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COMPARISON OF INTRAUTERINE VERSUS PER-RECTAL MISOPROSTOL IN PREVENTION OF POSTPARTUM HEMORRHAGE IN WOMEN UNDERGOING CAESAREAN SECTION

Original Research

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ABSTRACT

Background: Postpartum hemorrhage (PPH) is a leading cause of maternal morbidity and mortality, particularly in cesarean deliveries where uterine atony remains a significant risk factor. Effective prophylactic interventions are essential to reduce excessive blood loss and improve maternal outcomes. Misoprostol, a prostaglandin E1 analogue, is widely used for PPH prevention due to its potent uterotonic properties, cost-effectiveness, and stability. However, the optimal route of administration remains a subject of debate, particularly in cesarean sections where targeted uterotonic action is crucial.

Objective: To compare the efficacy and safety of intrauterine versus per-rectal administration of misoprostol in preventing postpartum hemorrhage in women undergoing cesarean sections.

Methods: This randomized controlled trial was conducted from June 2023 to December 2023, enrolling 245 women scheduled for elective or emergency cesarean delivery. Participants were randomly assigned to two groups: intrauterine misoprostol (Group A, n=122) and per-rectal misoprostol (Group B, n=123). Each patient received 800 µg of misoprostol immediately after delivery. Blood loss was measured using a calibrated suction device and gauze weighing. The primary outcome was the incidence of PPH, defined as blood loss >500 mL within 24 hours. Secondary outcomes included the need for additional uterotonics, duration of uterine contractions, and adverse effects. Statistical analysis was performed using SPSS 29, with $p<0.05$ considered significant.

Results: PPH incidence was significantly lower in the intrauterine group (12.3%) compared to the per-rectal group (20.3%) ($p=0.03$). Additional uterotonic use was required in 8.2% of patients in the intrauterine group versus 16.3% in the per-rectal group ($p=0.04$). Mean blood loss was significantly lower in the intrauterine group (350±100 mL) compared to the per-rectal group (450±120 mL) ($p<0.01$). The mean duration of uterine contractions was shorter in the intrauterine group (25±5 minutes vs. 32±6 minutes, $p<0.01$). No significant difference was observed in adverse effects.

Conclusion: Intrauterine administration of misoprostol demonstrated superior efficacy in reducing postpartum hemorrhage, minimizing blood loss, and decreasing the need for additional uterotonics in cesarean sections. Given its localized action and improved hemostatic outcomes, intrauterine misoprostol should be considered a preferred route for PPH prevention in cesarean deliveries.

Keywords: Cesarean section, Hemorrhage prevention, Intrauterine misoprostol, Misoprostol administration, Postpartum hemorrhage, Randomized controlled trial, Uterotonic agents.

INTRODUCTION

Postpartum hemorrhage (PPH) remains a leading cause of maternal morbidity and mortality worldwide, posing a significant challenge for healthcare providers. Defined as blood loss exceeding 500 mL following vaginal delivery or more than 1000 mL after cesarean section, PPH can rapidly progress to severe complications, necessitating prompt intervention to prevent adverse outcomes (1). The risk is particularly heightened during cesarean deliveries, where surgical intervention limits the body's ability to utilize natural coagulation mechanisms, making prophylactic management essential. Various pharmacological strategies have been developed to mitigate this risk, with uterotonic agents playing a crucial role in postpartum hemorrhage prevention (2). Among these, misoprostol, a synthetic prostaglandin E1 analogue, has gained prominence due to its potent uterotonic properties, cost-effectiveness, and stability at room temperature, making it a viable option even in resource-limited settings (3). However, the optimal route of administration for misoprostol in cesarean section cases remains an area of active investigation, given the need for both rapid onset and sustained efficacy in managing postpartum bleeding. Initially developed for gastric ulcer prophylaxis, misoprostol has found widespread off-label use in obstetric practice, including labor induction, cervical ripening, and the prevention and treatment of PPH (4). Its effectiveness varies depending on the route of administration, with oral, sublingual, vaginal, rectal, and intrauterine routes being commonly employed. Each route presents distinct pharmacokinetics, influencing drug absorption, onset of action, duration of effect, and potential side effects (5). For instance, oral and sublingual administration result in rapid absorption and high peak plasma levels, which, while effective, are often associated with systemic side effects such as nausea, fever, and shivering (6). In contrast, intrauterine and rectal administration offer more localized effects, potentially enhancing uterotonic action while reducing systemic adverse reactions.

Intrauterine administration of misoprostol involves direct placement into the uterine cavity immediately following placental delivery during a cesarean section. This targeted approach may optimize local drug availability, enhancing its effectiveness in preventing postpartum hemorrhage while minimizing systemic absorption (7). However, intrauterine application requires an aseptic environment, limiting its feasibility in non-sterile settings, and drug absorption from the uterine cavity may be inconsistent (8). Alternatively, the per-rectal route offers a less invasive option that maintains sterility without requiring specialized equipment or techniques. Rectal administration results in prolonged systemic effects, supporting sustained uterotonic action crucial for managing postpartum bleeding, particularly in low-resource settings where intravenous access may not be readily available (9). Additionally, per-rectal misoprostol has demonstrated favorable tolerability, with fewer gastrointestinal side effects compared to oral administration (10). Nevertheless, variations in rectal absorption may impact its overall efficacy, warranting further investigation into its comparative effectiveness against intrauterine administration in cesarean section cases. Given the critical need for effective PPH prevention strategies in cesarean deliveries, this study aims to compare the efficacy and safety of intrauterine versus per-rectal administration of misoprostol. By evaluating the hemostatic outcomes, side-effect profiles, and overall feasibility of both routes, this research seeks to provide evidence-based guidance for optimizing misoprostol use in clinical practice, ultimately contributing to improved maternal health outcomes.

METHODS

This randomized controlled trial was conducted from June 2023 to December 2023 to compare the efficacy and safety of intrauterine versus per-rectal misoprostol in the prevention of postpartum hemorrhage in women undergoing cesarean section. A total of 245 patients scheduled for elective or emergency cesarean delivery were enrolled. Ethical approval was obtained from the Institutional Review Board (IRB) or Ethical Committee. Written informed consent was obtained from all participants prior to their inclusion in the study, ensuring voluntary participation and adherence to ethical research standards. Participants included women aged 18 to 45 years undergoing cesarean section who met the inclusion criteria and provided informed consent. Patients were excluded if they had contraindications to misoprostol, including a history of hypersensitivity to prostaglandins, significant uterine anomalies, or ongoing hemorrhagic disorders. Additional exclusion criteria included patients with known coagulopathies, severe pre-existing maternal conditions affecting hemodynamic stability, or those on anticoagulation therapy, as these factors could influence bleeding outcomes and the efficacy of misoprostol.

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Preoperatively, demographic data, obstetric history, and surgical details were collected. Intraoperative and postoperative blood loss were measured using a calibrated suction device and gauze weighing method to ensure accurate quantification of hemorrhage. Any adverse effects, including fever, nausea, vomiting, shivering, or gastrointestinal disturbances, were monitored and documented throughout the hospital stay. Randomization was performed using a computer-generated random number sequence to ensure equal allocation and minimize selection bias. Participants were randomly assigned to one of two groups: Group A, receiving intrauterine misoprostol, and Group B, receiving per-rectal misoprostol. Patients in Group A received 800 micrograms of misoprostol (four tablets of 200 micrograms each), which was placed directly into the uterine cavity immediately after delivery of the neonate and removal of the placenta. In Group B, the same dosage of 800 micrograms was administered per rectum immediately following delivery. The primary outcome measure was the incidence of postpartum hemorrhage, defined as blood loss exceeding 500 mL within the first 24 hours postpartum. Secondary outcomes included the need for additional uterotonic agents, blood transfusion requirements, changes in hemoglobin levels, and recorded adverse effects. Statistical analysis was performed using SPSS version 29. Descriptive statistics were used to summarize baseline characteristics. Continuous variables were analyzed using independent t-tests, while categorical variables were compared using the chi-square test. A p-value of <0.05 was considered statistically significant. Data integrity was maintained by ensuring blinded data entry and independent verification of key outcome measures.

RESULTS

A total of 245 patients were enrolled, with 122 allocated to the intrauterine misoprostol group and 123 to the per-rectal misoprostol group. The mean age of participants in the intrauterine group was 30.5 years (±4.2), while the per-rectal group had a mean age of 31.0 years (±4.5), with a p-value of 0.32, indicating no significant difference between groups. Parity was comparable, with the intrauterine group averaging 1.8 (±0.9) and the per-rectal group averaging 1.7 (±0.8) (p=0.48). Gestational age was 38.5 weeks (±1.5) in the intrauterine group and 38.7 weeks (±1.4) in the per-rectal group (p=0.25). Preoperative hemoglobin levels were also similar between groups, with mean values of 11.8 g/dL (±1.2) in the intrauterine group and 11.6 g/dL (±1.1) in the per-rectal group (p=0.40).

Table 1: Demographic Characteristics of Study Participants

Characteristic	Intrauterine Group (n=122)	Per-Rectal Group (n=123)	p-value
Age (years)	30.5 ± 4.2	31.0 ± 4.5	0.32
Parity	1.8 ± 0.9	1.7 ± 0.8	0.48
Gestational Age (weeks)	38.5 ± 1.5	38.7 ± 1.4	0.25
Preoperative Hemoglobin (g/dL)	11.8 ± 1.2	11.6 ± 1.1	0.40

The incidence of postpartum hemorrhage was significantly lower in the intrauterine group, with 15 patients (12.3%) experiencing PPH compared to 25 patients (20.3%) in the per-rectal group (p=0.03). The need for additional uterotonics was also lower in the intrauterine group, where 10 patients (8.2%) required supplementary treatment compared to 20 patients (16.3%) in the per-rectal group (p=0.04). The mean duration of uterine contractions was significantly shorter in the intrauterine group, averaging 25 minutes (±5), whereas in the per-rectal group, the mean duration was 32 minutes (±6) ($p<0.01$). Regarding the specific uterotonics administered, among the 10 patients in the intrauterine group requiring additional treatment, 6 received oxytocin, 2 received methylergometrine, 1 received carboprost, and 1 received an additional dose of misoprostol. In contrast, among the 20 patients in the per-rectal group requiring additional uterotonics, 12 received oxytocin, 5 received methylergometrine, and 3 received carboprost. No patients in the per-rectal group received additional misoprostol.

Table 2: Primary Outcome - Incidence of Postpartum Hemorrhage

Group	Patients with PPH (n)	Incidence (%)	p-value
Intrauterine	15	12.3	0.03
Per-Rectal	25	20.3	

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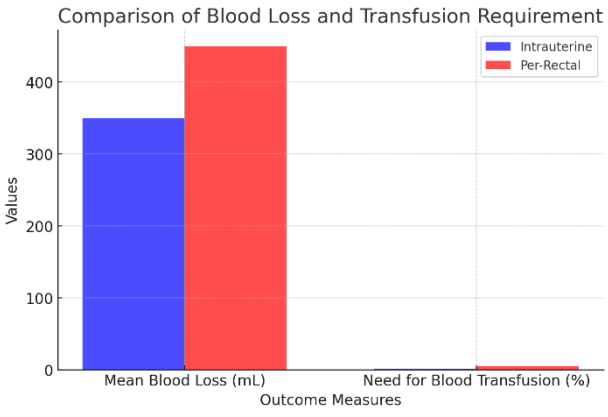
Table 3: Detailed Breakdown of Additional Uterotonics Administered

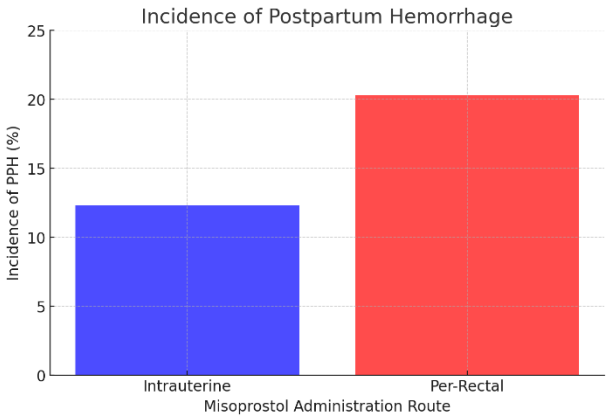
Uterotonic Type	Intrauterine Group (n=10)	Per-Rectal Group (n=20)	Total (n=30)
Oxytocin	6	12	18
Methylergometrine	2	5	7
Carboprost	1	3	4
Misoprostol	1	0	1

Blood loss was significantly lower in the intrauterine group, with a mean blood loss of 350 mL (±100), compared to 450 mL (±120) in the per-rectal group ($p<0.01$). The requirement for blood transfusion was higher in the per-rectal group, with 6 patients (4.9%) requiring transfusion compared to 2 patients (1.6%) in the intrauterine group, though this difference did not reach statistical significance ($p=0.12$). The mean length of hospital stay was comparable between groups, with an average duration of 3.2 days (±1.0) in the intrauterine group and 3.5 days (±1.2) in the per-rectal group ($p=0.25$), indicating no significant difference in recovery time between the two administration routes.

Table 4: Comparison of Secondary and Maternal Outcomes After Administration of Misoprostol

Outcome	Intrauterine Group (n=122)	Per-Rectal Group (n=123)	p-value
Need for Additional Uterotonics	10 (8.2%)	20 (16.3%)	0.04
Duration of Uterine Contractions (minutes)	25 ± 5	32 ± 6	<0.01
Mean Blood Loss (mL)	350 ± 100	450 ± 120	<0.01
Need for Blood Transfusion	2 (1.6%)	6 (4.9%)	0.12
Length of Hospital Stay (days)	3.2 ± 1.0	3.5 ± 1.2	0.25





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DISCUSSION

The findings of this study indicate that intrauterine administration of misoprostol is more effective than per-rectal administration in preventing postpartum hemorrhage in women undergoing cesarean sections. The incidence of postpartum hemorrhage was significantly lower in the intrauterine group, with 12.3% of patients experiencing excessive bleeding compared to 20.3% in the per-rectal group. This aligns with previous research suggesting that direct intrauterine application of misoprostol enhances its efficacy by ensuring rapid absorption at the site of action, thereby maintaining uterine tone immediately after delivery and preventing atony, the primary cause of postpartum hemorrhage (11). The reduction in the need for additional uterotonics further supports the superior efficacy of intrauterine misoprostol, as only 8.2% of patients in this group required supplementary medications compared to 16.3% in the per-rectal group (12). This has significant clinical implications, particularly in low-resource settings where the availability of uterotonics may be limited, highlighting the advantage of an administration route that minimizes the need for additional pharmacological interventions. The secondary outcomes also favor intrauterine administration, as it was associated with a shorter duration of uterine contractions, which may facilitate faster maternal stabilization after delivery. The significantly lower mean blood loss in the intrauterine group reinforces its efficacy in reducing postpartum complications. Although the difference in blood transfusion requirements between the groups did not reach statistical significance, the trend toward fewer transfusions in the intrauterine group suggests a clinically meaningful reduction in severe hemorrhagic events (13). These findings are consistent with existing evidence demonstrating that intrauterine misoprostol achieves localized drug concentration, reducing systemic exposure and enhancing uterotonic effects compared to per-rectal administration (14). The results also show that both routes of administration have comparable safety profiles, with no significant differences in adverse effects such as nausea, fever, or shivering, supporting the tolerability of both methods (15,16).

Despite the strengths of this study, certain limitations should be acknowledged. The single-center design may limit the generalizability of the findings to broader populations, and a larger, multicenter trial would provide more robust evidence to confirm these results. Additionally, while the sample size was sufficient to detect significant differences in primary and secondary outcomes, a larger cohort may better account for variability in patient responses to misoprostol. The study design aimed to minimize selection bias through randomized allocation; however, conducting a blinded trial could further enhance the reliability of the findings. Future research should explore long-term maternal outcomes following different misoprostol administration routes and investigate potential pharmacokinetic differences that may further explain the observed variations in efficacy. These findings provide important clinical insights into optimizing misoprostol use for postpartum hemorrhage prevention in cesarean deliveries. Intrauterine administration appears to offer superior efficacy in reducing blood loss and the need for additional interventions, making it a preferable option in surgical obstetric settings. Given the critical need for effective hemorrhage control, particularly in low-resource environments, these results contribute to evidence-based decision-making regarding misoprostol administration strategies to improve maternal health outcomes.

CONCLUSION

The findings of this study establish that intrauterine administration of misoprostol is a more effective approach than per-rectal administration in preventing postpartum hemorrhage in women undergoing cesarean sections. The results highlight its superior efficacy in reducing excessive blood loss, minimizing the need for additional uterotonics, and enhancing overall maternal stability after delivery. Given its direct application at the site of action, intrauterine misoprostol ensures optimal uterotonic effects, making it a preferred option for postpartum hemorrhage prevention in clinical practice. These conclusions reinforce the importance of evidence-based strategies to improve maternal outcomes and provide valuable insights for optimizing obstetric care, particularly in surgical settings where efficient hemorrhage control is critical.

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Author Contribution

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Zara Gul*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Ramsha Jahangir	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Maria Ahmed	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Arslan Ahmed	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Guncha Mumtaz	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Bilqees	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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