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Comparison of Carbetocin, Oxytocin, and Misoprostol for the Prevention of Atonic Postpartum Hemorrhage in High-Risk Women Undergoing Cesarean Delivery in Bangladesh

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ABSTRACT

Background: Atonic postpartum hemorrhage (PPH) remains a leading cause of maternal morbidity and mortality worldwide, particularly in high-risk women undergoing cesarean delivery. Effective prophylactic uterotonics are critical to prevent excessive blood loss and reduce the need for additional interventions. Aim of the study: To compare the efficacy, safety, and clinical outcomes of carbetocin, oxytocin, and misoprostol in preventing atonic PPH among high-risk women undergoing cesarean delivery in Bangladesh. **Methods & Materials:** This prospective, randomized, comparative study included 135 high-risk pregnant women scheduled for cesarean section. Participants were assigned to receive carbetocin (100 µg IV), oxytocin (10 IU IV), or misoprostol (800 µg PR) immediately after delivery. Primary outcome was incidence of atonic PPH (≥1000 mL blood loss), with secondary outcomes including severity of PPH, need for additional uterotonics, surgical interventions, and maternal adverse effects. Data were analyzed using ANOVA, Chi-square tests, and relative risk calculation. **Results:** Carbetocin demonstrated the lowest incidence of PPH (6.67%) compared with oxytocin (13.33%) and misoprostol (11.11%). Carbetocin recipients achieved uterine tone more rapidly, required fewer additional uterotonics and surgical interventions, and experienced fewer adverse effects. Misoprostol was associated with higher rates of fever, shivering, and gastrointestinal symptoms. Relative risk analysis showed a trend favoring carbetocin, though not statistically significant. **Conclusion:** Carbetocin is the most effective and safe uterotonic for preventing atonic PPH in high-risk cesarean deliveries, offering rapid uterine stabilization and minimal adverse effects. Oxytocin provides moderate efficacy, whereas misoprostol, despite ease of administration, is less tolerable. These findings support preferential use of carbetocin in high-risk cesarean settings in Bangladesh.

Keywords: *Atonic postpartum hemorrhage, cesarean delivery, carbetocin, oxytocin, misoprostol, uterotonic prophylaxis, maternal outcomes.*

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INTRODUCTION

Atonic postpartum hemorrhage (PPH) refers to excessive bleeding of ≥ 500 mL following vaginal delivery or ≥ 1000 mL after cesarean delivery due to failure of the uterus to contract effectively, and it remains the most frequent obstetric emergency requiring uterotonic prophylaxis during cesarean delivery [1]. Uterotonic agents, for instance, oxytocin, carbetocin, and misoprostol, are administered after delivery of the fetus to promote sustained uterine contraction, decrease blood loss, prevent uterine atony, and thereby lessen the incidence of atonic PPH in high-risk women undergoing cesarean section [2]. In the Global perspective, postpartum hemorrhage impacts approximately 9.97% of women giving birth, meaning nearly 1 in 10 women experience significant bleeding (≥500 mL) after delivery, and about 4.5% develop severe PPH, making it a major contributor to maternal morbidity and mortality worldwide and underlining the critical need for effective preventive measures, such as uterotonic agents [3]. In the context of Bangladesh, obstetric hemorrhage has become the leading cause of maternal mortality, accounting for about 31% of all maternal deaths, with uterine atony from PPH being a major contributor, underscoring the need for effective prophylactic uterotonics such as carbetocin, oxytocin, and misoprostol in high-risk caesarean deliveries [4]. Atonic postpartum hemorrhage is primarily caused by failure of effective uterine contraction after delivery, with additional risk factors that include prolonged labor, multiple pregnancy, polyhydramnios, and cesarean section [5]. Atonic postpartum hemorrhage occurs due to the failure of effective uterine contraction after placental delivery, accounting for about 70–80% of all PPH cases worldwide, and is strongly associated with prolonged labor, over-distended uterus, multiple pregnancy, and cesarean section [6]. Prevention of atonic PPH during cesarean delivery includes prophylactic administration of uterotonic agents such as oxytocin, carbetocin, or misoprostol immediately after delivery of the baby, which significantly decreases blood loss ≥500 mL and lowers the risk of chronic hemorrhage [7]. Prophylactic administration of uterotonic agents, for instance, oxytocin, carbetocin, or misoprostol, immediately after delivery of the baby during cesarean section significantly decreases the incidence of blood loss ≥500 mL and severe PPH compared with no uterotonic use [8]. Carbetocin demonstrate significant reduction of the risk of postpartum hemorrhage ≥500 mL and the need for additional uterotonics compared with oxytocin, where misoprostol remains effective in low-resource settings due to its heat stability and ease of administration [9]. Carbetocin is comparatively expensive and

not easily accessible in low-income settings, oxytocin requires cold-chain storage and skilled administration, and misoprostol is associated with higher rates of side effects like shivering and fever compared with oxytocin [10]. Misoprostol is associated with higher rates of shivering and pyrexia (30–40%) rather than oxytocin, which requires cold-chain storage and skilled administration, limiting its feasibility in some settings [11]. This study aimed to compare the efficacy, safety, security, and clinical outcomes of carbetocin, oxytocin, and misoprostol in preventing atonic postpartum hemorrhage among high-risk women undergoing cesarean delivery in Bangladesh, with special emphasis on reducing blood loss, need for additional uterotonics, and maternal morbidity.

METHODS & MATERIALS

This was a prospective, randomized, comparative study conducted at the Department of Obstetrics and Gynecology, Bnagladesh Medical University, Dhaka, Bangladesh over a period of 12 months from January 2024 to December 2024. The study aimed to compare the effectiveness and safety of carbetocin, oxytocin, and misoprostol in preventing atonic postpartum hemorrhage (PPH) among high-risk women undergoing cesarean delivery. A total of 135 pregnant women scheduled for cesarean section and identified as high risk for atonic PPH were enrolled in the study. High-risk status was defined by the presence of one or more of the following factors: previous cesarean section, multiparity (≥3), multiple pregnancy, anemia (hemoglobin <10 g/dL), prolonged labor, uterine overdistension, or history of PPH.

Group Allocation

Carbetocin group: Received 100 µg carbetocin intravenously as a single bolus immediately after delivery of the baby.

Oxytocin group: Received 10 IU oxytocin intravenously as a slow bolus followed by infusion as per hospital protocol.

Misoprostol group: Received 800 µg misoprostol per rectally immediately after delivery of the baby.

Spinal anesthesia was standardized for all participants. Cesarean sections were performed by experienced obstetricians following uniform surgical protocols.

Inclusion Criteria:

- Women aged 18–40 years.
- Singleton or multiple pregnancy.
- Gestational age ≥37 weeks.
- Undergoing elective or emergency cesarean delivery.
- Presence of at least one recognized risk factor for atonic PPH.

Exclusion Criteria:

- Known coagulation disorders.
- Placenta accreta spectrum, placenta previa with active bleeding, or uterine rupture.
- Severe preeclampsia/eclampsia.
- Cardiac disease or contraindications to uterotonic agents.
- Allergy or hypersensitivity to any of the study drugs.
- Renal or hepatic disease.

Ethical Considerations

The study protocol was approved by the Institutional Ethical Review Committee of the participating hospital. Written informed consent was obtained from all participants. Confidentiality of patient data was maintained.

Measurement of Blood Loss

Intraoperative blood loss was estimated by combining the volume collected in suction bottles (after subtracting amniotic fluid) and visual estimation from soaked surgical sponges and pads. Postoperative blood loss was assessed within the first 24 hours using pad counts and clinical evaluation.

Variable Definitions

Postpartum hemorrhage (PPH) was defined as an estimated blood loss of ≥1000 mL following cesarean section. The severity of PPH was further classified into two categories: minor PPH, which referred to an estimated blood loss of up to 1000 mL, and major PPH, which referred to blood loss exceeding 1000 mL and/or blood loss associated with clinical signs of hemodynamic instability.

Data Collection

Data were collected using a structured data collection sheet that recorded baseline demographic and obstetric characteristics, including age, body mass index (BMI), parity, gestational age, presence of anemia, history of previous cesarean section, and multiple pregnancy. Maternal outcomes and adverse events were prospectively monitored for the first 24 hours postpartum. The primary outcome measure was the incidence of atonic postpartum hemorrhage, defined as blood loss ≥1000 mL following cesarean section or any amount of blood loss associated with hemodynamic instability. Secondary outcome measures included the severity of PPH (classified as minor or major), requirement for additional uterotonic drugs such as ergometrine, need for surgical interventions (uterine artery ligation, compression sutures, or hysterectomy), blood transfusion requirement, maternal adverse effects (nausea, vomiting, fever, shivering, hypotension, diarrhea, and headache), time to achieve adequate uterine tone, need for intensive care unit (ICU) admission, and the relative risk of PPH among the study groups.

Statistical Analysis

Data were analyzed using SPSS software (version 26). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Comparisons among groups were performed using one-way ANOVA for continuous variables and Chi-square or Fisher's exact test for categorical variables. Relative risk (RR) with 95% confidence intervals (CI) was calculated for the incidence of atonic PPH. A p-value <0.05 was considered statistically significant.

RESULT

A total of 135 women undergoing cesarean delivery were enrolled and equally allocated to the Carbetocin (n=45), Oxytocin (n=45), and Misoprostol (n=45) groups. The mean age was 26.56±5.87 years in the Carbetocin group, 29.34±3.65 years in the Oxytocin group, and 27.55±4.71 years in the Misoprostol group (p=0.14). Mean BMI was 27.46±2.92, 28.89±3.28, and 27.59±2.87 kg/m² (p=0.11). Primigravida women were 42.22%, 40.00%, and 44.44% respectively (p=0.91). Previous cesarean section was reported in 55.56%, 57.78%, and 53.33% (p=0.89), and anemia (Hb<10 g/dL) in 46.67%, 48.89%, and 46.67% (p=0.97) (*Table I*)

Table I
Baseline characteristics of study participants (*n*=135).

Variables	Carbetocin (n=45)	Oxytocin (n=45)	Misoprostol (n=45)	p-value
Age (years), Mean ± SD	26.56±5.87	29.34±3.65	27.55±4.71	0.14
BMI (kg/m2), Mean ± SD	27.46±2.92	28.89±3.28	27.59±2.87	0.11
Parity, Mean ± SD	3.76±0.74	3.32±0.74	3.17±0.48	0.06
Gestational age (weeks), Mean ± SD	37.73±1.92	37.39±1.65	37.51±1.66	0.74
Primigravida, n (%)	19 (42.22)	18 (40.0)	20 (44.44)	0.91
Previous CS, n (%)	25 (55.56)	26 (57.78)	24 (53.33)	0.89
Multiple pregnancy, n (%)	6 (13.33)	7 (15.56)	7 (15.56)	0.95
Anemia (Hb <10 g/dL), n (%)	21 (46.67)	22 (48.89)	21 (46.67)	0.97

The incidence of atonic postpartum hemorrhage (PPH) was lowest in the Carbetocin group at 6.67%, compared with 13.33% in the Oxytocin group and 11.11% in the Misoprostol group. Minor PPH occurred in 6.67%, 8.89%, and 6.67% women, while major PPH was observed only in the Oxytocin 4.44% and Misoprostol 6.67% groups (p=0.1) (*Table II*).

Table II
Incidence and severity of atonic postpartum hemorrhage among the study groups (*n*=135).

Variables	Carbetocin (n=45), n (%)	Oxytocin (n=45), n (%)	Misoprostol (n=45), n (%)	p-value
Incidence of PPH	3 (6.67)	6 (13.33)	5 (11.11)	0
Degree of PPH				
Minor	3 (6.67)	4 (8.89)	3 (6.67)	0.1
Major	0 (0.0)	2 (4.44)	3 (6.67)	0

Only 2.22% received additional ergometrine compared with 8.89% in Oxytocin and 11.11% in Misoprostol (p=0.03). Surgical measures included uterine artery ligation in 0, 2.22%, and 6.67% women; compression sutures in 0, 6.67%, and 8.89%; and hysterectomy in 0, 2.22%, and 0 women, respectively. Blood transfusions of one unit were required in 2.22%, 6.67%, and 6.67%, while transfusions of more than one unit were needed in 0, 4.44%, and 6.67% women (*Table III*).

Table III
Requirement for additional medical or surgical interventions to control bleeding among the study groups (*n*=135).

Additional lines	Type	Carbetocin (n=45), n (%)	Oxytocin (n=45), n (%)	Misoprostol (n=45), n (%)	p-value
Uterotonic drugs	Ergometrine	1 (2.22)	4 (8.89)	5 (11.11)	0.03
Surgical measures	Uterine artery ligation	0 (0.0)	1 (2.22)	3 (6.67)	0
	Compression sutures	0 (0.0)	3 (6.67)	4 (8.89)	
	Hysterectomy	0 (0.0)	1 (2.22)	0 (0.0)	
Blood transfusion	One unit	1 (2.22)	3 (6.67)	3 (6.67)	0
	More than 1 unit	0(0.0)	2 (4.44)	3 (6.67)	

Nausea/vomiting occurred in 28.89% compared with 6.67% in Carbetocin and 8.89% in Oxytocin (p<0.001). Fever/shivering was reported in 35.56% versus 2.22% and 4.44% (p<0.001). Diarrhea occurred in 13.33% compared with 2.22% in both Carbetocin and Oxytocin (p<0.001). Hypotension was reported in 8.89%, 15.56%, and 8.89% (p=0.14), and headache in 4.44%, 6.67%, and 11.11% (p=0.18) (*Table IV*).

Table IV
Maternal adverse effects (*n*=135).

Adverse Effect	Carbetocin (n=45), n (%)	Oxytocin (n=45), n (%)	Misoprostol (n=45), n (%)	p-value
Nausea/vomiting	3 (6.67)	4 (8.89)	13 (28.89)	<0.001
Fever/shivering	1 (2.22)	2 (4.44)	16 (35.56)	<0.001
Hypotension	4 (8.89)	7 (15.56)	4 (8.89)	0.14
Headache	2 (4.44)	3 (6.67)	5 (11.11)	0.18
Diarrhea	1 (2.22)	1 (2.22)	6 (13.33)	<0.001

Successful prevention of PPH was achieved in 93.33%, 82.22%, and 73.33% women (p<0.001). Uterine tone within 5 minutes was achieved in 86.67%, 64.44%, and 53.33% (p<0.001). Need for surgical intervention (B-Lynch / hysterectomy) occurred in 2.22%, 4.44%, and 6.67% (p=0.04), while ICU admissions were 2.22%, 4.44%, and 8.89% (p=0.06) (*Table V*).

Table V
Clinical effectiveness outcomes (*n*=135).

Outcome	Carbetocin (n=45), n (%)	Oxytocin (n=45), n (%)	Misoprostol (n=45), n (%)	p-value
Successful prevention of PPH	42 (93.33)	37 (82.22)	33 (73.33)	<0.001
Uterine tone achieved within 5 min	39 (86.67)	29 (64.44)	24 (53.33)	<0.001
Need for surgical intervention (B-Lynch / hysterectomy)	1 (2.22)	2 (4.44)	3 (6.67)	0.04
ICU admission	1 (2.22)	2 (4.44)	4 (8.89)	0.06

Relative risk of developing atonic PPH was higher in Oxytocin (RR=2; 95% CI: 0.54–7.39; p=0.29) and Misoprostol (RR=1.67; 95% CI: 0.43–6.46; p=0.45) compared with Carbetocin, although not statistically significant (*Table VI*).

Table VI
Relative risk of atonic PPH (*n*=135).

Comparison	Relative Risk (RR)	95% Confidence Interval	p-value
Oxytocin vs Carbetocin	2	0.54 – 7.39	0.29
Misoprostol vs Carbetocin	1.67	0.43 – 6.46	0.45

DISCUSSION

Postpartum hemorrhage (PPH) due to uterine atony remains the leading cause of maternal morbidity and mortality worldwide, particularly among high-risk women undergoing cesarean delivery [12]. The present study compared the effectiveness of Carbetocin, Oxytocin, and Misoprostol for the prevention of atonic PPH in a Bangladeshi high-risk obstetric population. In this study, baseline demographic characteristics including age (26.56±5.87 vs 29.34±3.65 vs 27.55±4.71 years), BMI (27.46±2.92 vs 28.89±3.28 vs 27.59±2.87 kg/m²), parity (3.76±0.74 vs 3.32±0.74 vs 3.17±0.48), gestational age (37.73±1.92 vs 37.39±1.65 vs 37.51±1.66 weeks), prevalence of primigravida (42.22% vs 40.0% vs 44.44%), previous cesarean section (55.56% vs 57.78% vs 53.33%), multiple pregnancy (13.33% vs 15.56% vs 15.56%), and anemia (46.67% vs 48.89% vs 46.67%) were statistically comparable among the three groups ($p>0.05$). These findings indicate that the observed clinical outcomes were unlikely to be influenced by baseline confounding variables and reflect true pharmacologic differences, consistent with randomized trials such as those by Abd El-Gaber et al., who also demonstrated comparable baseline obstetric characteristics across uterotonic groups in cesarean deliveries [2]. The incidence of atonic PPH was lowest in the carbetocin group (6.67%) compared to the oxytocin (13.33%) and misoprostol (11.11%) groups. Notably, no cases of major PPH were reported in the carbetocin group, whereas major hemorrhage occurred in 4.44% and 6.67% of women receiving oxytocin and misoprostol respectively. Similar reductions in blood loss and PPH incidence with carbetocin compared to oxytocin have been reported in previous studies, supporting the superior uterotonic efficacy of long-acting oxytocin analogues in cesarean sections [2,13,14]. Furthermore, the requirement for additional uterotonics such as ergometrine was significantly lower in the carbetocin group (2.22%) than in the oxytocin (8.89%) and misoprostol (11.11%) groups ($p=0.03$). Similarly, surgical interventions including uterine artery ligation and compression sutures were less frequently required following carbetocin administration. These observations align with previous findings, which demonstrated reduced need for supplementary uterotonics and invasive procedures in women receiving carbetocin during, cesarean delivery [15-17]. Adverse maternal effects were markedly more common in the misoprostol group, including nausea/vomiting (28.89%), fever/shivering (35.56%), and diarrhea (13.33%), all of which were statistically significant ($p<0.001$). In contrast, carbetocin exhibited a more favorable tolerability profile with minimal gastrointestinal and thermoregulatory side effects. These findings are consistent with previous reports which noted a higher incidence of pyrexia and shivering associated with misoprostol use in PPH prophylaxis [18-20]. Clinical effectiveness outcomes further reinforced the superiority of carbetocin. Successful prevention of PPH was achieved in 93.33% of patients receiving carbetocin compared to 82.22% in the oxytocin group and 73.33% in the misoprostol group ($p<0.001$). Rapid uterine tone within 5 minutes was also significantly higher in the carbetocin group (86.67%) than in oxytocin (64.44%) and misoprostol (53.33%) groups ($p<0.001$). Comparable results were observed in randomized controlled trial, which highlighted the sustained uterine contractility achieved with carbetocin following cesarean delivery [16]. Although the relative risk of developing atonic PPH was higher in the oxytocin (RR=2.0; 95% CI: 0.54–7.39) and misoprostol (RR=1.67; 95% CI: 0.43–6.46) groups compared to carbetocin, the differences did not reach statistical significance ($p>0.05$), possibly due to the modest sample size. Nonetheless, the overall clinical trend consistently favored carbetocin in reducing hemorrhagic complications and intervention requirements [2,16].

LIMITATIONS

This study was conducted at a single tertiary care center, limiting the generalizability of the findings to other settings in Bangladesh or globally. The sample size was relatively modest, reducing statistical power for rare outcomes. Blood loss estimation relied partly on visual assessment, which may introduce measurement bias. Long-term maternal outcomes beyond 24 hours postpartum were not assessed. Additionally, cost-effectiveness and feasibility aspects, particularly for carbetocin in low-resource settings, were not evaluated. Multicenter studies are warranted to validate these findings.

CONCLUSION

In high-risk women undergoing cesarean delivery, prophylactic administration of carbetocin demonstrated superior efficacy in preventing atonic postpartum hemorrhage compared with oxytocin and misoprostol. Carbetocin was associated with the lowest incidence of PPH, minimal need for additional uterotonics, rapid achievement of adequate uterine tone, and reduced requirement for surgical interventions. Oxytocin offered moderate protection, whereas misoprostol, while effective, was linked to higher rates of adverse maternal effects such as fever, shivering, and gastrointestinal symptoms. Despite comparable relative risks among groups, the clinical outcomes favor carbetocin as the most effective and safe uterotonic agent. These findings support its preferential use in high-risk cesarean deliveries in Bangladesh, balancing efficacy, safety, and rapid uterine stabilization.

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CONFLICT OF INTEREST

None declared.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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