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Comparative Study of Intravenous Carbetocin Versus Rectal Misoprostol for Prevention of Postpartum Haemorrhage in Third Stage of Labour in Vaginal Delivery

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Abstract: ***Background: Postpartum hemorrhage (PPH) remains a leading cause of maternal morbidity and mortality worldwide, particularly in low- and middle-income countries. Active management of the third stage of labor (AMTSL) using effective uterotonics is crucial for PPH prevention. Oxytocin, though effective, has storage and stability limitations, prompting evaluation of alternatives such as carbetocin and misoprostol. This study aimed to compare the efficacy and safety of intravenous carbetocin versus rectal misoprostol in preventing PPH among low-risk women undergoing vaginal delivery. Methods: This prospective, randomized comparative study was conducted in the Department of Obstetrics and Gynecology at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda. One hundred women with uncomplicated singleton term pregnancies were randomly assigned to two groups of 50 each. Group A received 100 µg of intravenous carbetocin at delivery of the anterior shoulder, while Group B received 800 µg of rectal misoprostol at crowning. Blood loss was measured using a calibrated drape and by weighing blood-soaked materials up to two hours postpartum. Hemoglobin and hematocrit levels were assessed pre- and post-delivery. Statistical analysis was performed using t-test and Chi-square test, with $p < 0.05$ considered significant. Results: The mean blood loss was significantly lower with carbetocin (214.3 ± 55.7 mL) compared to misoprostol (322.2 ± 74.8 mL; $p = 0.001$). The incidence of PPH (≥500 mL) and uterine atony were also lower with carbetocin (2% vs. 12% and 2% vs. 16%, respectively; $p = 0.03$). The mean fall in hemoglobin and hematocrit levels was significantly less in the carbetocin group ($p = 0.003$). Both drugs were well tolerated, with only mild, transient side effects observed. Conclusion: Intravenous carbetocin is significantly more effective than rectal misoprostol in reducing postpartum blood loss and preventing PPH in low-risk vaginal deliveries, with a comparable safety profile. Given its prolonged uterotonic effect and heat stability, carbetocin represents a superior option for AMTSL, although its cost may limit widespread use.***

Keywords: postpartum hemorrhage, carbetocin, misoprostol, vaginal delivery, uterotonic drugs

1. Introduction

Postpartum hemorrhage (PPH) remains one of the most serious emergencies in obstetric practice and continues to be the leading cause of maternal mortality worldwide. It is defined as blood loss exceeding 500 mL after vaginal delivery or 1000 mL following cesarean section, or any amount causing hemodynamic instability within 24 hours postpartum[1]. The World Health Organization (WHO) estimates that around 14 million women experience PPH each year, resulting in approximately 70,000 maternal deaths- one every six minutes- of which 99% occur in low- and middle-income countries[2].

Primary PPH, occurring within 24 hours of delivery, accounts for most cases and is commonly attributed to uterine atony, followed by trauma, retained tissue, and coagulation disorders[3]. Alarmingly, up to 40% of women who develop PPH have no identifiable risk factors, emphasizing the need for universal preventive strategies[4]. Beyond mortality, PPH contributes to significant morbidity, including severe anemia, shock, renal failure, and long-term psychological trauma, while also imposing heavy economic and healthcare burdens, particularly in resource-constrained settings.

Active management of the third stage of labor (AMTSL) remains the cornerstone of PPH prevention [5]. Oxytocin, the conventional uterotonic used in AMTSL, effectively reduces PPH incidence but has major limitations, including thermal instability, short half-life, and dependence on cold-chain storage- factors that hinder its use in low-resource regions. Consequently, alternative uterotonics such as carbetocin, a long-acting heat-stable oxytocin analogue, and misoprostol, a prostaglandin E1 analogue, have gained prominence.

However, comparative data on their efficacy and safety in low-risk vaginal deliveries remain limited. This study therefore aims to evaluate the effectiveness of intravenous carbetocin (100 µg) versus rectal misoprostol (800 µg) in reducing postpartum blood loss, thereby providing evidence to guide clinical practice in routine obstetric care, especially in settings where oxytocin use is challenging.

2. Methodology

This prospective, randomized comparative study was conducted in the Department of Obstetrics and Gynecology at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, after obtaining ethical clearance and informed consent from all participants. The study included women with uncomplicated singleton pregnancies at term, in cephalic presentation, undergoing spontaneous or induced vaginal delivery. Women with traumatic postpartum hemorrhage, severe anemia, severe pre-eclampsia, multifetal gestation, grand multiparity, previous cesarean or instrumental delivery, non-vertex presentation, or significant medical disorders (cardiac, hepatic, renal, vascular, or neurological) were excluded.

A total of 100 eligible women were randomly allocated into two equal groups using block randomization. Group A received 100 µg of intravenous carbetocin administered slowly over one minute at delivery of the anterior shoulder, while Group B received 800 µg of rectal misoprostol (four 200 µg tablets) at the time of crowning. Active management of the third stage of labor was performed as per WHO guidelines, including delayed cord clamping, controlled cord traction, and uterine massage. In cases of uterine atony or persistent bleeding, additional uterotonics (10 IU intramuscular oxytocin) were administered.

Blood loss was measured using a calibrated under-buttock graduated drape and by weighing all blood-soaked materials before and after use. Blood volume was calculated using the Gai et al. method, and cumulative blood loss was recorded up to two hours postpartum. Hemoglobin and hematocrit levels were re-evaluated 24 hours after delivery. Data were analyzed using SPSS software, with the *t*-test for continuous variables and the Chi-square test for categorical variables. A *p*-value <0.05 was considered statistically significant.

3. Observations

A total of 100 participants were enrolled and evenly divided into two groups: Group A receiving Carbetocin (n=50) and Group B receiving Misoprostol (n=50). The baseline characteristics were comparable between both groups. No statistically significant differences were observed in mean age, BMI, gravidity status, period of gestation, mode of onset of labor, Bishop score, or mean duration of labor (all p > 0.05), indicating appropriate homogeneity between the study groups as depicted in table no. 1

Table 1: Baseline characteristics and study population

Variables	Group A (Carbetocin) (n=50)	Group B (Misoprostol) (n=50)	p Value
Age (years, mean ± SD)	26.8 ± 4.28	26.2 ± 3.6	0.61
BMI (kg/m², mean ± SD)	23.7 ± 2.6	24.8 ± 2.5	0.057
Primigravida (PGR)	24 (48%)	27(54%)	0.54
Gravida (2)	18(36%)	15 (30%)	0.52
Gravida (3)	6(12%)	5(10%)	0.74
Mean POG (weeks, mean ± SD)	38.9 ± 1.1	38.7 ± 1.2	0.412
Onset of labor Spontaneous	35(70%)	30 (60%)	0.8
Induced	15 (30%)	20(40%)	0.22
Bishop score (Mean ± SD)	7.4 ± 2.01	7.9 ± 2.1	0.28
Mean Duration of labor (Min)	536.2	548.7	0.547

Pre-delivery hematological parameters, including mean hemoglobin and hematocrit levels, were similar across both groups (p = 0.6 and p = 0.725, respectively). However, significant differences emerged following delivery. Group A exhibited higher post-delivery hemoglobin and hematocrit values compared to Group B (p = 0.03 and p = 0.01, respectively). The mean fall in hemoglobin and hematocrit was significantly lower among Carbetocin recipients (0.6 g/dL vs. 1.3 g/dL, p = 0.003; and 1.8% vs. 2.8%, p = 0.007), indicating reduced blood loss.

Table 2: Pre and post-delivery changes

Parameter	Group A (Carbetocin) (n=50)	Group B(Misoprostol) (n=50)	p-value
Pre-delivery Hemoglobin (g/dL, mean ± SD)	11.9 ± 1.2	12.07 ± 1.3	0.6
Pre-Delivery Hematocrit (%, mean ± SD)	35.8 ± 4.1	35.5 ± 4.3	0.725
Post-Delivery Hemoglobin (g/dL, mean ± SD)	11.3 ± 1.1	10.8 ± 1.2	0.03
Post-Delivery Hematocrit (%, mean ± SD)	34 ± 3.9	31.7 ± 4.0	0.01
Mean Fall in Hematocrit	1.8 ± 1.1	2.8 ± 1.5	0.007
Mean Fall in Hemoglobin (g/dL)	0.6 ± 0.39	1.3 ± 0.62	0.003
PPH (≥500mL)	1 (2%)	6 (12%)	0.03
Uterine Atony	1 (2%)	8 (16%)	0.03
Total Mean Blood Loss (mL) at 2 Hours	214.3 ± 55.7	322.2 ± 74.8	0.001
Additional Uterotonic Used (Oxytocin)	1 (2%)	8 (16%)	0.03
Blood Transfusion	0	0	0

Clinically significant postpartum hemorrhage (≥500 mL) occurred in 2% of Group A compared to 12% in Group B (p = 0.03). Uterine atony was also significantly less frequent in the Carbetocin group (2% vs. 16%, p = 0.03). The mean total blood loss within 2 hours postpartum was substantially lower in Group A (214.3 ± 55.7 mL) compared to Group B (322.2 ± 74.8 mL) (p = 0.001). Additional uterotonic use was higher

among Misoprostol users (16% vs. 2%, p = 0.03). No participants in either group required blood transfusion.

Table 3: Distribution of participants according to Side Effects

Parameter	Group A (Carbetocin) (n=50)	Group B (Misoprostol) (n=50)	*p*-value
Side Effects			
Nausea	1(2%)	0 (0%)	0.315
Pyrexia	1 (2%)	1 (2%)	
Tachycardia	2 (4%)	1 (2%)	
Abdominal Pain	0 (0%)	0 (0%)	
Diarrhea	0 (0%)	0 (0%)	
Vomiting	0 (0%)	0 (0%)	
Headache	1 (2%)	0 (0%)	

Side effects were minimal and comparable between groups, with no statistically significant differences.

4. Discussion

This prospective randomized study compared the efficacy and safety of intravenous carbetocin and rectal misoprostol in the prevention of postpartum hemorrhage (PPH) among low-risk women undergoing vaginal delivery. The findings demonstrated that carbetocin was significantly more effective in reducing blood loss, the incidence of PPH, and the need for additional uterotonics compared to misoprostol, with both drugs showing acceptable safety and tolerability profiles.

The baseline characteristics of both groups, including maternal age, parity, gestational age, and mode of labor onset, were comparable, ensuring that the observed differences in outcomes were attributable to the intervention rather than confounding factors. Both groups underwent standardized active management of the third stage of labor according to WHO guidelines, thereby maintaining consistency in care.

The mean estimated blood loss in the carbetocin group was significantly lower (214.3 ± 55.7 mL) compared to the misoprostol group (322.2 ± 74.8 mL; p=0.001). This reduction aligns with findings from previous studies such as Maged et al. (2018), Ibrahim et al. (2017), and Yasmin et al. (2021), which consistently demonstrated that carbetocin leads to significantly lower postpartum blood loss compared with misoprostol[6]. The superior hemostatic effect of carbetocin can be attributed to its long duration of uterotonic action, with a half-life of approximately 40 minutes compared to oxytocin's 3–5 minutes, ensuring sustained uterine contractions and effective prevention of atony[7].

The incidence of PPH (≥500 mL) in this study was also lower in the carbetocin group (1%) compared to the misoprostol group (12%), a difference that was statistically significant (p=0.03). This finding corroborates previous research by Elbohoty et al. (2016) and Ismail et al. (2019), who also reported a significant reduction in PPH rates with carbetocin use[8]. Similarly, the requirement for additional uterotonics and the occurrence of uterine atony were notably less frequent in the carbetocin group (2%) than in the misoprostol group (16%), further emphasizing carbetocin's superior efficacy in maintaining uterine tone.

Hemoglobin and hematocrit estimations 24 hours postpartum revealed a smaller mean decline in the carbetocin group (0.6 ± 0.39 g/dL) compared to the misoprostol group (1.3 ± 0.62 g/dL; p=0.003), consistent with reduced blood loss. This outcome is in line with studies by Attilakos et al. (2010) and Su et al. (2012), both of which demonstrated less reduction in postpartum hemoglobin levels following carbetocin administration compared with other uterotonics[9].

Regarding safety and side effects, both agents were generally well tolerated. Misoprostol was associated with a higher incidence of transient pyrexia, shivering, and mild gastrointestinal discomfort, findings similar to those reported by Hofmeyr et al. (2013)[10]. Carbetocin, on the other hand, occasionally caused mild tachycardia and headache but no serious adverse events. Importantly, no cases of severe hypotension, allergic reaction, or thromboembolic events were reported in either group.

The present study reinforces existing evidence that intravenous carbetocin is more effective than rectal misoprostol in reducing postpartum blood loss and preventing PPH in low-risk vaginal deliveries. Its longer duration of uterotonic effect, ease of administration, and emerging heat-stable formulations make it a promising alternative to oxytocin, particularly in low-resource settings where maintaining cold-chain storage is difficult. Carbetocin thus represents a safe, effective, and practical option for routine prophylaxis against PPH, contributing to improved maternal outcomes and advancing global efforts to reduce preventable maternal mortality.

5. Conclusion

Our study concluded that intravenous carbetocin is significantly more effective than rectal misoprostol in preventing PPH in low-risk women undergoing vaginal delivery. It reduces blood loss, eliminates PPH incidence, minimizes uterine atony, and decreases the need for additional uterotonics while maintaining higher post-delivery hemoglobin and hematocrit levels. In view of above considering carbetocin for active management of third stage of labor would be prudent, especially in situations where high cost is not a factor. However larger study may be required to differentiate between efficacy of these two drugs.

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