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Hemorrhage-Related Outcomes Among Women Receiving Three Prophylactic Uterotonic Regimens During Cesarean Delivery: An Observational Study

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Abstract

Background and objective

Postpartum hemorrhage (PPH) is an important cause of maternal morbidity. Hemorrhage-related outcomes among women receiving different prophylactic uterotonic regimens during cesarean delivery warrant investigation in routine clinical settings. The objective of this study is to describe and compare hemorrhage-related maternal outcomes among women receiving oxytocin, misoprostol, or carbetocin prophylaxis during cesarean delivery.

Methods

This single-center prospective observational study included 150 women undergoing cesarean delivery at Sri Krishna Medical College and Hospital, Muzaffarpur, India. Participants were recruited using predefined quotas of 50 women per prophylactic uterotonic group. Medication selection was clinician-directed without randomization. For the revised exploratory analysis, PPH was classified using estimated cumulative blood loss ⩾500 mL within 24 hours after delivery, irrespective of cause. Other outcomes included estimated blood-loss categories, postoperative hemoglobin concentrations, additional oxytocin administration, blood transfusion, surgical interventions, and adverse events. Analyses were exploratory and unadjusted.

Results

Blood-loss-defined PPH occurred in four women (8%) receiving carbetocin, eight (16%) receiving oxytocin, and 31 (62%) receiving misoprostol. Estimated blood loss exceeding 1,000 mL occurred in one (2%), four (8%), and 10 (20%) women, respectively. Additional oxytocin was administered to seven (14%), 12 (24%), and 25 (50%) women, while blood transfusion was recorded in four (8%), 10 (20%), and 17 (34%) women, respectively. The overall association between prophylactic regimen and blood-loss-defined PPH was statistically significant ($\chi^2 = 41.53$, $p < 0.001$). These findings were unadjusted and subject to potential confounding.

Conclusion

Blood-loss-defined PPH and other recorded hemorrhage-related outcomes varied across the three clinician-selected prophylactic regimens. These exploratory findings do not establish causal treatment superiority because of the nonrandomized design, potential confounding, and limitations of retrospective outcome classification. Further studies with prespecified outcomes and appropriate adjustment for baseline differences are required.

Categories: Therapeutics, Obstetrics/Gynecology, Public Health
Keywords: carbetocin, cesarean delivery, misoprostol, oxytocin, postpartum hemorrhage, uterotonics

Introduction

Postpartum hemorrhage (PPH) remains an important cause of preventable maternal morbidity and mortality worldwide. Uterine atony is a major contributor to bleeding following cesarean delivery, and prophylactic uterotonic administration forms an essential component of obstetric care. The World Health Organization (WHO) recommends the use of quality-assured uterotonics for PPH prevention, with the choice of agent influenced by clinical circumstances, availability, and health-system considerations [1].

Oxytocin is widely used for PPH prevention because of its established uterotonic efficacy, although appropriate storage and administration are important considerations [1]. Carbetocin, a long-acting oxytocin analog, has been evaluated as an alternative to oxytocin during cesarean delivery [2]. Misoprostol, a prostaglandin E1 analog, offers a non-injectable option for PPH prophylaxis, although adverse effects such

as fever and shivering require consideration [1,3]. The comparative effectiveness and safety of these agents have been examined in clinical studies, supporting the importance of evaluating their outcomes in routine obstetric practice [2,3].

Previous randomized trials and systematic reviews have investigated the comparative effects of these agents during cesarean delivery. Attilakos et al. evaluated carbetocin and oxytocin, while Elbohoty et al. compared carbetocin, misoprostol, and oxytocin [2,3]. However, outcomes observed during routine clinical practice may be influenced by patient characteristics, operative urgency, treatment-selection decisions, and differences in clinical management.

The present study aimed to describe and compare recorded maternal hemorrhage-related outcomes among women receiving three prophylactic uterotonic regimens during routine cesarean delivery at a tertiary-care hospital in Bihar, India. Because treatment selection was clinician-directed rather than randomized, the analyses were considered exploratory and were not intended to establish causal superiority of any regimen.

Materials And Methods

Study design and participant selection

This single-center, prospective, nonrandomized observational comparative study was conducted in the Department of Obstetrics and Gynecology at Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India, from August 20, 2023, to December 2024.

Participants were recruited using a non-probability quota sampling technique, with a predefined target of 50 participants in each of the three prophylactic uterotonic groups. Eligible women undergoing elective or emergency cesarean delivery were included according to the prophylactic uterotonic administered during routine clinical care: oxytocin, misoprostol, or carbetocin.

The choice of prophylactic medication was determined independently by the treating clinician based on routine clinical practice. No researcher-directed treatment allocation or randomization was performed. Recruitment continued until the predetermined sample of 150 participants, comprising 50 women in each exposure group, was achieved.

Eligibility criteria

The reported inclusion criteria were singleton pregnancy, gestational age beyond 37 weeks, and elective or emergency cesarean delivery.

The reported exclusion criteria included severe anemia, renal or hepatic disease, bleeding disorders, abnormal placentation, uterine overdistension, diabetes mellitus, severe preeclampsia, eclampsia, systemic lupus erythematosus, and known hypersensitivity to the study medications.

These criteria are summarized in Table *1*. However, the available summary documentation does not provide consistently verifiable operational thresholds for all exclusions or fully describe the original timing and procedure for assessing eligibility. These uncertainties were considered limitations of reproducibility and participant selection.

Eligibility category	Criterion
Inclusion	Singleton pregnancy
	Gestational age greater than 37 weeks
	Elective or emergency cesarean delivery
Exclusion	History of renal or hepatic disease
	History of bleeding disorders
	Severe anemia
	Antepartum hemorrhage associated with abnormal placentation, including low-lying placenta, placenta previa, or placenta accreta/percreta
	Uterine overdistension, including polyhydramnios or fetal macrosomia
	Diabetes mellitus
	Severe preeclampsia or eclampsia
	Systemic lupus erythematosus
	Known allergy to oxytocin, misoprostol, or carbetocin

TABLE 1: Inclusion and exclusion criteria for study participants

Eligibility criteria were based on the study protocol.

Prophylactic uterotonic regimens

The reported prophylactic regimens were intramuscular oxytocin (10 IU), sublingual misoprostol (600 micrograms), or slow intravenous carbetocin (100 micrograms). Administration was described as occurring after neonatal delivery.

The available summary does not establish the precise interval between neonatal delivery, placental delivery, and drug administration; the exact duration of intravenous carbetocin administration; or complete details of concomitant prophylaxis and other co-interventions.

The study therefore compares the recorded clinical outcomes associated with these specific regimens as administered during routine care, rather than isolating the pharmacological effect of one uterotonic molecule from differences in dose, route, or other clinical management.

Estimated blood-loss assessment

The source study describes estimation of operative blood loss by weighing surgical gauze, mops, and vaginal swabs before and after use, with an approximately 1 g increase in weight treated as equivalent to 1 mL of blood. Suction-container volumes were assessed after adjustment for amniotic and irrigation fluids, and estimated clot volume was incorporated.

For the revised analysis, the recorded cumulative estimated blood loss within 24 hours after delivery was used to classify hemorrhage-related outcomes. Blood loss was categorized as 0-499 mL, 500-1,000 mL, and greater than 1,000 mL. The individual components of estimated blood loss and consistency of measurement procedures across different clinical care areas could not be independently verified from the available aggregate data.

Blood-loss-defined PPH

For the revised exploratory analysis, PPH was classified as estimated cumulative blood loss ⩾500 mL within 24 hours after delivery, irrespective of the underlying cause. This threshold corresponds to the ⩾500 mL blood-loss component of the 2025 WHO diagnostic recommendations [1]. The classification was applied retrospectively to the recorded blood-loss categories and was not part of the original clinical diagnostic protocol.

The originally recorded clinician-documented atonic PPH diagnoses were retained as a separate descriptive

outcome. Because a uniform operational diagnostic definition was not documented for these clinical diagnoses, they were not equated with the retrospectively classified blood-loss-defined PPH outcome or used to establish treatment superiority. The additional WHO diagnostic criterion of blood loss ⩾300 mL accompanied by abnormal hemodynamic signs was not evaluated because the necessary individual-level clinical observations were not consistently available. No new cause-specific classification into atonic, traumatic, or other forms of PPH was performed.

Hemoglobin assessment and additional interventions

Hemoglobin concentrations were recorded before cesarean delivery and approximately 48 hours postoperatively.

The study recorded the number of women receiving additional oxytocin, blood transfusion, or uterine artery ligation in each exposure group. Packed red blood cell (PRBC) transfusion quantities were summarized as the total number of units administered and mean units per transfused woman in each group. However, transfusion timing relative to postoperative hemoglobin sampling, perioperative fluid administration, and complete rescue-treatment regimens were not consistently documented.

Postoperative hemoglobin was therefore interpreted as a recorded laboratory outcome potentially influenced by transfusion and fluid management rather than as an independent measure of hemorrhage severity.

The additional-oxytocin outcome specifically represented subsequent documented oxytocin administration. It was not assumed to represent all possible rescue uterotonic medications.

Adverse-event assessment

The available study summary documented fever, shivering, nausea or vomiting, diarrhea, and headache following prophylactic uterotonic administration.

The observation period, standardized diagnostic thresholds, and procedures for attributing these events to individual medications were not fully specified. Accordingly, these outcomes were described as adverse events recorded after prophylaxis rather than confirmed medication-induced adverse reactions.

Events not systematically reported in the available summary were not assumed to have been absent.

Study size and statistical analysis

Before recruitment, a total sample-size target of 150 participants was predefined, with an equal quota of 50 participants for each prophylactic uterotonic group. This planned quota determined the final recruitment target. The study was designed to compare recorded maternal outcomes across the three exposure groups.

A formal power calculation supporting a specified minimum detectable difference could not be verified from the available documentation. Accordingly, between-group comparisons were interpreted as exploratory, with recognition that the sample might be insufficient to detect modest differences.

Categorical outcomes were summarized using frequencies and percentages, and continuous variables were reported as means and standard deviations where available.

Mean preoperative and 48-hour postoperative hemoglobin concentrations were compared separately across the three independent exposure groups using one-way analysis of variance (ANOVA). Group sizes were equal (n = 50 each), and the reported standard deviations were reasonably similar across groups. However, participant-level normality and outlier diagnostics could not be independently verified from the available aggregate data. No paired change-score or baseline-adjusted hemoglobin analysis was performed; therefore, these comparisons were interpreted as exploratory.

For the retrospectively classified blood-loss-defined PPH outcome (estimated cumulative blood loss ⩾500 mL within 24 hours after delivery), the overall association across the three exposure groups was assessed using Pearson's chi-square test. All expected cell frequencies exceeded five. Exploratory pairwise comparisons were expressed as unadjusted absolute risk differences with 95% confidence intervals calculated using the Newcombe method. These comparisons were not adjusted for multiple testing.

No multivariable adjustment for potential confounders or confirmatory correction for multiple outcome comparisons was performed. Statistical significance was not interpreted as evidence of causal superiority, and nonsignificant baseline comparisons were not considered proof of equivalence.

The absence of individual-level data for several clinically important variables prevented reliable assessment of residual confounding and more detailed adjusted analyses.

Ethical considerations

The research proposal was reviewed and approved by the Institutional Ethics Committee of Sri Krishna Medical College, Muzaffarpur, at its meeting held on August 4, 2023. This decision was subsequently documented in an institutional letter issued on May 22, 2025 (reference number 1412/25). The date of the letter represents the issuance of documentation of the earlier committee decision rather than a new approval granted in 2025. Participant recruitment commenced on August 20, 2023, following the reported committee approval. Written informed consent was obtained from participants before enrollment.

Results

Participant characteristics

A total of 150 women were included, with 50 participants in each prophylactic uterotonic group. Mean maternal ages were 23.36 ± 3.61 years in the carbetocin group, 23.84 ± 3.27 years in the oxytocin group, and 23.32 ± 3.78 years in the misoprostol group. Other recorded baseline characteristics are summarized in Table 2. According to the recorded gestational-age categories, gestation below 38 weeks was recorded in 10 (20%), seven (14%), and six (12%) women, respectively; 38-39 weeks in 19 (38%), 22 (44%), and 24 (48%); and 40-42 weeks in 21 (42%), 21 (42%), and 20 (40%). These descriptive summaries should not be interpreted as demonstrating equivalence of baseline hemorrhage risk between groups.

Characteristic	Carbetocin (n = 50)	Oxytocin (n = 50)	Misoprostol (n = 50)
Mean age, years (mean ± SD)	23.36 ± 3.61	23.84 ± 3.27	23.32 ± 3.78
Age 21-30 years	40 (80%)	41 (82%)	38 (76%)
Primigravida	31 (62%)	29 (58%)	28 (56%)
Booked for antenatal care	4 (8%)	4 (8%)	3 (6%)
Rural residence	50 (100%)	47 (94%)	45 (90%)
Gestational age <38 weeks	10 (20%)	7 (14%)	6 (12%)
Gestational age 38-39 weeks	19 (38%)	22 (44%)	24 (48%)
Gestational age 40-42 weeks	21 (42%)	21 (42%)	20 (40%)

TABLE 2: Baseline maternal characteristics and gestational-age distribution across the three prophylactic uterotonic groups

Data are presented as n (%) unless otherwise indicated. Each group included 50 participants. Gestational age refers to gestational age at cesarean delivery.

SD: standard deviation

PPH and blood loss

Using the retrospectively applied estimated blood-loss threshold of ⩾500 mL within 24 hours after delivery, PPH was identified in four women (8%) in the carbetocin group, eight women (16%) in the oxytocin group, and 31 women (62%) in the misoprostol group. The overall unadjusted three-group association was statistically significant (Pearson's $\chi^2(2, N = 150) = 41.53$, $p < 0.001$; Cramér's $V = 0.526$).

In exploratory pairwise comparisons, the absolute risk difference for carbetocin versus oxytocin was -8.0 percentage points (95% CI, -21.4 to 5.3), while that for carbetocin versus misoprostol was -54.0 percentage points (95% CI, -67.1 to -36.4). These comparisons were unadjusted and were not corrected for multiple testing.

Estimated blood loss greater than 1,000 mL was recorded in one woman (2%) in the carbetocin group, four women (8%) in the oxytocin group, and 10 women (20%) in the misoprostol group. The blood-loss-defined PPH outcome was derived from the recorded estimated blood-loss categories and did not require classification by the underlying cause of hemorrhage (Table 3).

Outcome	Carbetocin (n = 50)	Oxytocin (n = 50)	Misoprostol (n = 50)
Blood-loss-defined PPH ≥500 mL	4 (8%)	8 (16%)	31 (62%)
Clinician-recorded atonic PPH	7 (14%)	10 (20%)	22 (44%)
Blood loss 0-499 mL	46 (92%)	42 (84%)	19 (38%)
Blood loss 500-1,000 mL	3 (6%)	4 (8%)	21 (42%)
Blood loss >1,000 mL	1 (2%)	4 (8%)	10 (20%)

TABLE 3: Blood-loss-defined postpartum hemorrhage and estimated blood-loss categories by prophylactic uterotonic group

Data are presented as n (%). Blood-loss-defined PPH was retrospectively classified as estimated cumulative blood loss ≥500 mL within 24 hours after delivery. The blood-loss-defined PPH row represents the sum of the 500-1,000 mL and >1,000 mL categories. The three blood-loss categories are mutually exclusive, with exactly 1,000 mL included in the 500-1,000 mL category. The originally clinician-recorded atonic PPH diagnoses were retained as a separate descriptive outcome without a verified uniform clinical diagnostic threshold. Individual-level overlap between the clinician-recorded diagnoses and blood-loss categories could not be established from the available aggregate data.

PPH: postpartum hemorrhage

The originally recorded clinician-documented atonic PPH diagnoses were reported in seven women (14%) in the carbetocin group, 10 women (20%) in the oxytocin group, and 22 women (44%) in the misoprostol group. These diagnoses were retained as a separate descriptive outcome and were not considered equivalent to the retrospectively classified blood-loss-defined PPH outcome.

Preoperative and postoperative hemoglobin concentrations

Mean preoperative hemoglobin concentrations were 10.95 ± 0.99 g/dL, 11.26 ± 1.20 g/dL, and 11.41 ± 1.22 g/dL in the carbetocin, oxytocin, and misoprostol groups, respectively (reported overall p = 0.128). At approximately 48 hours after delivery, the corresponding means were 9.13 ± 0.95 g/dL, 8.59 ± 0.89 g/dL, and 8.16 ± 0.95 g/dL (reported overall p < 0.001; Table *4*). These group-level summaries do not establish individual paired hemoglobin changes. Because the timing of blood transfusion relative to hemoglobin assessment and perioperative fluid administration was incompletely documented, postoperative hemoglobin differences cannot be attributed exclusively to estimated blood loss or to the prophylactic regimen.

Hemoglobin measure	Carbetocin (n = 50)	Oxytocin (n = 50)	Misoprostol (n = 50)	p-value
Preoperative Hb (g/dL)	10.95 ± 0.99	11.26 ± 1.20	11.41 ± 1.22	0.128
48-hour postoperative Hb (g/dL)	9.13 ± 0.95	8.59 ± 0.89	8.16 ± 0.95	<0.001

TABLE 4: Preoperative and 48-hour postoperative hemoglobin concentrations by prophylactic uterotonic group

Data are presented as mean ± standard deviation. p-values represent overall comparisons across the three prophylactic uterotonic groups. Postoperative hemoglobin concentrations may be influenced by blood transfusion and perioperative intravenous fluid administration.

Hb: hemoglobin

Additional interventions

Additional oxytocin was administered to seven women (14%) in the carbetocin group, 12 women (24%) in the oxytocin group, and 25 women (50%) in the misoprostol group. Blood transfusion was recorded in four women (8%), 10 women (20%), and 17 women (34%), respectively.

Among the four transfused women in the carbetocin group, three received one unit of PRBCs each, and one received 2 units, giving a total of 5 units and a mean of 1.25 units per transfused woman. In the oxytocin group, eight women received 1 unit each and two received 2 units each, giving a total of 12 units and a mean of 1.20 units per transfused woman. In the misoprostol group, 11 women received 1 unit each and six

received 2 units each, giving a total of 23 units and a mean of 1.35 units per transfused woman.

Uterine artery ligation was performed in no women in the carbetocin group, three women (6%) in the oxytocin group, and seven women (14%) in the misoprostol group (Table 5). These findings represent recorded interventions during clinical care, and their frequencies may also reflect differences in clinical decision-making and baseline patient characteristics.

Intervention	Carbetocin (n = 50)	Oxytocin (n = 50)	Misoprostol (n = 50)
Women receiving additional oxytocin	7 (14%)	12 (24%)	25 (50%)
Women receiving PRBC transfusion	4 (8%)	10 (20%)	17 (34%)
Total PRBC units transfused	5	12	23
Mean PRBC units per transfused woman	1.25	1.2	1.35
Women undergoing uterine artery ligation	0 (0%)	3 (6%)	7 (14%)

TABLE 5: Additional oxytocin administration, packed red blood cell transfusion, and uterine artery ligation by prophylactic uterotonic group

Data are presented as n (%) unless otherwise indicated. Mean transfusion units were calculated among women receiving PRBC transfusion, not among all participants. Additional oxytocin was administered following initial prophylaxis. Subsequent therapeutic interventions were performed according to clinical requirements.

PRBC: packed red blood cells

Adverse events recorded after prophylactic uterotonic administration

Fever was recorded in 10 women (20%) in the misoprostol group, one woman (2%) in the carbetocin group, and no women (0%) in the oxytocin group. Shivering was recorded in eight women (16%) in the oxytocin group, four women (8%) in the carbetocin group, and three women (6%) in the misoprostol group. Other recorded events included nausea or vomiting, diarrhea, and headache (Table 6). Because standardized observation periods, adverse-event definitions, and formal assessments of causality were not fully documented, these events are described as occurring after administration rather than as proven medication-related adverse reactions.

Recorded event	Carbetocin (n = 50)	Oxytocin (n = 50)	Misoprostol (n = 50)
Nausea or vomiting	3 (6%)	3 (6%)	2 (4%)
Diarrhea	1 (2%)	2 (4%)	3 (6%)
Shivering	4 (8%)	8 (16%)	3 (6%)
Headache	4 (8%)	4 (8%)	3 (6%)
Fever	1 (2%)	0 (0%)	10 (20%)

TABLE 6: Adverse events recorded after prophylactic uterotonic administration

Data are presented as n (%) of 50 women per group. Adverse-event categories were not necessarily mutually exclusive. Events were recorded following prophylactic uterotonic administration; temporal association does not establish medication causality. Standardized surveillance periods and uniform diagnostic thresholds were not fully documented.

Discussion

This prospective observational study evaluated hemorrhage-related outcomes among 150 women receiving three clinician-selected prophylactic uterotonic regimens during cesarean delivery. Using the retrospectively applied estimated blood-loss threshold of ⩾500 mL within 24 hours after delivery, PPH was recorded in 8%, 16%, and 62% of the carbetocin, oxytocin, and misoprostol groups, respectively. The overall association between prophylactic regimen and blood-loss-defined PPH was statistically significant. However, these findings represent unadjusted observational associations and should not be interpreted as evidence of causal

treatment superiority.

Although the carbetocin group had a lower observed PPH frequency than the oxytocin group, the exploratory pairwise comparison did not establish a statistically conclusive difference. The revised blood-loss-defined outcome provides a consistent numerical classification across all three groups, but was applied retrospectively rather than specified as the original primary outcome. Moreover, clinician-directed treatment selection and potential differences in baseline hemorrhage risk limit the interpretation of between-group differences.

Previous studies, including randomized trials by Attilakos et al. and Elbohoty et al., have examined the comparative effects of prophylactic uterotonics during cesarean delivery [2,3]. Evidence from systematic reviews and meta-analyses provides additional context for interpreting these findings. Jaffer et al. evaluated pharmacological strategies for preventing PPH following cesarean delivery in a network meta-analysis [4]. Conde-Agudelo et al. examined the effects of misoprostol on intraoperative and postoperative hemorrhage in a systematic review and meta-analysis [5]. These studies illustrate the importance of considering both hemorrhage-related outcomes and the characteristics of the prophylactic regimens.

More recent meta-analyses have specifically compared carbetocin and oxytocin in low-risk and high-risk cesarean deliveries [6,7]. Delavallade et al. also evaluated these agents among women at increased risk of hemorrhage [8]. Broader evidence is available from a Cochrane network meta-analysis examining uterotonic agents for prevention of PPH [9], and a Cochrane review focused on carbetocin [10]. Differences in study populations, outcome definitions, and clinical protocols should be considered when comparing these findings with those of the present observational study.

Additional randomized studies have investigated carbetocin and oxytocin during emergency cesarean delivery [11] and elective cesarean delivery using different dosing regimens [12]. Çetin et al. evaluated three prophylactic uterotonic regimens in a randomized clinical trial [13]. Brun et al. examined different oxytocin administration approaches in comparison with carbetocin [14], while Tureli et al. investigated carbetocin and oxytocin during elective cesarean delivery [15].

These studies evaluated prophylactic uterotonics across different patient populations and treatment protocols. In contrast, the present study included both elective and emergency cesarean deliveries, with prophylaxis selected by treating clinicians rather than through randomization. Differences in baseline hemorrhage risk, operative urgency, gestational-age distribution, medication doses, administration routes, and outcome definitions may explain variations between our findings and those of previous studies. Furthermore, clinician-directed medication selection may have been influenced by patient characteristics, drug availability, or physician preference, introducing potential confounding by indication. Therefore, the observed differences should be interpreted as exploratory associations rather than evidence of causal treatment superiority.

The recorded use of additional oxytocin, blood transfusion, and surgical intervention may reflect clinical decisions as well as bleeding severity. These interventions were not necessarily administered according to uniform thresholds, and their frequencies cannot be interpreted as independent measures of the intrinsic effectiveness of each prophylactic regimen.

Postoperative hemoglobin concentrations may be influenced by perioperative fluid administration and blood transfusion. Although the number of PRBC units administered was recorded, the timing of transfusion relative to postoperative hemoglobin measurement and details of perioperative fluid administration were not consistently documented. Therefore, between-group differences in postoperative hemoglobin should not be attributed solely to differences in blood loss.

Reported adverse-event frequencies varied across the three groups. However, standardized surveillance periods and procedures for attributing adverse events to individual medications were not consistently documented. Therefore, these findings should be interpreted as events recorded after prophylactic administration rather than confirmed medication-induced adverse reactions.

Strengths of the study

The study evaluated three prophylactic uterotonic regimens in a tertiary-care setting and reported several clinically relevant outcomes, including estimated blood loss, retrospectively classified blood-loss-defined PPH, hemoglobin concentrations, additional treatment, blood transfusion, surgical intervention, and adverse events. The data provide a descriptive account of outcomes associated with these regimens in routine clinical practice.

Limitations of the study

This single-center, nonrandomized observational study included 50 participants in each of three exposure groups using a predefined non-probability quota sampling approach. Although recruitment targets were

established before enrollment, quota sampling does not ensure baseline comparability between the exposure groups.

Treatment selection was clinician-directed, introducing potential selection bias and confounding by indication. Important baseline factors, including operative urgency, cesarean indication, labor characteristics, and prior uterotonic exposure, were not reported by treatment group, preventing reliable adjustment for these differences.

The PPH outcome was retrospectively classified using an estimated blood-loss threshold of ⩾500 mL rather than a prespecified primary-outcome definition. Although this provided a consistent numerical criterion across the three groups, the full WHO diagnostic algorithm, including the assessment of abnormal hemodynamic signs at lower blood-loss volumes, was not applied. The available aggregate data also limited independent verification of measurement consistency and cause-specific classification of hemorrhage.

Postoperative hemoglobin values may have been affected by transfusion and fluid management. Furthermore, the criteria for subsequent uterotonic administration, blood transfusion, and surgical intervention were not fully standardized in the available documentation.

Although the recruitment target was predefined, a formal sample-size calculation based on a specified primary outcome could not be verified. Multiple exploratory comparisons were performed without confirmatory adjustment for multiple testing. These factors limit statistical precision, while the single-center design, residual confounding, and incomplete outcome standardization limit reproducibility, generalizability, and causal interpretation.

Accordingly, the findings should be interpreted as hypothesis-generating descriptions of recorded clinical outcomes rather than definitive estimates of the comparative effectiveness or safety of the three prophylactic regimens.

Clinical implications

The observed differences highlight the importance of standardized outcome assessment, patient risk stratification, and documentation of prophylactic and rescue uterotonic regimens. Because the treatment groups were not randomized and several potential confounders were unmeasured, these findings do not provide sufficient evidence to change established prophylactic protocols. Further appropriately designed comparative studies are needed.

Conclusions

In this single-center prospective observational study, the frequency of retrospectively classified blood-loss-defined PPH and other hemorrhage-related outcomes varied among women receiving clinician-selected prophylactic oxytocin, misoprostol, or carbetocin during cesarean delivery. Differences in additional oxytocin administration, blood transfusion requirements, and postoperative hemoglobin concentrations were also observed.

However, these exploratory comparisons were unadjusted and remain subject to selection bias, potential confounding, and limitations associated with retrospective outcome classification. The findings do not establish causal superiority of any prophylactic uterotonic regimen. Further studies using prespecified diagnostic criteria, appropriate sample-size planning, and adjustment for baseline clinical differences are required before making comparative clinical recommendations.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Ankita Sinha, Poonam ., Pallawi Singh

Acquisition, analysis, or interpretation of data: Ankita Sinha, Poonam .

Drafting of the manuscript: Ankita Sinha, Poonam .

Critical review of the manuscript for important intellectual content: Ankita Sinha, Poonam ., Pallawi Singh

Supervision: Ankita Sinha, Poonam .

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee, Sri Krishna Medical College, Muzaffarpur issued approval 1412/25; dated August 4, 2023. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **AI use statement:** The authors used OpenAI ChatGPT (GPT-6) as follows: language polishing, structure or formatting, methodological or statistical suggestions, data cleaning or exploratory analysis, drafting summaries in Abstract, Introduction, Materials and Methods, Results, Discussion, Conclusions, tables, and references. All AI-assisted content was reviewed by the authors for scientific accuracy and consistency with the study records. Reported numerical results and aggregate statistical calculations were checked, references were verified against the cited publications, and the manuscript was reviewed for factual accuracy and appropriate interpretation. No patient-level data were generated or altered using AI. The authors confirm that they have reviewed and verified all AI-assisted content and take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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Poonam and Ankita Sinha contributed equally to this work and should be considered co-first authors.

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