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COMPARISON OF SUBLINGUAL AND VAGINAL MISOPROSTOL FOR CERVICAL RIPENING BEFORE EVACUATION OF FIRST TRIMESTER MISCARRIAGE

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Abstract

Background: Missed miscarriage is a common early-pregnancy complication that often requires uterine evacuation. Inadequate cervical ripening prior to evacuation can elevate the chances of cervical injury, uterine perforation and partial evacuation. The purpose of this study was to compare the efficacy and time needed in cervical ripening with sublingual and vaginal misoprostol prior to first- trimester missed miscarriage evacuation. **Methods:** This was a randomized controlled trial carried out in the Department of Obstetrics and Gynecology, CDA Hospital. Women (n = 200) with first trimester missed miscarriage were randomly assigned in two groups. Group A was treated with sublingual misoprostol 600µg and Group B was treated with vaginal misoprostol 800µg. Additional 400µg doses were administered at 6-hours intervals as required, to a maximum of two doses. Sufficient cervical ripening was determined as the passage of a Hegar dilator 8 mm and above through the internal os without resistance in 5 hours. Data were analyzed using SPSS software. **Results:** There were no significant differences in baseline demographic and clinical characteristics. The sublingual and vaginal groups were found to have successful cervical ripening in 96 and 80%, respectively ($p<0.001$). The mean of time to cervical ripening was also significantly lower in the sublingual group (4.02 ±0.57 hours) compared to the vaginal group (4.47 ±0.61 hours; $p<0.001$). **Conclusion:** sublingual misoprostol demonstrated greater efficacy and shorter ripening time, suggesting potential suitability for rapid cervical preparation prior to evacuation.

Keywords: Missed Miscarriage; Misoprostol; Sublingual; Vaginal; Cervical Ripening; First Trimester; Uterine Evacuation.

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INTRODUCTION

Missed miscarriage, or intrauterine death of the fetus without expulsion of products of conception, is a frequent obstetric complication that is experienced in early pregnancy [1]. It frequently requires evacuation of the uterus especially when the spontaneous expulsion fails.

Nevertheless, the process can be complicated by insufficient cervical dilatation, which can result in cervical trauma, uterine perforation, and incomplete evacuation [2]. Consequently, cervical ripening before evacuation is a crucial measure to enhance the safety and outcome of the procedure [2].

A synthetic analogue of prostaglandin E1, misoprostol is now commonly applied in cervical ripening because it is affordable, stable at room temperature, and available in a variety of administration routes including oral, sublingual, buccal, and vaginal [3]. Its pharmacologic effect contains the cervix softening, augmentation of uterine contractility, and expelling of uterine contents [4].

The sublingual route is one of the different routes and is more bioavailable and absorbed rapidly because it does not undergo first-pass hepatic metabolism, leading to faster action [5]. Vaginal delivery, on the contrary, offers prolonged local release of drugs, and a higher concentration at the cervix, with possible better efficacy and less systemic side effects [6]. Recent trials and randomized controlled trials have shown similar efficacy of sublingual and vaginal misoprostol in cervical ripening and induction of labor though variation in onset, patient comfort, and side-effects have been observed.

Similar success rates in vaginal and sublingual misoprostol in achieving desired obstetric outcomes were reported in a study, and both routes were reported as a success in clinical practice [7]. In a study by Saxena et al. has found that the sublingual route of misoprostol administration had a higher efficacy of 96% in achieving adequate cervical ripening, compared to 80% efficacy with the vaginal route before evacuation of first trimester missed miscarriage [8].

Moreover, systematic reviews and meta-analyses indicate that the administration route is a significant clinical outcome, such as time to expulsion and the overall success rate [9]. There is evidence that vaginal misoprostol might be more successful in certain locations, but sublingual administration is a rapid acting agent that is easy to administer and more acceptable by patients.

Although international data is available, clinical practice variability exists because of the population of patients, dose regimens, and study methodology. Thus, the study was intended to compare the efficacy of sublingual and vaginal misoprostol in cervical ripening prior to evacuation of first trimester missed miscarriage in a controlled clinical environment, as well as creating context-specific evidence to inform individualized patient management.

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METHODOLOGY

This was a randomized controlled trial carried out in the department of Obstetrics and Gynecology at CDA Hospital within a duration of six months following institutional ethical review committee approval (Reference No: IRB-128 dated: 09-12-2025). The WHO sample size calculator determined a sample size of 200 patients, with 95% confidence, 5% level of significance (two-sided) and 90 percent power based on previously reported efficacy rates of 96 percent with sublingual misoprostol and 80 percent with vaginal misoprostol [8]. Two hundred women were recruited on non-probability consecutive sampling basis and randomly assigned to two equal groups (n=100 each) by blocked randomization.

Inclusion criteria included women between the ages of 18 and 40 years old, who have a singleton pregnancy, gestational age of between 7 and 13 weeks as determined by ultrasound, any parity and those with diagnosed missed miscarriage as per operational definition. Pregnancies in women with molar or ectopic history, known hypersensitivity to misoprostol, hypertension, glaucoma or sickle cell anemia were excluded. Baseline demographic and clinical data, such as age, gestational age, parity, body mass index (BMI), education level, profession, residential status, and comorbidities (diabetes mellitus, thyroid disease, bleeding disorders, uterine anomalies/fibroids, and history of pelvic infections), were collected using a structured proforma after signing a written informed consent.

Group A was administered 600µg of misoprostol sublingually and Group B was administered 800µg of misoprostol vaginally with 2.5 ml of hydroxyethyl gel applied to the posterior vaginal fornix. Another dose of 400ug misoprostol was given at 6-hour intervals to a maximum of two doses in both groups in cases of inadequate response. No regular premedication was given, but analgesics were given when needed. Intra-operative cervical dilatation was measured with Hegar dilators and sufficient cervical ripening was established as the passage of a dilator 8 mm or more through the internal os without resistance during 5 hours of misoprostol application.

The first was efficacy of cervical ripening and the second was time taken to attain adequate dilatation. Statistical analysis was done with SPSS version 26. Mean ± standard deviation was used to state the quantitative variables such as age, gestational age, BMI, parity, and time to cervical ripening and the independent samples t-tests were used to compare the variables. Interpretation of categorical variables was in the form of frequencies and percentages and was compared using the chi-square test. The main result, efficacy of cervical ripening, was compared in the groups by chi-square test. Time to cervical ripening was compared using the independent samples t-test. Moreover, binary logistic regression was conducted to estimate the independent effect of treatment group on efficacy with or without the adjustment of possible confounders. A p-value of less than 0.05 was considered significant.

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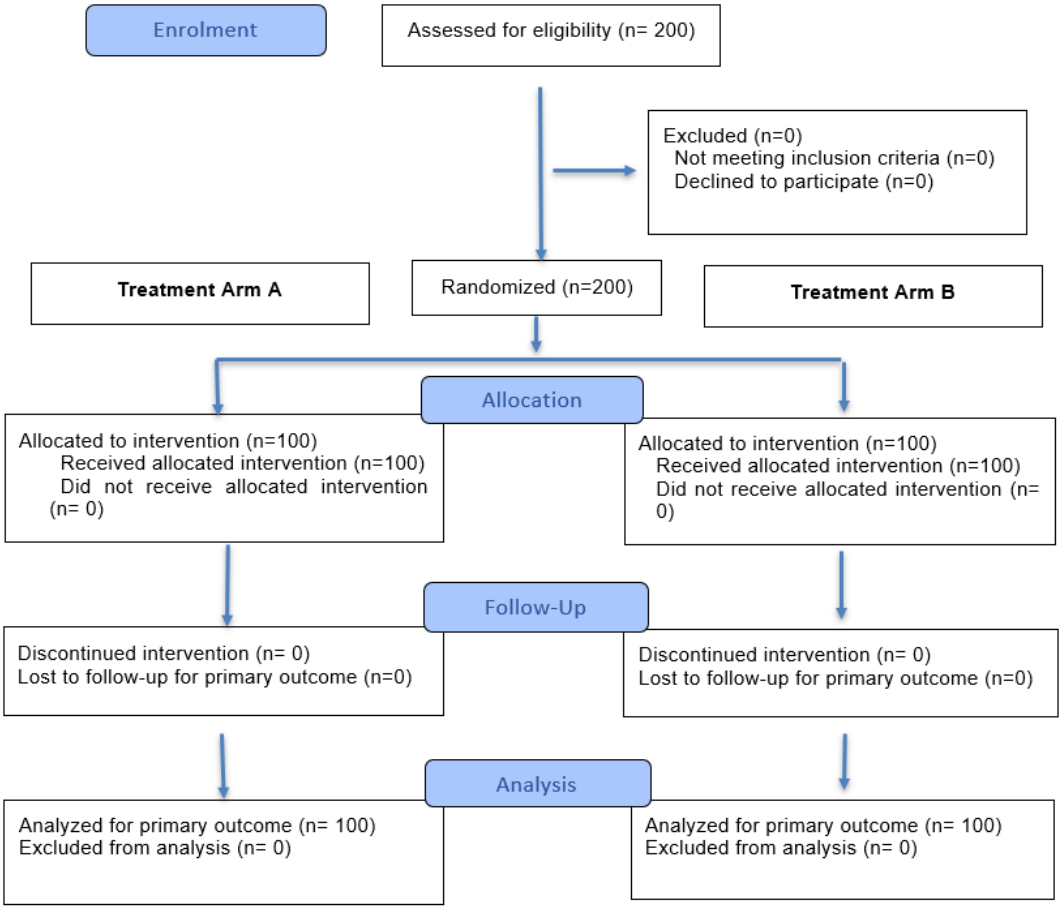

Figure 1: Flow diagram of participant recruitment, allocation, follow-up, and analysis

RESULTS

A total of 200 patients were included in the study and randomly allocated into two equal groups, with 100 patients each in the sublingual and vaginal misoprostol groups. All enrolled participants completed the study. Baseline demographic and clinical characteristics of the study population are presented in Table 1. There were no statistically significant differences between the two groups with respect to age, gestational age, parity, and body mass index ($p>0.05$).

Table 1: Baseline Continuous Variables

Variable	Sublingual (n=100)	Vaginal (n=100)	p-value
Age (years)	29.35 ± 5.00	28.88 ± 4.81	0.499
Gestational age (weeks)	9.97 ± 1.38	9.84 ± 1.32	0.484
Parity	1.45 ± 1.31	1.45 ± 1.33	1.000
BMI (kg/m²)	26.86 ± 3.56	26.52 ± 3.43	0.490

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The distribution of categorical variables in the overall study population is summarized in Table 2.

Table 2: Distribution of Categorical Variables (n=200)

Variable	Category	Frequency	Percentage (%)
Residential status	Rural	82	41.0
	Urban	118	59.0
Education	Educated	134	67.0
	Uneducated	66	33.0
Profession	Housewife	154	77.0
	Job	46	23.0
Diabetes	Yes	27	13.5
	No	173	86.5
Thyroid disease	Yes	15	7.5
	No	185	92.5
Bleeding disorder	Yes	9	4.5
	No	191	95.5
Uterine anomalies/fibroids	Yes	19	9.5
	No	181	90.5
Pelvic infection	Yes	31	15.5
	No	169	84.5

Comparison of categorical baseline variables between the two groups is shown in Table 3. No statistically significant differences were observed between the groups ($p>0.05$).

Table 3: Comparison of Baseline Categorical Variables Between Groups

Variable	Sublingual n (%)	Vaginal n (%)	p-value
Residential (Rural)	40 (40.0)	42 (42.0)	0.774
Education (Educated)	68 (68.0)	66 (66.0)	0.764
Profession (Housewife)	76 (76.0)	78 (78.0)	0.737
Diabetes (Yes)	14 (14.0)	13 (13.0)	0.836
Thyroid disease (Yes)	8 (8.0)	7 (7.0)	0.788
Bleeding disorder (Yes)	5 (5.0)	4 (4.0)	0.733
Uterine anomalies/fibroids (Yes)	10 (10.0)	9 (9.0)	0.809
Pelvic infection (Yes)	16 (16.0)	15 (15.0)	0.845

The efficacy of cervical ripening is presented in Table 4. A significantly higher proportion of patients in the sublingual group achieved successful cervical ripening compared to the vaginal group (96.0% vs 80.0%, $p<0.001$).

Table 4: Comparison of Efficacy Between Groups

Outcome	Sublingual (n=100)	Vaginal (n=100)	p-value
Efficacy (Yes)	96 (96.0%)	80 (80.0%)	<0.001
Efficacy (No)	4 (4.0%)	20 (20.0%)	

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The time required to achieve cervical ripening is shown in Table 5. The mean time to cervical ripening was significantly shorter in the sublingual group compared to the vaginal group (p<0.001).

Table 5: Time to Cervical Ripening

Variable	Sublingual	Vaginal	p-value
Time (hours)	4.02 ± 0.57	4.47 ± 0.61	<0.001

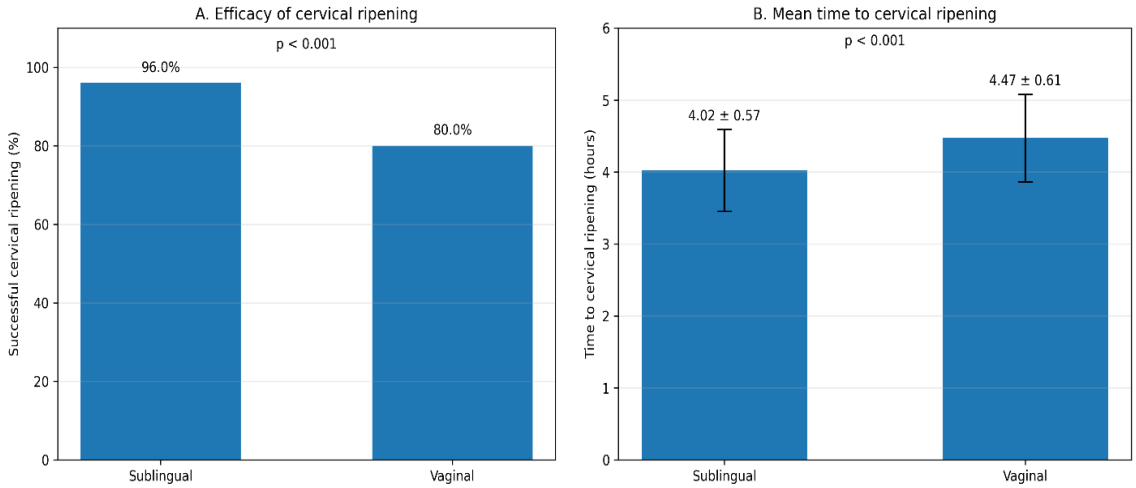

Figure 2: Graphical comparison of efficacy and mean time to cervical ripening between the two groups

DISCUSSION

The current research shows that sublingual misoprostol was much more effective than vaginal misoprostol in cervical ripening before first-trimester missed miscarriage evacuation. Adequate cervical ripening was achieved in 96.0% of women in the sublingual group and 80.0% in the vaginal group. The mean time to ripening was shorter with the sublingual group (4.02 ± 0.57 hours) compared to the vaginal group (4.47 ±0.61 hours). These findings suggest that, in this clinical context, the sublingual route was both more effective and faster for cervical preparation. Notably, the groups were similar in age, gestational age, parity, BMI, and baseline variables. This supported the trial's internal validity and clarified that the observed difference was due to the route of administration rather than baseline imbalance.

The main strength of this study is its focus on a more limited and clinically specific question: cervical ripening before evacuation, not total medical expulsion. This distinction matters when comparing the results to existing literature. Ghosh et al. showed that miscarriage management outcomes depend on both route and clinical outcome measured, confirming the need for route-specific results to match treatment goals. Similarly, Mizrachi et al. reported significant global uncertainty about the best dosing and

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route, with wide variation in misoprostol regimens to induce early pregnancy loss. Against this background, the current study offers specific evidence for women under planned evacuation after a missed miscarriage, where quick, dependable cervical priming is needed.

The present results are also supported by direct comparative literature on cervical preparation. Malik et al. compared sublingual and vaginal misoprostol as means of cervical preparation preceding first-trimester surgical abortion and found a similar pattern to the one in the present study, with greater effectiveness and greater cervical dilation in the sublingual arm but more frequent systemic side effects. The importance of this parallel is that it hints that the benefit of the sublingual route may not be specific to a single institution or population, but perhaps represents a larger pharmacodynamics advantage when the endpoint is rapid cervical preparation to instrumentation. [12]

At the same time, the findings of the current study appear to contrast with parts of the recent literature on the medical management of missed miscarriage and early pregnancy loss. Majeed et al. (2025) concluded that vaginal misoprostol had a higher rate of success and a lesser induction-to-expulsion period than oral misoprostol when used to induce first-trimester missed abortion [13]. Likewise, Tarleton et al. highlight that, when misoprostol is administered alone and without mifepristone to induce early pregnancy loss, sublingual or vaginal administration can be used, but combination therapy with mifepristone and misoprostol should be the rule of thumb [14]. Other real-world studies and systematic reviews have demonstrated a consistent better success rate and a reduced rate of treatment failure with combination regimens versus misoprostol alone [15,16]. Nevertheless, such studies compared full uterine evacuation, a decrease in the need to repeat treatment, or surgery elimination, but not a short interval of cervical readiness to evacuation. To this end, the apparent inconsistency is more probably the result of differences in endpoint than a real contradiction in the evidence base [17,18].

This endpoint difference is core in the interpretation of the present study. Successful passage of a Hegar dilator 8 mm through the internal os without resistance in 5 hours was considered a success in the current study; in contrast, prolonged exposure, sustained uterotonic effect, and eventual complete expulsion were the dominant outcome measures in medication-only management of early pregnancy loss. With this definition, immediate action becomes more significant than local exposure. This could be the reason why the sublingual regimen was more effective than the vaginal regimen in the present study, even though the vaginal group was given a higher initial dose. Practically speaking, these results indicate that the route of administration might be more important than dose escalation in cases where the endpoint of interest is rapid cervical priming prior to surgery [13,14].

The general literature on early-pregnancy loss also shows that response to treatment is dependent on patient and pregnancy factors, which can be used as a helpful background to understand the reported results. MISOPRED score created by Bar-Noy et al. indicated that nulliparity, previous spontaneous abortion, gestational age, vaginal bleeding,

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abdominal pain, and mean sac diameter were significant predictors of misoprostol success [19]. Cohen et al. found that women with a history of retained placenta had a lower success rate of misoprostol treatment for early pregnancy failure [20]. Although Meister et al. indicated that the overall success rate was 86% with misoprostol, and post-treatment endometrial thickness might be predictive [15]. Colleselli-Turtscher et al. also demonstrated high efficacy of mifepristone-misoprostol therapy and found lower gestational age to be an independent predictor of successful medical therapy [21]. The combined evidence of these studies is that route does not dictate response to misoprostol, but is adjusted by underlying patient factors, gestational peculiarities, and therapeutic purpose. This also justifies the necessity to contextualize the superiority of sublingual misoprostol in the current study in the context of pre-evacuation cervical ripening.

The findings of the current research have practical implications in terms of service delivery. A protocol offering faster and more consistent cervical ripening could enhance theatre throughput, wait times to evacuation, and, perhaps, the technical complexity of the procedure. These benefits can be especially useful in high-traffic hospitals in the public sector and in day-care gynecology units, where shorter preoperative periods can be useful. Secondly, sublingual delivery does not require vaginal insertion, which could enhance acceptability in certain women and decrease pelvic manipulation. However, patient satisfaction, adverse effects, analgesic requirement, intraoperative blood loss, or even procedural complications like cervical injury or incomplete evacuation were not evaluated in the current study. Thus, the current results support the efficacy and speed of the sublingual route, but they do not determine an overall superiority of all clinical and patient-centered outcomes [12,22].

There are also a number of limitations of the current study. First, it was carried out at one center, which can be a limitation to generalizability. Second, the sample size was sufficient to yield the primary outcome, but the study failed to indicate stratified subgroup analyses of potentially relevant modifiers, including parity, BMI, comorbidities, or specific gestational-age groups. Third, binary logistic regression was indicated in the methodology to adjust for confounding, but adjusted results on the regression were not shown in the synopsis, which restricts the interpretation of the independent treatment effect to unadjusted group comparison. Fourth, the research was on immediate cervical ripening and time to dilatation, but not on operative ease, safety outcomes, repeat evacuation necessity, and patient-reported experience. These constraints do not nullify the results, but they imply that conclusions must be drawn in relation to the particular endpoint under analysis.

CONCLUSION

In conclusion, the present study concluded that sublingual misoprostol is more effective and faster than vaginal misoprostol for cervical ripening before evacuation of a first-trimester missed miscarriage. This study suggests that the choice of route should depend

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on the treatment goal. If the aim is quick cervical preparation before a procedure, sublingual misoprostol may be more suitable. However, if the goal is complete expulsion without surgery and a lower chance of treatment failure, vaginal misoprostol or combination regimens may be more effective.

References

1) Quenby S, Gallos ID, Dhillon-Smith RK, Podesek M, Stephenson MD, Fisher J, Brosens JJ, Brewin J, Ramhorst R, Lucas ES, McCoy RC. Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. The Lancet. 2021 May 1; 397(10285):1658-67. Doi: 10.1016/S0140-6736(21)00682-6

2) Farhadian Y, Friedman M, Tarashandegan D, Mor L, Cohen I, Gluck O, Kerner R, Keidar R, Weiner E, Sagiv R. Complications Following Late Second-Trimester Dilatation and Evacuation: A Retrospective Cohort Comparison of Missed and Induced Abortions. International Journal of Women's Health. 2026 Dec 31:1-0. Doi: https://doi.org/10.2147/IJWH.S561941

3) Godakandage Y, Furukan R. Oral Misoprostol vs Intravaginal Dinoprostone for Pre-Induction Cervical Ripening in Post-Term, Uncomplicated Pregnancies: A Randomized Controlled Trial. Open Journal of Obstetrics and Gynecology. 2024; 14(12):1807-20. Doi: https://doi.org/10.4236/ojog.2024.1412150

4) Eminov E, Eminov A. Comparison of the effectiveness and safety of vaginal and sublingual low-dose misoprostol versus vaginal dinoprostone for labor ınduction: A retrospective cohort study. PLoS One. 2025; 20(10):e0336025. Doi: 10.1371/journal.pone.0336025.

5) Bahraminejad S, Almoazen H. Sublingual and buccal delivery: a historical and scientific prescriptive. Pharmaceutics. 2025 Aug 20; 17(8):1073. Doi: 10.3390/pharmaceutics17081073

6) Vorontsova Y, Haas DM, Flannery K, Masters AR, Silva LL, Pierson RC, Yeley B, Hogg G, Guise D, Heathman M, Quinney SK. Pharmacokinetics of vaginal versus buccal misoprostol for labor induction at term. Clinical and Translational Science. 2022 Aug; 15(8):1937-45. Doi: https://doi.org/10.1111/cts.13306

7) Atemie Gordon, Harry T. Clement, Porbeni-Fumudoh B. Offiong, Okumoko A Maureen, Ani C MaryJane, Nwanze C Nnamdi, Akanatei I Daniel, Warisuo S. Ariwelo. Fetomaternal Outcomes Following Sub-Lingual and Vaginal Misoprostol for Induction of Labour: A Randomized Controlled Trial. International Journal of Medical Science and Clinical Research Studies. 2025; 5(12):2071-9. Doi: https://doi.org/10.47191/ijmscrs/v5-i12-22

8) Saxena P, Salhan S, Sarda N. Sublingual versus vaginal route of misoprostol for cervical ripening prior to surgical termination of first trimester abortions. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2006 Mar 1; 125(1):109-13. Doi: 10.1016/j.ejogrb.2005.07.022

9) Pergialiotis V, Panagiotopoulos M, Constantinou T, Vogiatzi Vokotopoulou L, Koumenis A, Stavros S, Voskos A, Daskalakis G. Efficacy and safety of oral and sublingual versus vaginal misoprostol for induction of labour: a systematic review and meta-analysis. Archives of gynecology and obstetrics. 2023 Sep; 308(3):727-75. Doi: 10.1007/s00404-022-06867-9

10) Ghosh J, Papadopoulou A, Devall AJ, Jeffery HC, Beeson LE, Do V, et al. Methods for managing miscarriage: a network meta-analysis. Cochrane Database Syst Rev. 2021; 6(6):CD012602. Doi: 10.1002/14651858.CD012602.pub2

11) Mizrachi Y, Donyo N, Khatib N, Weiner E, Svirsky R, Benshalom-Tirosh N, et al. Misoprostol treatment for early pregnancy loss: an international survey. Reprod Biomed Online. 2021; 42(5):997-1005. Doi: 10.1016/j.rbmo.2021.02.009.

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.21067535

12) Malik N, Chawla D, Sharma N, Soni M, Singhal A, Talwar N. Sublingual vs. vaginal misoprostol for cervical preparation before surgical abortion in the first trimester. New Indian J OBGYN. 2023; 10(1):116-120. doi:10.21276/obgyn.2023.10.1.20.

13) Majeed K, Syed H, Murtaza M, Hanif ZM, Ali H. Efficacy and safety of oral versus vaginal misoprostol for medical management of first trimester missed abortion: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2025; 305:92-99. doi:10.1016/j.ejogrb.2024.12.009.

14) Tarleton JL, Benson LS, Moayedi G, Trevino J. Society of Family Planning Clinical Recommendation: medication management for early pregnancy loss. Contraception. 2025; 144:110805. doi:10.1016/j.contraception.2024.110805.

15) Meister L, Künnemann I, Fettke F, Lux A, Ignatov A. Medical treatment of miscarriage using misoprostol-a retrospective study. Arch Gynecol Obstet. 2024; 310(4):2115-2121. Doi: 10.1007/s00404-024-07628-6.

16) Benson LS, Gunaje N, Holt SK, Gore JL, Dalton VK. Outcomes after early pregnancy loss management with mifepristone plus misoprostol vs misoprostol alone. JAMA Netw Open. 2024; 7(10):e2435906. doi:10.1001/jamanetworkopen.2024.35906.

17) Friedman M, Mor L, Shazar R, Paul N, Kerner R, Keidar R, et al. Treatment of early pregnancy loss with mifepristone and misoprostol compared with misoprostol only. Obstet Gynecol. 2025; 145(2):204-209. doi:10.1097/AOG.0000000000005800.

18) Pirrami RG, Reinert JP, Li P, Krenzelok EP, Spinler SA. Efficacy and safety of mifepristone and misoprostol compared to misoprostol alone for the resolution of miscarriage and intrauterine fetal death: a systematic review and meta-analysis. Ann Pharmacother. 2025; 59(7):636-647. doi:10.1177/10600280241289968

19) Bar-Noy T, Limonad O, Gandelsman E, Shrim A, Sharabi H, Zarecki R, et al. The MISOPRED score: development and validation of a clinical scoring system to predict the effectiveness of misoprostol treatment for early pregnancy loss. PLoS One. 2024; 19(5):e0303607. doi:10.1371/journal.pone.0303607.

20) Cohen A, Gutman-Ido E, Karavani G, Albeck A, Rosenbloom JI, Shushan A, et al. The association between history of retained placenta and success rate of misoprostol treatment for early pregnancy failure. BMC Womens Health. 2023; 23(1):523. doi:10.1186/s12905-023-02666-9

21) Colleselli-Türtscher V, Hafenmayr M, Ciresa-König A, Trinker M, Maier S, Toth B, et al. Retrospective cohort study comparing success of medical management of early pregnancy loss in pregnancies conceived with and without medical assistance. Fertil Steril. 2024; 121(5):824-831.

22) World Health Organization. Clinical practice handbook for quality abortion care. Geneva: World Health Organization; 2023.