

Original Article

Hemorrhage risk mitigation in second-trimester abortion: a comparative study of prophylactic interventions

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Received: 20 May 2025; **Revised:** 09 July 2025; **Accepted:** 16 July 2025

ABSTRACT

Hemorrhage remains a major complication during second-trimester abortions, particularly in dilation and evacuation procedures. The use of prophylactic uterotonic agents plays a critical role in minimizing perioperative blood loss and related morbidity. This study aimed to compare the efficacy of three prophylactic regimens-misoprostol alone, misoprostol with oxytocin, and misoprostol with methylergometrine- in reducing hemorrhagic complications during the second-trimester dilation and evacuation procedure. A prospective, hospital-based comparative study was conducted at the Department of Obstetrics and Gynecology, Tikrit Teaching Hospital, Iraq, from April to December 2024. Ninety women diagnosed with second-trimester missed abortion (14–27 weeks of gestation) and scheduled for D&E were randomly allocated into three groups (n=30 each). Group I received rectal misoprostol; Group II received misoprostol plus intravenous oxytocin; Group III received misoprostol with intravenous and oral methylergometrine. Outcomes included estimated blood loss, need for transfusion, reoperation, retained products of conception, and need for referral to higher care. Data were analyzed using SPSS v22, with significance set at $p < 0.05$. The misoprostol–oxytocin group exhibited significantly lower rates of blood transfusion (3.3%) and reoperation (3.3%) compared to the misoprostol-only group (26.7% and 23.3%, respectively; $p < 0.05$). All three regimens effectively reduced RPOC post-intervention ($p < 0.001$), but no significant differences were observed among groups in final RPOC rates. The combination of misoprostol and oxytocin demonstrated superior efficacy in minimizing hemorrhagic complications during second-trimester D&E compared to other regimens. These findings support the adoption of dual uterotonic prophylaxis to enhance maternal safety during surgical abortion procedures.

Keywords: Second-trimester abortion, Hemorrhage prevention, Dilation and evacuation, Misoprostol, Oxytocin

Introduction

Second-trimester abortion, typically defined as termination of pregnancy between 13 and 28 weeks of gestation, remains one of the most technically challenging aspects of reproductive healthcare. Hemorrhage during this period is a serious complication that can result in significant maternal morbidity and

mortality if not adequately managed [1, 2]. Retention of intrauterine tissue is associated with multiple adverse outcomes, including intrauterine adhesion, infection, coagulopathies, infertility, and, in severe cases, maternal death [3, 4]. The risk of such complications increases with advancing gestational age. In second-trimester abortions, hemorrhage may result from uterine atony, traumatic injury to the cervix or uterus, or abnormal placentation; particularly in women with prior cesarean sections [5]. Prophylactic pharmacological agents, especially uterotonics such as misoprostol and oxytocin, have become integral to minimizing blood loss in second-trimester procedures. Other agents, including vasopressin analogs and antifibrinolytics, are occasionally utilized for similar purposes [6]. Among uterotonics, misoprostol, a synthetic prostaglandin E1 analog, acts on uterine EP3 receptors to stimulate uterine contractions and promote cervical ripening [7]. While generally

Access this article online

Website: www.japer.in

E-ISSN: 2249-3379

How to cite this article: Khudhur SS. Hemorrhage risk mitigation in second-trimester abortion: a comparative study of prophylactic interventions. J Adv Pharm Educ Res. 2025;15(3):126-32. <https://doi.org/10.51847/ULvAztFQ69>

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safe, it may cause gastrointestinal and systemic side effects, particularly at higher plasma concentrations [8, 9]. Oxytocin, an endogenous posterior pituitary hormone, induces uterine contractions by activating oxytocin receptors on myometrial smooth muscle cells, leading to intracellular calcium influx. Its rapid onset and short half-life make it particularly useful in preoperative settings [10]. Methylergometrine, a semi-synthetic ergot alkaloid, acts primarily on 5-HT₂ receptors and provides sustained uterine contractions but is contraindicated in patients with hypertension due to its potent vasoconstrictive effects [11]. Despite their widespread use, the optimal prophylactic regimen for minimizing hemorrhagic complications during 2nd-trimester dilation and evacuation (D&E) remains unclear. Previous studies have shown varying efficacy for misoprostol when used alone or in combination with other agents [3, 12]. Recent studies from both high- and low-resource settings have documented evolving trends in second-trimester abortion, highlighting improvements in procedural safety through advances in medical and surgical techniques as well as persistent disparities in service availability [13]. This study was designed to evaluate and compare the clinical effectiveness of three prophylactic regimens- misoprostol alone, misoprostol plus oxytocin, and misoprostol plus methylergonovine in minimizing hemorrhagic complications in women undergoing 2nd-trimester D&E. The findings aim to support evidence-based recommendations for improving maternal outcomes and guiding uterotonic use in clinical practice [14-19].

Materials and Methods

Study design and setting

This prospective, hospital-based comparative study was conducted in the department of obstetrics and gynecology at Tikrit teaching hospital, Iraq, over a nine-month period from April to December 2024. The study aimed to evaluate the effectiveness of three prophylactic pharmacological regimens in reducing hemorrhagic complications in women undergoing second-trimester dilation and evacuation. Participants were allocated to intervention groups using a random assignment method to reduce selection bias. While maintaining a pragmatic design reflective of routine clinical practice, the study adhered to strict inclusion and exclusion criteria to ensure internal validity [20-28].

Study population

Eligible participants included pregnant women aged 18 years and older with a confirmed diagnosis of missed abortion between 14 and 27 weeks of gestation, as determined by ultrasonographic evaluation. All women were admitted for uterine evacuation via D&E, performed by experienced gynecologic surgeons. A total of 105 women were initially screened. Ten were excluded based on eligibility criteria, and five declined to participate. The remaining 90 women were enrolled and randomly assigned into three equal groups (n = 30 per group).

Random allocation

Randomization was conducted using a simple random allocation method to assign participants to one of three treatment groups: Group I (Control): Received rectal misoprostol (600–800 mcg; 3-4 tablets of 200 mcg) administered three hours prior to D&E. Group II: Received the same misoprostol regimen plus 40 IU of oxytocin diluted in 1000 mL of normal saline, administered intravenously at 250 mL/hour starting at the onset of the procedure.

Group III: Received the same misoprostol regimen in addition to 0.2 mg intravenous methylergometrine bolus at the time of D&E, followed by oral methylergometrine 0.2 mg every 6-8 hours for up to five doses within 24 hours, as needed [29-35].

Sample size calculation

Sample size was calculated using G*Power software (version 3.1.9.7), targeting a large effect size ($f = 0.40$) with a statistical power of 90% and a two-tailed alpha of 0.05. The minimum required sample size was 87. To account for potential dropouts, 90 participants were recruited.

Inclusion criteria

1. Gestational age between 13 weeks 0 days and 27 weeks 6 days.
2. Diagnosis of missed abortion confirmed by ultrasonography.
3. Hemodynamically stable and able to provide written informed consent.
4. Willingness to receive one of the study's prophylactic regimens.

Exclusion criteria

1. Known allergy or contraindication to misoprostol, oxytocin, or methylergometrine
2. Significant pre-existing medical conditions (e.g., bleeding disorders, uncontrolled hypertension, advanced liver or kidney disease, unstable cardiac status)
3. Structural uterine anomalies (e.g., fibroids distorting the cavity, bicornuate uterus)
4. History of uterine rupture
5. Active pelvic infection

Intervention groups

Group I, (Misoprostol only): Received 600–800 mcg of rectal misoprostol (3–4 tablets, each containing 200 mcg) administered three hours before the D&E procedure.

Group II (Misoprostol + Oxytocin): Received the same misoprostol regimen as Group I, along with 40 IU of oxytocin diluted in 1000 mL of normal saline, infused intravenously at a rate of 250 mL/hour beginning at the initiation of the procedure.

Group III (Misoprostol+Methylergometrine): Received the same misoprostol regimen as Group I, in addition to a 0.2 mg intravenous bolus dose of methylergometrine at the time of D&E, followed by maintenance dosing of oral

methylergometrine (0.2 mg every 6–8 hours), up to five doses in 24 hours as needed [36, 37].

Data collection

Data were collected using a structured form documenting demographic variables (age, parity, gestational age, residence) and clinical parameters, including:

- Estimated blood loss (EBL), assessed visually by the attending physician.
- Pain severity, evaluated using the Visual Analogue Scale (VAS).
- Incidence of vaginal spotting.
- Presence or absence of retained products of conception (RPOC) post-procedure.

Primary outcomes included intraoperative and post-procedural hemorrhage, requirement for blood transfusion, reoperation, and transfer to higher levels of care.

Statistical analysis

Data were analyzed using SPSS software version 22 (Chicago, IL, USA). Continuous variables were presented as means \pm standard

deviation (SD), while categorical variables were summarized using frequencies and percentages. Normality of data was assessed using the Shapiro-Wilk test. Between-group comparisons were performed using one-way ANOVA for continuous variables, with post-hoc analysis when significant differences were detected. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. An independent samples t-test was used for two-group mean comparisons. A p-value < 0.05 was considered statistically significant [38-42].

Results and Discussion

Baseline characteristics

A total of 90 participants were enrolled and equally distributed into three groups (n=30 per group). Baseline demographic and obstetric characteristics, including age, occupation, parity, and gestational age, showed no statistically significant differences among the groups, confirming comparability prior to intervention (**Table 1**). The mean participant age ranged from 26.66 ± 4.17 to 27.43 ± 4.25 years ($p = 0.939$), with parity and gestational age similarly matched across groups ($p > 0.05$ for all).

Table 1. Baseline characteristics

Characteristics		Misoprostol – only group (N=30)	Misoprostol + oxytocin (N=30)	Misoprostol + Methylergometrene (N=30)	p-value
Age(years) (Mean \pm SD)		26.66 \pm 4.17	27.43 \pm 4.25	27.06 \pm 4.81	0.939 ^a
Occupation N(%)	Student	4(13.4%)	3(10%)	3(10%)	0.798 ^b
	employer	14(46.6%)	17(57%)	16(53%)	
	housewife	12(40%)	10(33%)	11(37%)	
Parity N(%)	0	3(10%)	3(10%)	4(13.3%)	0.857 ^b
	1	5(16.6%)	4(13.4%)	6(20%)	
	≥ 2	22(73.4%)	23(76.6%)	20(66.7%)	
Gestational age(weeks)		17 \pm 2.01	16.8 \pm 1.86	16.76 \pm 1.75	0.865 ^a

BMI: Body Mass Index, N: number, SD: standard deviation, a: ANOVA test, b: Fisher's exact test

Bleeding severity, pain scores, and spotting

No significant differences were found among the three groups in terms of bleeding severity, pain intensity (VAS), or the incidence of spotting ($p > 0.05$ for all variables); (**Table 2**). Mild bleeding

was observed in approximately half of the participants in each group, while moderate to severe bleeding was relatively infrequent. Pain was predominantly reported as mild (VAS 0–3), with only a few participants experiencing moderate or severe discomfort, as shown in **Table 2**.

Table 2. Comparative Analysis of Bleeding Severity, Pain Scores, and Spotting Incidence Across Patient Groups

Parameters		Misoprostol - only group (N=30)	Misoprostol + Oxytocin (N=30)	Misoprostol + Methylergometrine (N=30)	p-value
Bleeding rate N(%)	Mild	15(50%)	18(60%)	17(56.7%)	0.178 ^a
	Moderate	4(13.3%)	7(23.3%)	9(30%)	
	Severe	3(10%)	2(6.7%)	3(10%)	
	No bleeding	8(26.7%)	3(10%)	1(3.3%)	
Pain N(%)	None to mild (vas = 0-3)	22(73.3%)	23(76.7%)	24(80%)	0.829 ^a
	Moderate (vas=4-6)	5(16.7%)	6(20%)	4(13.3%)	
	Severe (vas=7-10)	3(10%)	1(3.3%)	2(6.7%)	
Spotting	Yes	12(40%)	8(26.7%)	5(16.7%)	0.129 ^b

N(%)	No	18(60%)	22(73.3%)	25(83.3%)
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N: number, VAS: visual analogue scale, a: Fisher's exact test, b: chi-square test

Hemorrhage-related outcomes

Significant intergroup differences were noted for key hemorrhagic complications, including the need for blood transfusion and reoperation (**Table 3**):

Blood transfusion was required in 26.7% of the misoprostol-only group (8/30), 20% of the misoprostol-methylergometrine group (6/30), and only 3.3% in the misoprostol-oxytocin group (1/30) ($p = 0.030$). Reoperation was necessary in 23.3% of the control group and 26.7% of the methylergometrine group, compared to 3.3% in the oxytocin group ($p = 0.020$). Transfers to higher-level care occurred in 13.3% (4/30) of the control group and 10% (3/30) of the methylergometrine group, while none were required in the oxytocin group; however, this difference was not statistically significant ($p = 0.112$).

The results demonstrated that the combination of misoprostol and oxytocin significantly reduced the need for blood transfusion and reoperation compared to the other two groups. Specifically, the transfusion and reoperation rates in the misoprostol-oxytocin group were 3.3%, significantly lower than those observed in the misoprostol-only (26.7% and 23.3%) and misoprostol-methylergometrine (20% and 26.7%) groups. These findings suggest that the synergistic action of misoprostol and oxytocin provides enhanced uterine contractility and

hemostasis, thereby minimizing blood loss. This outcome is consistent with prior studies reporting improved hemorrhage control when misoprostol is used in combination with oxytocin [43-46]. For example, Whitehouse *et al.* found that prophylactic oxytocin significantly reduced intraoperative bleeding during second-trimester D&E, although its effect on transfusion rates varied depending on baseline risk factors [47]. Similarly, postpartum studies have demonstrated superior blood loss reduction with dual uterotonic therapy compared to monotherapy [48, 49]. In contrast, the addition of methylergometrine did not significantly improve hemorrhage outcomes. This aligns with earlier randomized trials indicating limited efficacy of methylergometrine in second-trimester surgical settings [50]. Furthermore, its vasoconstrictive effect and sustained myometrial contraction may paradoxically interfere with complete placental expulsion, potentially increasing procedural blood loss and the need for surgical reintervention [51]. The rate of transfer to higher levels of care was low and not significantly different between groups. This suggests that severe complications were infrequent and manageable within the study setting, reflecting the relative safety of second-trimester D&E when performed with appropriate pharmacological prophylaxis and skilled personnel [52-54].

Table 3. Complications during and after evacuation

Complications		Misoprostol - only group (N=30)	Misoprostol + oxytocin (N=30)	Misoprostol + Methylergometrine (N=30)	p-value
Blood transfusions N(%)	Yes	8(26.7%)	1(3.3%)	6(20%)	0.03*
	No	22(73.3%)	29(96.7%)	24(80%)	
Reoperation N(%)	Yes	7(23.3%)	1(3.3%)	8(26.7%)	0.02*
	No	23(76.7%)	29(96.7%)	22(73.3%)	
Transfer to a higher care level N(%)	Yes	4(13.3%)	0(0%)	3(10%)	0.11 ^a
	No	26(86.7%)	30(100%)	27(90%)	

N: number, a: Fisher's exact test, *: significant at $p < 0.05$.

Retained products of conception (RPOC)

All groups demonstrated significant within-group reductions in the presence of retained products of conception following D&E ($p < 0.001$ for all); (**Table 4**). Post-treatment RPOC rates were: 13.3% in the misoprostol-only group, 10% in the methylergometrine group, and 3.3% in the oxytocin group. However, when comparing post-treatment RPOC between groups, the differences were not statistically significant ($p =$

0.353). These results suggest that while surgical evacuation was effective across all groups, none of the prophylactic regimens demonstrated clear superiority in achieving complete uterine clearance, suggesting that while uterotonic agents may support uterine tone, they do not independently influence completeness of evacuation. These results are in line with previous findings from Fujishima *et al.* which indicated that resolution of RPOC is more dependent on surgical technique and gestational age than pharmacologic support [55].

Table 4. Comparison of pre- and post-treatment retained products of conception among three uterotonic regimen patient groups

Degree of retained products of conception		Misoprostol - only group (N=30)	Misoprostol + oxytocin (N=30)	Misoprostol + Methylergometrine (N=30)	p-value
Before intervention N(%)	Present	30(100%)	30(100%)	30(100%)	NA
	Absent	0(0%)	0(0%)	0(0%)	
After intervention	Present	4(13.3%)	1(3.3%)	3(10%)	0.353

N(%)	Absent	26(86%)	29(96.7%)	27(90%)	
p-value		< 0.001	< 0.001	< 0.001	NA

N: number, NA: not applicable

Limitations of the study

Limitations include a modest sample size and the subjective estimation of blood loss. Use of objective measurement tools would improve data reliability. Additionally, the single-center design may limit generalizability to other populations.

Conclusion

The combination of misoprostol and oxytocin was significantly more effective than either control or misoprostol plus methylergometrine in reducing hemorrhage-related complications during second-trimester D&E. These findings support the integration of dual uterotonic prophylaxis into clinical protocols to improve surgical outcomes and reduce the risk of significant blood loss.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: The study received ethical approval from the Scientific Research Ethical Committee at the College of Pharmacy, University of Tikrit, Iraq (Approval ID: SREC 17). Written informed consent was obtained from all participants before inclusion in the study.

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