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A comparative study of injection oxytocin with injection carbetocin in the management of postpartum haemorrhage

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Abstract

Background: Postpartum hemorrhage (PPH) is a leading cause of maternal mortality, particularly in developing countries. Active management of the third stage of labor with uterotonic agents is critical in reducing PPH incidence. This study compared the efficacy and safety of carbetocin, a synthetic oxytocin analogue, to oxytocin in preventing PPH among term pregnancies in a tertiary care hospital in Gujarat, India.

Methods: A prospective randomized controlled trial was conducted over 12 months, enrolling 80 women with singleton term pregnancies. Participants were randomly assigned to receive either 100 mcg of carbetocin intravenously (Group A) or 10 IU of oxytocin intramuscularly (Group B) following delivery. Primary outcomes included estimated blood loss, hemoglobin decline, uterine tone, and requirement for additional uterotonics or blood transfusions. Adverse effects were also recorded.

Results: The carbetocin group demonstrated significantly lower mean blood loss (567.7±160.9 ml vs. 625.5±122.4 ml, P=0.003) and hemoglobin decline at 48 hours post-delivery (10.5±0.9 g/dl vs. 9.8±1.2 g/dl, P=0.002). Fewer participants in the carbetocin group required additional uterotonics (10% vs. 25%, P=0.047) or blood transfusions (7.5% vs. 25%, P=0.034). Both groups exhibited comparable safety profiles.

Conclusion: Carbetocin significantly reduces blood loss and improves clinical outcomes compared to oxytocin, with similar safety, suggesting its potential as a preferred uterotonic agent in resource-limited settings.

Keywords: Carbetocin, oxytocin, postpartum hemorrhage, uterotonics, randomized controlled trial

Introduction

Labor, though a physiological process, can cause significant morbidity and mortality, primarily due to excessive blood loss during delivery [1]. Spontaneous vaginal delivery involves three stages, with the third stage being critical for parturition. Complications like postpartum hemorrhage (PPH) can arise suddenly, even after an uneventful second stage [2]. In India, the maternal mortality ratio stands at 103 per 100,000 live births, with over half of these deaths linked to childbirth-related hemorrhage, including PPH [3]. Defined as blood loss exceeding 500 ml after the third stage of labor, PPH can cause hypovolemia and maternal death within hours if untreated [4]. High anemia prevalence among Indian mothers exacerbates blood loss severity during cesarean sections and heightens PPH risks [5].

The third stage of labor is managed through active or physiological approaches. Active management, endorsed by the WHO, involves administering oxytocic drugs, early cord clamping, and controlled cord traction, significantly reducing PPH incidence [6]. Physiological management relies on maternal effort, gravity, and nipple stimulation without pharmacological intervention [7]. Oxytocin, the most widely used uterotonic, is a nine-amino acid peptide hormone stimulating uterine contractions by acting on smooth muscle receptors and prostaglandin formation [8]. While effective, oxytocin requires prolonged IV infusions due to its short half-life and may cause adverse effects like hypotension, nausea, arrhythmias, and water intoxication [9].

Carbetocin, a synthetic oxytocin analogue, offers advantages over oxytocin, including a longer half-life (40 minutes), quicker onset of sustained uterine contraction (2-3 minutes), and reduced need for stringent storage [10]. Studies indicate carbetocin enhances uterine tone, reduces blood loss, minimizes additional uterotonic requirements, and lowers PPH risk compared to oxytocin.

Despite its benefits, oxytocin remains the standard for PPH prevention in India, with limited adoption of carbetocin in healthcare facilities [11-13].

This study aims to compare oxytocin and carbetocin for PPH prevention in women delivering at a tertiary care hospital in Gujarat, India.

Materials and Methods

Study setting

The current study was an institution-based prospective randomized controlled trial conducted at the Department of Obstetrics and Gynecology of the GMERS medical college and general hospital, Gotri, Vadodara, Guajarat for 12 months, from May 2023 to May of 2024.

Study sample and randomization method

The study population consisted of mothers with full-term pregnancies admitted to the labor room of the study institution in order to undergo delivery.

The study utilized two groups of patients. Group A (study group) included mothers delivering in the study institution during the period of study and receiving 100 mcg of Carbetocin IV after the delivery of the baby. Group B (control group) were mothers delivering in the study institution at the same time period receiving the standard management after delivery, i.e., 10 IU of oxytocin IM.

Inclusion criteria

The inclusion criteria for the study population were

1. Women with singleton pregnancies.
2. Women with vertex, breech, OP position with gestational age of ≥37 weeks
3. Women presenting to the study institution for their delivery by either spontaneous vaginal delivery, lower segment cesarean section.
4. Prophylactic instrumental delivery for prev CS

Exclusion criteria

The exclusion criteria for the participants that were considered for the current study were as follows

1. Women with chronic diseases such as hypertension, cardiac diseases, chronic liver and kidney diseases
2. Women undergoing delivery via instrumental delivery for prolonged second stage of labor.
3. Women with a history of hypersensitivity to any of the study drugs such as carbetocin, oxytocin analogues.
4. Women presenting in preterm labor.
5. Women with overdistended uterus due to polyhydramnios, multiple pregnancy, large for gestational age babies.
6. Intrauterine fetal death.
7. Grand multipara.
8. Severe anemia.
9. Previous classical cs.

Methodology

A randomization procedure using envelope method was utilized for the selection and allocation of patients that presented to the labor room. They were explained aoout the study. Detailed history was taken and examination was done for those who consented and after checking eligibility they were assigned to either of the two study groups. At the time of admission and recruitment to the study, each of the participants were asked to choose between one of two envelopes containing the names of the two study groups. Each woman chose one of the two envelopes and were then subsequently assigned to the study group to either receive carbetocin or oxytocin respectively. Mothers recruited to Group A were given a bolus dose of 100 mcg of Injection Carbetocin IV after the delivery of the baby. On the other hand, those mothers in Group B were given 10 IU of Injection Oxytocin IM.

After approval from the institutional ethical committee, mothers coming for delivery at the study institution and fulfilling the inclusion criteria were recruited to group A consecutively. For each mother recruited into the study group, 1 matched control mothers were recruited for group B. The control mothers were matched with the mothers of the carbetocin group with respect to their age (±2 years) and gestational age (±1 completed week).

Mothers recruited to group A were given a bolus dose of 100 mcg of carbetocin via IV after the delivery of the baby. On the other hand, those mothers in the control group were given 10 IU of oxytocin IM after the delivery of the baby. The blood loss following delivery was estimated via visual estimation and pictorial blood assessment chart. The fall in the hemoglobin level was measured by estimating hemoglobin of the mothers before the delivery and at 48 hours of the delivery. The systolic and diastolic blood pressure, uterine position, and uterine tone of the mothers of the two study groups were monitored and compared immediately after delivery, 1 hour, 6 hours and 24 hours of delivery.

Sample size

The sample size was calculated based on findings of the study conducted by Kabir *et al.* [14]. The sample size was calculated using the formula: N = 2. n

Where,

$N = Z_{1-\alpha}^2 [p_1(1-p_1) + p_2(1-p_2)] / (p_1 - p_2)^2$

And

p_1 = Proportion of participants developing the outcome of interest in the carbetocin group

p_2 = Proportion of participants developing the outcome of interest in the control group

Considering the requirement of additional uterotonics as outcome variable, the sample size was calculated. The p_1 was considered to be 7%, and the p_2 was considered to be 3% at 95% significance level, the calculated sample size for each study group was 36, which was rounded off to 40. Thus, the total sample size for the present study was 80.

Data management and statistical analysis

The collected data were checked for consistency, completeness and entered into Microsoft Excel (MS-EXCEL, Microsoft Corp.) data sheet. Analyzed with the statistical program Statistical Package for the Social Sciences (IBM SPSS, version 22). Data were organized and presented using the principles of descriptive and inferential statistics. The data were categorized and expressed in proportions. The continuous data were expressed as mean±SD. The data were graphically presented in the form of tables, vertical bars, horizontal bar, pie diagram. Where analytical statistics were performed, a p-value of <0.05 was considered to be statistically significant for the purpose of the study. For analytical statistics, Chi-square test was used for categorical data and student's t-test was used for continuous data.

Ethical consideration

The Institutional Ethics Committee of GMERS Medial College and Hospital, Gotri reviewed and approved the project before it was carried out. All of the participants were informed in their own language about the study and their rights for participation before providing data for the researcher-administered questionnaire. They were informed about the participant's role and rights, to clarify that their participation was voluntary, the information was treated confidentially, and they could withdraw from the study at any time. After the collection of data, the data was cleaned, anonymized and stored in a password protected spreadsheet for data analysis.

Results

The study included 80 participants evenly distributed between the carbetocin and oxytocin groups. The mean age of participants was comparable, with no significant difference observed between the groups (26.4±2.8 vs. 25.4±3.1 years, P=0.152). Most participants were aged 26-30 years. Socioeconomic status, assessed using the modified Kuppuswamy scale, showed a predominance of participants from the upper-middle class in both groups, with no significant intergroup difference (P=0.974). Gestational age at admission was similar across groups, averaging 37.8±0.8 weeks in the carbetocin group and 38.1±1.1 weeks in the oxytocin group (P=0.188). Parity distribution revealed a slight predominance of multiparous women (>2 parity), with no significant difference between groups (P=0.990). (Table 1)

Regarding antenatal care, a higher proportion of participants in the oxytocin group were booked (80% vs. 67.5%), although the difference was not statistically significant (P=0.205). Previous lower segment cesarean section (LSCS) history was slightly more common in the oxytocin group (30% vs. 22.5%, P=0.446). Mode of delivery was evenly split between vaginal delivery and LSCS in both groups (60% LSCS, P=1.000). (Table 1)

Significantly lower mean blood loss was observed in the carbetocin group compared to the oxytocin group (567.7±160.9 ml vs. 625.5±122.4 ml, P=0.003). Additionally, fewer participants in the carbetocin group experienced blood loss exceeding 500 ml during vaginal delivery (6.2% vs. 18.6%, P=0.047) and blood loss over 1000 ml during LSCS (4.2% vs. 16.8%, P=0.039). No cases of severe postpartum hemorrhage (PPH) were reported in either group. (Table 2)

The mean hemoglobin drop at 48 hours post-delivery was significantly lower in the carbetocin group (10.5±0.9 g/dl vs. 9.8±1.2 g/dl, P=0.002). Systolic blood pressure was comparable between groups, but diastolic pressure was significantly lower at 2 hours in the oxytocin group (P=0.025). Uterine atonicity was less frequent in the carbetocin group at delivery (7.5% vs. 20%, P=0.010), and fewer participants required additional uterotonics (10% vs. 25%, P=0.047) or blood transfusions (7.5% vs. 25%, P=0.034). (Table 2)

The incidence of side effects, including nausea, vomiting, dizziness, and hypotension, was similar between groups, with no statistically significant differences (P=0.471), (Table 3).

Discussion

In this study, the effectiveness of two widely used uterotonic agents, oxytocin and carbetocin, in preventing postpartum hemorrhage (PPH) was evaluated among women undergoing vaginal or caesarean deliveries at a tertiary hospital in Gujarat, India. A prospective comparative design was employed with two groups of 40 term singleton pregnancies. The first group received 100 mcg of carbetocin intravenously after delivery, while the second group was administered 10 IU of oxytocin intramuscularly after the delivery of the anterior shoulder. Both groups were monitored for 48 hours post-delivery for PPH, with immediate management provided if needed.

Most participants were aged 26-30 years, aligning with findings from Indian studies [14, 15]. However, the observed age distribution in this study was much lower than the >30 years average maternal age reported in studies from developed countries [16, 17]. This age disparity reflects socio-cultural differences between developing and developed regions. The mean gestational ages in the carbetocin and oxytocin groups were 37.8±0.8 weeks and 38.1±1.1 weeks, respectively, consistent with findings from similar studies.

Higher parity (>2) was noted in both groups, reflecting the challenges of population control in India, despite progress in reducing fertility rates. The prevalence of <4 antenatal visits in 32.5% and 20% of the carbetocin and oxytocin groups, respectively, highlights gaps in antenatal care, although efforts to improve care delivery are evident. Antenatal care is vital in reducing maternal complications, including PPH. Several risk factors for PPH, such as previous lower segment cesarean section (LSCS) deliveries, were evaluated. Prior LSCS was noted in 22.5% of carbetocin and 30% of oxytocin group mothers, reflecting global trends of increasing cesarean deliveries [18, 19]. Approximately 60% of mothers in both groups underwent LSCS, driven by both elective preferences and obstetric risk factors.

Carbetocin demonstrated superior efficacy in reducing PPH. Average blood loss in the carbetocin group was 567.7±160.9 ml compared to 625.5±122.4 ml in the oxytocin group. Significantly fewer patients in the carbetocin group experienced blood loss >500 ml during vaginal delivery (6.2% vs. 18.8%) and >1000 ml during LSCS (4.2% vs. 16.8%). Carbetocin also resulted in a smaller drop in hemoglobin levels (11.8±0.7 g/dl vs. 9.8±1.2 g/dl in the oxytocin group). These findings align with studies by Matthijsse, Kabir, and others [14, 17, 20, 21]. These findings indicate a clear superiority of the carbetocin in preventing the development of PPH as compared to oxytocin. However, oxytocin was found to be an effective drug, as demonstrated by the fact that none of the participants experienced severe PPH (>2000 ml), similar to what was reported by Jin *et al*. [19].

It was observed that carbetocin group patients furthermore required fewer additional uterotonics (10% vs. 25%) and blood transfusions (7.5% vs. 25%), consistent with findings by Larciprete and Hollebloom *et al*. [17, 22]. Adverse events like nausea and vomiting were slightly higher in the carbetocin group, but hypotension was exclusively observed in the oxytocin group (7.5%). The safety profiles of both drugs were comparable. Thus, the study demonstrated that as compared to oxytocin, carbetocin was associated with significantly reduced blood loss during delivery and a lower decline in hemoglobin levels over 48 hours. Carbetocin also showed better hemodynamic stability, more rapid uterine contraction, and reduced need for additional uterotonics and blood transfusions compared to oxytocin.

Tables

Table 1: Distribution of sociodemographic characteristics of the participants (N=80)

Parameter	Carbetocin group (N,%)	Oxytocin group (N,%)	P-Value
Mean age (years)	26.4±2.8	25.4±3.1	0.152
Socioeconomic status			
Upper	11 (27.5)	10 (25)	0.974
Upper middle	15 (37.5)	16 (40)	
Middle	6 (15)	7 (17.5)	
Lower middle	8 (20)	7 (17.5)	
Lower	0 (0)	0 (0)	
Parity			
1	13 (32.5)	12 (30)	0.990
2	13 (32.5)	12 (30)	
>2	14 (35)	16 (40)	
Booking status			
Booked	27 (67.5)	32 (80)	0.205
Un-booked	13 (32.5)	8 (20)	
Previous LSCS			
Yes	9 (22.5)	12 (30)	0.446
No	31 (77.5)	28 (70)	
Mode of delivery			
Vaginal delivery	16 (40)	16 (40)	1.000
Lower segment cesarean section	24 (60)	24 (60)	

Table 2: Distribution of delivery related characteristics of the participants (N=80)

Parameter	Carbetocin group (N,%)	Oxytocin group (N,%)	P-Value
Mean blood loss (ml)	567.7±160.9	625.5±122.4	0.003*
Severe PPH	0 (0)	0 (0)	-
Average hemoglobin level (gm/dl)			
At baseline	11.3±0.8	11.8±0.7	0.617
At 48 hours	10.5±0.9	9.8±1.2	0.002*
Average systolic blood pressure (mmHg)			
At baseline	121.9±11.8	122±13.6	0.972
At 2 hours	118.8±8.3	119.2±4.1	0.302
At 12 hours	119.9±10.9	121.7±7.5	0.401
At 24 hours	116.8±10.6	120.2±8.9	0.114
Average diastolic blood pressure (mmHg)			
At baseline	79.1±8.2	78.2±10.3	0.676
At 2 hours	77.4±5.9	73.8±8.1	0.025*
At 12 hours	79.1±6.9	79.7±6.3	0.649
At 24 hours	78±7.4	76.8±4.5	0.388
Uterine atonicity			
At delivery	3 (7.5)	8 (20)	0.010*
At 2 hours	0 (0)	0 (0)	1.000
At 12 hours	0 (0)	0 (0)	1.000
At 24 hours	0 (0)	0 (0)	1.000
Additional uterotonics required			
Yes	4 (10)	10 (25)	0.047*
No	36 (90)	30 (75)	
Blood transfusion required			
Yes	3 (7.5)	10 (25)	0.034*
No	37 (92.5)	30 (75)	

*Statistically significant

Table 3: Distribution of adverse event-related characteristics of the participants (N=80)

Adverse events	Carbetocin group (N,%)	Oxytocin group (N,%)	P-Value
Nausea	3 (7.5)	2 (5)	0.471
Vomiting	2 (5)	1 (2.5)	
Dizziness	1 (2.5)	1 (2.5)	
Hypotension	0 (0)	3 (7.5)	
None	34 (85)	33 (82.5)	

Conclusion

The findings of the study indicate that carbetocin demonstrated superior efficacy and stability in preventing PPH, with a comparable safety profile, underscoring its potential as a preferred uterotonic agent in Indian clinical settings.

Conflict of Interest

Not available

Financial Support
Not available

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