40.13	392.89 ± 47.34	**0.00004** (Unpaired t test)
Number of women with post-partum blood loss > 500 ml	10	18	0.14
Number of women requiring additional uterotonic agents	14	18	0.55
Number of women requiring blood transfusion	2	6	0.28
Number of women requiring manual removal of placenta	0	2	0.50
Number of women requiring additional surgical procedure	2	5	0.44
S- Significant NS- Non-Significant			

Group A had considerably lower blood loss than Group B (362.53 ± 40.13 ml vs. 392.89 ± 47.34 ml, P = 0.00004). Non-statistically significant variations were found in the number of women with post-partum blood loss > 500 ml, needing extra uterotonic medications, blood transfusions, manual placenta removal, or other surgical operations.

Figure 1: Comparison of Efficacy in PPH

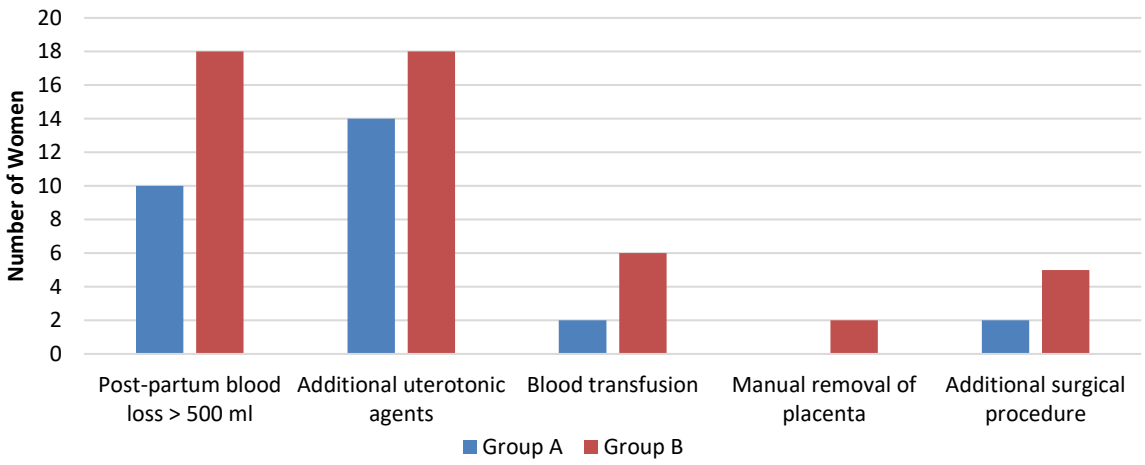

Table 3: Comparison of neonatal outcomes between Group A (carbetocin) and Group B (oxytocin group)

Outcome	Group A (n = 75)	Group B (n = 75)	P-Value (Fisher's exact test)
Number of new-borns requiring resuscitation	5	8	0.56
Number of new-borns requiring mechanical ventilation resuscitation	5	2	0.44

In Group A, 5 neonates need resuscitation compared to 8 in Group B, although the difference is not statistically significant (P = 0.56). Group A also has more newborns that need mechanical ventilation than Group B (5 vs. 2), but the difference is not statistically significant (P = 0.44).

Table 4: Comparison of frequency of different adverse events between Group A (carbetocin) and Group B (oxytocin group)

Adverse Events	Group A (n = 75)	Group B (n = 75)	P-Value (Fisher's exact test)
Abdominal pain	3	9	0.13
Nausea & Vomiting	5	12	0.12
Chest pain	3	2	>0.99
Flushing	6	10	0.43

Abdominal pain, nausea, vomiting, chest pain, and flushing are not significantly different between groups. Specific symptoms included abdominal discomfort in 3 women versus 9 in Group B (P = 0.13), nausea and vomiting in 5 women versus 12 in Group B (P = 0.12), chest pain in 3 women versus 2 in Group B (P > 0.99), and flushing in 6 women versus 10 in Group B.

DISCUSSION

The study compares carbetocin with oxytocin in demographics, blood loss management, neonatal outcomes, and postpartum adverse events. A well-matched baseline demographic and clinical profile between the two groups ensured that the study's findings were robust and not influenced by starting disparities. This study's comparisons depend on parity to accurately assess each drug's results.

The carbetocin group had much less mean blood loss than the oxytocin group. This suggests that carbetocin may reduce postpartum bleeding, a major cause of maternal mortality. A large reduction in blood loss could make carbetocin the primary treatment for postpartum hemorrhage in clinical settings.

The number of women with blood loss over 500 ml, those requiring additional uterotonic agents, blood transfusions, manual placenta removal, or additional surgical procedures did not differ between carbetocin and oxytocin groups. Carbatocin may be better at managing blood loss, although it performs similarly to oxytocin in other clinical outcomes. Practitioners must consider this when assessing each drug's benefits and drawbacks.

These findings align with the studies of Rath W et al., which indicated that the extended duration of carbetocin's action resulted in comparable incidence rates.[14]

Both groups had similar neonatal outcomes, with no significant variations in resuscitation or mechanical breathing rates. This consistency suggests that carbetocin and oxytocin do not impact infant health outcomes, confirming that both medications are safe. This study helps guide therapeutic decisions to protect infant safety without compromising maternal advantages.

No significant differences were found in adverse events between groups. Carbatocin and oxytocin had equal incidence rates of abdominal pain, nausea, vomiting, chest pain, and flushing, suggesting similar safety profiles. This information is crucial for health practitioners since it shows that these medications can be chosen based on blood loss reduction without increased side effects.

Jackson Jr. KW et al. found that uterotonics are the best strategy to prevent postpartum haemorrhage, hence oxytocin is widely used.[15] India's rural areas struggle to maintain the cold chain needed for oxytocin activity. Heat-stable carbetocin is lifesaving in such situations.

Maged AM et al. found that a single intramuscular or intravenous carbetocin dose is equally helpful.[16] Malm M et al. found the IV or IM injection of carbetocin to be safe with little side effects. This allows its use in basic healthcare.[17] In India, carbetocin costs higher than oxytocin. Due to its one-dose efficacy and lack of cold chain requirement, carbetocin is advantageous in India.

Avoiding atony postpartum hemorrhage requires powerful uterotonic medicines. Theunissen FJ et al. found that low- and middle-income nations often have uterotonic agent quality difficulties.[18] The latest data shows that 45.6% to 74.2% of oxytocin specimens in these countries failed quality testing due to insufficient active component.[19,20] Thus, uterotonic drug potency and quality must be improved to stop postpartum hemorrhage.

Beyond clinical practice, this study affects health policy. Carbetocin may improve postpartum hemorrhage management due to its considerable reduction in mean blood loss. Carbatocin in clinical guidelines may improve maternal health and lower severe postpartum hemorrhage healthcare expenditures. These findings may help policymakers update treatment guidelines and ensure carbetocin availability in maternity care to improve mother health.

This study compares carbetocin to oxytocin's efficacy and safety, although it has significant drawbacks. The sample size is suitable for early comparisons but may not be large enough to detect rare adverse events or subtle outcomes. The study also ignores long-term maternal and newborn health impacts by focusing on immediate postpartum outcomes. The single-center design may also limit generalizability to other demographics or healthcare environments. Further research with bigger, more diverse populations and longer follow-ups is needed to validate and overcome these shortcomings.

CONCLUSION

As a conclusion, this study underlines the fact that carbetocin considerably reduces mean blood loss in postpartum women when compared to oxytocin, indicating that it is more effective in the management of postpartum hemorrhage. The two medications, on the other hand, exhibit equivalent outcomes with regard to various postpartum metrics, newborn health, and adverse events, which indicates that their safety profiles are equal. The inclusion of carbetocin in clinical guidelines for the management of postpartum hemorrhage is supported by these findings, which highlight the potential of carbetocin to improve maternal care without compromising the safety of neonates.

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