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Comparison of Misoprostol versus Carbetocin for Prevention of Postpartum Hemorrhage in Cesarean Section: A Prospective Comparative Study.

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Abstract

Background: Postpartum hemorrhage (PPH) remains one of the leading causes of maternal mortality worldwide. Uterine atony accounts for nearly 80% of cases. Prophylactic uterotonics during the third stage of labor significantly reduce blood loss. While carbetocin is a long-acting oxytocin analogue, misoprostol is a prostaglandin E1 analogue widely used due to its stability and cost-effectiveness.

Aim: To compare the efficacy and safety of misoprostol versus carbetocin in preventing postpartum hemorrhage in women undergoing cesarean section.

Materials and Methods: This prospective comparative study was conducted in the Department of Obstetrics and Gynaecology at S.N. Medical College, Agra. A total of 200 women undergoing cesarean section were randomized into two groups: Group A received 100 µg intravenous carbetocin and Group B received 800 µg rectal misoprostol after delivery of the baby. Primary outcomes included total blood loss, fall in hemoglobin, need for additional uterotonics, blood transfusion requirement, and adverse effects. Statistical analysis was performed using SPSS version 23.0, with $p<0.05$ considered significant.

Results: Mean total blood loss was significantly lower in the carbetocin group (348.6 ± 65.2 mL) compared to the misoprostol group (432.4 ± 78.5 mL) ($p<0.001$). The mean fall in hemoglobin was 0.82 ± 0.4 g/dL in Group A and 1.58 ± 0.6 g/dL in Group B ($p<0.001$). Additional uterotonics were required in 6% of patients in the carbetocin group versus 14% in the misoprostol group ($p=0.048$). Shivering and fever were significantly more common with misoprostol ($p<0.05$).

Conclusion: Carbetocin is more effective than misoprostol in reducing blood loss during cesarean section and is associated with fewer additional interventions. However, misoprostol remains a feasible alternative in low-resource settings due to its stability and cost advantages.

Keywords: Postpartum Hemorrhage, Misoprostol, Carbetocin, Cesarean Section, Uterotonics, Maternal Mortality

Introduction

Postpartum hemorrhage (PPH) is defined as blood loss ≥1000 mL following cesarean delivery or any blood loss causing hemodynamic instability within 24 hours postpartum (1). It remains a major contributor to maternal morbidity and mortality, particularly in developing countries. In India, PPH accounts for nearly one-third of maternal deaths (2).

Active management of the third stage of labor (AMTSL), including prophylactic administration of uterotonics, significantly reduces the risk of PPH (3).

Oxytocin is recommended as the first-line agent; however, its short half-life and requirement for cold-chain storage limit its utility in low-resource settings (4).

Misoprostol, a prostaglandin E1 analogue, is inexpensive, heat-stable, and can be administered orally, sublingually, vaginally, or rectally (5). It has been widely used in developing countries due to ease of administration and storage advantages (6). However, side effects such as fever and shivering are common.

Carbetocin is a long-acting synthetic oxytocin analogue with a half-life of approximately 40 minutes, producing sustained uterine contractions after a single dose (7). Heat-stable carbetocin formulations have expanded its use in low- and middle-income countries (8). Several trials have demonstrated its superiority over oxytocin in preventing PPH following cesarean section (9).

The present study was undertaken to compare the efficacy and safety of misoprostol versus carbetocin in preventing PPH during cesarean section.

Materials And Methods

This prospective randomized comparative study was conducted at the Department of Obstetrics and Gynaecology, S.N. Medical College, Agra, after obtaining institutional ethical clearance and informed consent.

Study Population

200 antenatal women (37–41 weeks gestation) undergoing elective or emergency cesarean section under spinal anesthesia were included.

Inclusion Criteria

1. Singleton pregnancy
2. Term gestation
3. No contraindication to uterotonics

Exclusion Criteria

1. Placenta previa or abruption
2. Coagulation disorders
3. Severe anemia (Hb <7 g/dL)
4. Hypersensitivity to study drugs

Intervention

1. **Group A (n=100):** 100 µg intravenous carbetocin single bolus after delivery.
2. **Group B (n=100):** 800 µg rectal misoprostol after delivery.

Outcome Measures

Primary outcomes:

1. Total blood loss (intraoperative + 24 hours postoperative)
2. Fall in hemoglobin level
3. Incidence of PPH

Secondary outcomes:

1. Need for additional uterotonics
2. Blood transfusion requirement
3. Adverse drug reactions

Statistical Analysis

Data were analyzed using SPSS version 23.0. Continuous variables were compared using Student's t-test, and categorical variables were analyzed using chi-square test. P-value <0.05 was considered statistically significant.

Results

Baseline demographic parameters (age, parity, BMI, gestational age) were comparable between groups (p>0.05).

Tables

Table 1: Baseline Demographic Characteristics of Study Participants

Parameter	Carbetocin Group (n=100)	Misoprostol Group (n=100)	p-value
Age (years)	25.4 ± 3.2	25.8 ± 3.5	0.462
Primigravida (%)	48 (48%)	52 (52%)	0.563
BMI (kg/m²)	28.6 ± 2.4	29.1 ± 2.7	0.218

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Parameter	Carbetocin Group (n=100)	Misoprostol Group (n=100)	p-value
Gestational Age (weeks)	37.5 ± 1.3	37.7 ± 1.5	0.336
Preoperative Hb (g/dL)	10.3 ± 1.4	10.2 ± 1.5	0.782
Preoperative Hct (%)	33.8 ± 4.1	34.0 ± 3.9	0.801

Interpretation: No statistically significant difference in baseline characteristics (p>0.05).

Table 2: Comparison of Blood Loss and Hematological Changes

Outcome Parameter	Carbetocin Group (n=100)	Misoprostol Group (n=100)	p-value
Intraoperative Blood Loss (mL)	308.2 ± 60.4	382.6 ± 72.8	<0.001
Postoperative Blood Loss (mL)	40.4 ± 12.6	49.8 ± 15.3	0.004
Total Blood Loss (mL)	348.6 ± 65.2	432.4 ± 78.5	<0.001
Postoperative Hb (g/dL)	9.48 ± 1.3	8.62 ± 1.4	<0.001
Mean Fall in Hb (g/dL)	0.82 ± 0.4	1.58 ± 0.6	<0.001
Mean Fall in Hct (%)	2.42 ± 1.2	3.08 ± 1.4	0.002

Interpretation: Carbetocin significantly reduced total blood loss and hemoglobin fall.

Table 3: Incidence of Postpartum Hemorrhage

Incidence of PPH	Carbetocin (n=100)	Misoprostol (n=100)	p-value
Yes	2 (2%)	6 (6%)	0.148
No	98 (98%)	94 (94%)	

Table 4: Requirement of Additional Interventions

Intervention	Carbetocin (n=100)	Misoprostol (n=100)	p-value
Additional Uterotonics	6 (6%)	14 (14%)	0.048
Balloon Tamponade	0	2 (2%)	0.156
Compression Sutures	1 (1%)	2 (2%)	0.561
Blood Transfusion	3 (3%)	8 (8%)	0.091
Hysterectomy	0	1 (1%)	0.316

Table 5: Adverse Drug Reactions

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Adverse Effect	Carbetocin (n=100)	Misoprostol (n=100)	p-value
Fever	8 (8%)	18 (18%)	0.031
Shivering	10 (10%)	26 (26%)	0.003
Nausea/Vomiting	9 (9%)	12 (12%)	0.487
Abdominal Pain	6 (6%)	9 (9%)	0.420
Hypotension	3 (3%)	2 (2%)	0.650
Tachycardia	7 (7%)	6 (6%)	0.771

Interpretation: Shivering and fever were significantly more common in the Misoprostol group.

Blood Loss

Mean total blood loss was significantly lower in Group A (348.6 ± 65.2 mL) compared to Group B (432.4 ± 78.5 mL) ($p<0.001$).

Hemoglobin Fall

Mean fall in hemoglobin:

- Carbetocin: 0.82 ± 0.4 g/dL
- Misoprostol: 1.58 ± 0.6 g/dL ($p<0.001$)

Incidence of PPH

- Carbetocin: 2%
- Misoprostol: 6% ($p=0.148$)

Additional Uterotonics

- Carbetocin: 6%
- Misoprostol: 14% ($p=0.048$)

Blood Transfusion

- Carbetocin: 3%
- Misoprostol: 8% ($p=0.091$)

Adverse Effects

Shivering and fever were significantly higher in the misoprostol group ($p<0.05$). Hypotension and tachycardia were comparable in both groups.

Discussion

This study demonstrated that carbetocin significantly reduces intraoperative and postoperative blood loss compared to misoprostol. The sustained uterotonic action of carbetocin likely contributes to improved uterine tone and reduced need for additional uterotonics (7,9).

Misoprostol, although less effective in reducing blood loss, remains advantageous due to heat stability, low cost, and ease of administration (5,6). Similar findings were reported by Larciprete et al., who showed superior efficacy of carbetocin over prostaglandins in high-risk cesarean sections (10).

Heat-stable carbetocin has shown non-inferiority to oxytocin in large WHO trials, making it an emerging alternative for PPH prevention (8).

However, cost considerations and availability may limit widespread use in resource-constrained settings.

Conclusion

Carbetocin is superior to misoprostol in reducing blood loss and requirement of additional uterotonics during cesarean section. It is associated with fewer side effects. Nevertheless, misoprostol remains a practical alternative in low-resource settings due to its affordability and storage advantages.

Further multicentric trials and cost-effectiveness analyses are recommended.

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