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Research Article

Sublingual versus Vaginal Misoprostol for Medical Management of First-Trimester Missed Miscarriage: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: The relative effectiveness and tolerability of sublingual and vaginal misoprostol for first-trimester missed miscarriage remain uncertain when treatment regimens and assessment intervals differ.

Objective: To compare complete evacuation, surgical evacuation, time to expulsion, and adverse effects between equal-dose sublingual and vaginal misoprostol regimens.

Methods: This manuscript synthesizes the supplied evidence extraction dated 2 October 2026. Reports were identified through web, registry and citation searching. Eligible studies were randomized trials of misoprostol alone for ultrasound-diagnosed first-trimester missed miscarriage or closely related early pregnancy failure. Only separable first-trimester outcomes were used from mixed gestational age populations. Formal database searches and independent duplicate extraction had not been completed. Study-specific risk ratios (RRs) and mean differences (MDs) with 95% confidence intervals (CIs) were presented without pooling because outcome definitions, assessment intervals, and data reliability differed. Risk of bias and certainty ratings were provisional.

Results: The supplied screening record contained 23 reports: 10 excluded, eight awaiting classification and five provisionally included trials. Four trials provided numerical complete evacuation data for 361 participants. Complete evacuation RRs were 0.95 (95% CI 0.52–1.73), 1.14 (0.87–1.49), 1.37 (1.06–1.77) and 0.05 (0.003–0.80); the last estimate depended on disputed denominators and continuity correction. Two trials reported less surgical evacuation with sublingual treatment, with RRs of 0.67 (0.40–1.12) and 0.62 (0.41–0.92). Time to expulsion findings differed: MD −8.5 hours (−11.5 to −5.5) and +3.6 hours (2.8–4.4). Heavy bleeding was more frequent with sublingual treatment in one trial, RR 4.00 (1.19–13.48). Provisional certainty was low or very low.

Conclusion: The extracted evidence does not establish consistent superiority of either route. A possible reduction in surgical evacuation with sublingual treatment must be weighed against uncertain effectiveness estimates and possible increases in adverse effects. Incomplete evidence identification, unresolved reporting discrepancies and methodological limitations prevent definitive conclusions.

Keywords: Misoprostol, Sublingual Administration, Vaginal Administration, Missed Miscarriage, Early Pregnancy Failure, Systematic Review, Narrative Synthesis.

INTRODUCTION

Missed miscarriage describes a nonviable pregnancy retained within the uterus. The trials considered here used ultrasound to establish pregnancy failure and included embryonic death and, in some studies, anembryonic pregnancy. Medical treatment aims to achieve expulsion without surgical evacuation while limiting bleeding, pain and other adverse effects. Complete expulsion is therefore important, but it is not the only outcome relevant to the comparative value of treatment. Misoprostol has been administered through both sublingual and vaginal routes in randomized comparisons. The practical difference between routes is accompanied by variation in dose, repeat dosing schedules and thresholds for declaring treatment unsuccessful. A route comparison within an individual trial uses the same nominal dose in both groups, but comparisons across trials may represent substantially different treatment strategies. A result assessed shortly after dosing cannot automatically be interpreted as equivalent to success assessed after several days or until the return of menstruation. [1–5]

The purpose of this review manuscript is to synthesize the currently extracted randomized evidence comparing sublingual with vaginal misoprostol alone for first trimester missed miscarriage. The review addresses complete evacuation, surgical evacuation, time to expulsion and adverse effects. It also evaluates how study design, incomplete reporting and differences in outcome assessment affect interpretation. Because the supplied evidence record documents unfinished searches and verification, this manuscript reports the current synthesis transparently and does not claim a completed comprehensive search or a meta-analysis.

METHODS

Review Framework and Evidence Provenance

The manuscript was prepared from the supplied document, Sublingual vs Vaginal Misoprostol for First-Trimester Missed Abortion: Evidence Tables and Figures, dated 2 October 2026. That document contained study characteristics, regimens, extracted outcomes, exclusion reasons, provisional risk of bias judgments, provisional certainty ratings and a screening record. PRISMA 2020 informed the organization and transparent reporting of available information; full PRISMA compliance is not claimed because the evidence identification process remains incomplete. [6] No registration identifier or accessible review protocol was supplied. A reference to a protocol in the extraction document was not treated as evidence of prospective registration or of a prespecified analytical decision.

Eligibility Criteria

The review question concerned women with ultrasound diagnosed first trimester missed miscarriage, including nonviable intrauterine pregnancy and anembryonic pregnancy where these were included by trial investigators. Eligible comparisons used sublingual versus vaginal misoprostol alone at equal doses within a reported randomized trial. Studies concerned with cervical preparation before planned surgery, second trimester treatment without separable first trimester findings, a different route comparison, or nonrandomized allocation were excluded from the randomized evidence synthesis. Retracted evidence was excluded. Studies with unverified allocation or unavailable arm level data remained excluded provisionally or awaited classification, as recorded in the supplied evidence document.

For Shah 2010, the overall trial recruited pregnancies below 20 weeks; only the subgroup at or below 12 weeks contributed to the main complete evacuation analysis. Whole trial tolerability findings were retained as contextual information and were not treated as first trimester specific estimates. Sonsanoh 2014 and El Sokkary 2016 were provisionally included even though their exact upper gestational limits were not established in the extraction record. This uncertainty was considered an applicability limitation rather than resolved by assumption.

Information Sources and Study Selection

The supplied screening record describes web, trial registry and citation searching and assessment of full text reports, abstracts, registry entries and secondary extractions. It records 23 reports assessed for eligibility, with five assessed through full text and 18 through other report types. Formal searches of PubMed, CENTRAL, Embase, Scopus, ClinicalTrials.gov and ICTRP had not been run as a reproducible systematic search. Search strings, source specific dates, database yields, deduplication procedures and independent screening procedures were not documented. The screening counts therefore describe the supplied record of identification through other methods and should not be interpreted as a completed database search.

Targeted online checks during manuscript preparation confirmed bibliographic details of included studies and methodological references. These checks were not used to reconstruct missing search history or to add outcome data to the supplied synthesis. Reports awaiting classification remained outside the numerical analyses. Figure 1 records the current screening counts without adding hypothetical database records.

Data Extraction and Outcomes

The supplied data were extracted by one reviewer; independent second reviewer verification was outstanding. Extracted fields included setting, allocation method, diagnostic criteria, gestational age, group sizes, dose, repeat interval, maximum cumulative dose, outcome definitions, follow-up and adverse effects. Complete evacuation was the principal outcome, using each trial's reported definition and assessment interval. Additional outcomes were surgical evacuation, time from first dose to expulsion and adverse effects. A common primary assessment time was not established in the source document.

Discrepancies were retained visibly. Dehbashi 2016 reported conflicting treatment group denominators and postrandomization exclusions. The working extraction used 27 sublingual and 25 vaginal participants because these denominators matched reported percentages, but this interpretation remains unconfirmed. El Sokkary 2016 reported 240 randomized participants and 160 analyzed participants without an adequate explanation for the difference. Inconsistent adverse effect rates between that report's Results and Discussion were not combined; the extraction used Results figures and withheld inconsistent diarrhoea counts.

Risk of Bias and Certainty of Evidence

The supplied assessment used the five RoB 2 domains for the complete evacuation outcome: randomization, deviations from intended interventions, missing outcome data, outcome measurement and selection of reported results. [7] Overall judgments were retained as provisional single reviewer assessments. They were not automatically extended to every secondary outcome. Absent trial registration or a protocol was treated as limited information concerning selective reporting, rather than proof of selective reporting.

The supplied GRADE summary rated certainty by outcome, considering risk of bias, inconsistency, indirectness and imprecision. [8] These ratings were retained as provisional because extraction verification and full eligibility assessment remain incomplete. No absolute pooled effect was estimated. Missing information about serious complications was treated as absence of adequate reporting, not evidence of absence of harm.

Effect Measures and Synthesis

For binary outcomes, RR was defined as the sublingual event risk divided by the vaginal event risk. An RR above 1 indicates more complete evacuation with sublingual treatment for the principal outcome, but more events with sublingual treatment for surgery or adverse effects. For continuous outcomes, MD was defined as the sublingual mean minus the vaginal mean; a negative value indicates a shorter expulsion interval with sublingual treatment.

The manuscript retained the study specific estimates and 95% CIs supplied in the extraction. For the zero event sublingual arm in Dehbashi 2016, the displayed RR used 0.5 added to all four cells; the observed event counts remained unchanged. This correction produces a finite descriptive estimate and does not resolve the denominator conflict. No meta-analysis was undertaken because a common clinically comparable endpoint had not been established, regimen and population differences were substantial, and important data integrity issues remained unresolved. Opposite directions of effect alone were not considered sufficient reason to rule out meta-analysis. No pooled heterogeneity statistic, subgroup meta-analysis or statistical sensitivity analysis was calculated. Funnel plot assessment and small study effect tests were not performed because only four trials contributed the principal numerical outcome.

RESULTS

Study Selection and Characteristics

The supplied screening record contained 23 reports. Ten were excluded, eight awaited classification and five were provisionally included: Tang 2003, Shah 2010, Sonsanoh 2014, El Sokkary 2016 and Dehbashi 2016. [1–5] Four studies contributed arm level numerical complete evacuation data, involving 361 participants: 41 in the eligible Shah subgroup, 120 in Sonsanoh, 160 analyzed in El Sokkary and 52 using Dehbashi's disputed working denominators. Tang randomized 80 participants but its arm level outcome counts

remained unverified in the supplied extraction. Consequently, the participant count for numerical synthesis is not the total randomized population of all included trials.

Trials were conducted in Hong Kong, Pakistan, Thailand, Egypt and Iran. Dose per administration ranged from 100 to 800 µg, repeat intervals ranged from three to six hours, and maximum cumulative dose ranged from 400 to 2,400 µg. The comparator dose was the same within each trial. All trials assessed misoprostol alone. Complete evacuation definitions and assessment intervals varied, including assessment within approximately 24 hours, 24 hours after the last dose, up to 48 hours after the third dose, and follow-up until return of menses. Tables 1 and 2 present these differences.

Figure 1 Screening record for identification through other methods

Stage	Reports
Reports identified via web, registry and citation searching	23
Reports assessed for eligibility (5 full text, 18 abstract, registry or secondary extraction)	23
Reports excluded with reasons in Supplementary table 1	10
Reports awaiting classification	8
Studies included in this preliminary synthesis	5
Studies contributing outcome data	4

The 23 report record comprises 10 excluded, eight awaiting classification and five provisionally included reports. Four included studies contribute numerical complete evacuation data. Formal database searching was not completed; this is a tabular screening flow, not a complete PRISMA database flow diagram. Counts are transcribed from the source rather than reconstructed from a report level screening log.

Supplementary table 1 Excluded reports

Report	Reason and evidence basis
Nasir (Sulaimani) 2011, J Sulaimani Med Coll 1:45–50	Nonrandomized: alternate allocation by order of admission; Full text
Latif 2014, Pak J Med Health Sci 8:434–7	Random allocation not established; Abstract; confirm with authors
BMRAT 2019, Biomed Res Ther 6:3391–5	Retrospective design; Abstract and full text
Islam Medical College trial	Cervical priming before planned surgical evacuation; Abstract
Warda, Egypt J Fertil Steril	Cervical priming before vacuum evacuation; Full text
Tang 2006, Hum Reprod	Wrong comparison: sublingual in both arms; Cochrane extraction table
NCT05088707 (Aswan)	Second-trimester population; Registry
Publication linked to NCT02686840	Retracted according to the supplied screening record
Eastern Nepal study, J Coll Med Sci Nepal 17(4)	Nonrandomized prospective study; Abstract
PAFMJ trial (CMH Malir)	Mixed first and second trimester termination; missed-abortion data not separable; Full text excerpt

Exclusions reproduce the supplied screening record. Latif's random allocation remains unestablished rather than definitively disproved. The exact retracted publication and retraction notice were not identified in the supplied record; this limits reproducibility of that exclusion.

Supplementary table 2 Reports awaiting classification

Report	Unresolved information
Tanha 2010, J Obstet Gynaecol Res 36:525–32	Full text; arm denominators
Souizi 2020, J Res Med Sci 25:72	Full text; sublingual and vaginal arm counts

Ehsan 2020, Pak J Med Health Sci	Confirm random allocation
NCT04604366 (Islamabad)	Locate results publication
NCT05001061 (Cairo)	Locate results publication
IRCT 9597 (Iran)	Locate results publication
Ain Shams thesis (Mohamad)	Check overlap with NCT02686840
IJRCOG study (first-trimester missed miscarriage)	Full text; study design

These reports were not added to numerical synthesis during manuscript drafting. The supplied record also mentions Lamba and Qadir as unlocated route comparison trials; they were not counted in the 23 report flow.

Table 1 Study characteristics

Study and setting	Participants and eligibility	Allocation and limitations
Tang 2003 Hong Kong	40 SL / 40 V; <13 weeks; nonviable pregnancy on ultrasound	Computer generated sequence; concealment not reported; numerical outcomes unverified
Shah 2010 Pakistan	25 / 25 overall; eligible ≤12 week subgroup 22 / 19	Sealed envelopes; opacity not stated; overall trial includes >12 weeks
Sonsanoh 2014 Thailand	60 / 60; early pregnancy failure; mean gestation 69 vs 68 days	Blocks of four; opaque sealed envelopes; upper gestational limit unconfirmed
El Sokkary 2016 Egypt	240 randomized; 80 / 80 analyzed; missed abortion including blighted ovum	Randomization method not described; 80 unexplained losses; upper gestational limit unconfirmed
Dehbashi 2016 Iran	52 total; working denominators 27 / 25; first trimester	Block allocation linked to admission timing; denominators conflict; exclusions unresolved

SL = sublingual; V = vaginal. Inclusion remains provisional where eligibility or denominators are unresolved.

Table 2 Regimens and outcome assessment

Study	Dose and schedule	Complete evacuation assessment
Tang 2003	600 µg every 3 h; ≤3 doses; maximum 1,800 µg	No surgery until menses; day 7 review
Shah 2010	400 µg every 3 h; ≤5 doses; maximum 2,000 µg in eligible subgroup	Expulsion without retained products on ultrasound; approximately 24 h
Sonsanoh 2014	800 µg every 6 h; ≤3 doses; maximum 2,400 µg	Complete expulsion without surgery or extra misoprostol; ≤48 h after third dose; 2 week visit
El Sokkary 2016	100 µg every 4 h; 4 doses; maximum 400 µg	No surgery; ultrasound interface <15 mm; 24 h after last dose
Dehbashi 2016	400 µg every 4 h until expulsion; maximum 2,000 µg	Complete expulsion or endometrium <10 mm without residue; within 24 h

Each trial used the same nominal dose in both administration groups. All regimens used misoprostol alone.

Risk of Bias

Tang, Shah and Sonsanoh were rated as having some concerns overall for complete evacuation. El Sokkary and Dehbashi were rated at high risk. Unexplained attrition affected El Sokkary, while conflicting denominators and allocation linked to admission timing affected Dehbashi. These two studies also produced the most divergent complete evacuation estimates, which reduces confidence in interpreting their contrast as a reliable route effect. Table 5 provides the provisional domain assessments.

Table 5 Provisional risk of bias for complete evacuation

Study	Randomization	Deviations	Missing data	Measurement	Reporting	Overall
Tang	Some concerns	Low	Low	Low	Some concerns	Some concerns
Shah	Some concerns	Low	Low	Low	Some concerns	Some concerns
Sonsanoh	Low	Low	Low	Some concerns	Some concerns	Some concerns
El Sokkary	Some concerns	Low	High	Low	Some concerns	High
Dehbashi	High	Some concerns	High	Some concerns	Some concerns	High

Single reviewer judgments retained from the supplied record. Independent assessment was not completed. Reporting concerns reflect limited protocol information and, for Shah, subgroup reporting; lack of registration alone does not establish selective reporting.

Complete Evacuation

In the first trimester subgroup of Shah 2010, complete evacuation occurred in 11 of 22 sublingual participants and 10 of 19 vaginal participants, RR 0.95 (95% CI 0.52–1.73). Sonsanoh 2014 reported 41 of 60 versus 36 of 60, RR 1.14 (0.87–1.49). Both confidence intervals included potentially relevant effects in either direction. El Sokkary 2016 reported 56 of 80 versus 41 of 80, RR 1.37 (1.06–1.77), favoring sublingual treatment at its reported assessment interval. This estimate must be interpreted alongside unexplained losses after randomization.

Dehbashi 2016 reported no complete evacuation among 27 sublingual participants and nine among 25 vaginal participants under the working denominator interpretation. The continuity corrected RR was 0.05 (0.003–0.80). The severe contrast, denominator inconsistency and uncertain allocation process limit the credibility of this estimate. Tang 2003 was described in secondary extraction as having 87.5% success in both groups; this percentage was not converted into verified event counts or incorporated in the numerical synthesis. No pooled complete evacuation estimate was produced. Table 3 and Figure 2 show the extracted numerical results.

Surgical Evacuation

Sonsanoh 2014 reported surgery in 16 of 60 sublingual participants and 24 of 60 vaginal participants, RR 0.67 (95% CI 0.40–1.12). El Sokkary 2016 reported 24 of 80 versus 39 of 80, RR 0.62 (0.41–0.92). The estimates pointed toward less surgery with sublingual treatment, although the first interval included no difference and the second trial had important attrition concerns. Whole trial surgery counts from Shah were not used because first trimester subgroup counts were unavailable. Surgery was not assumed to be the exact complement of complete evacuation across all studies, because additional treatment and outcome classifications differed.

Time to Expulsion

Sonsanoh reported means of 12.6 ± 3.9 hours among 51 sublingual participants who aborted and 21.1 ± 10.2 hours among 50 vaginal participants, MD −8.5 hours (95% CI −11.5 to −5.5). El Sokkary reported 12.6 ± 3.1 versus 9.0 ± 1.6 hours using 80 participants per group in the extraction, MD +3.6 hours (2.8–4.4). Thus, the reported direction differed between trials. Restriction to participants who expelled the pregnancy in Sonsanoh and uncertainty surrounding the outcome denominator in El Sokkary complicate comparisons. The estimates do not represent a uniform randomized population time to event analysis. Whole trial timing data from Shah were excluded from the first trimester numerical synthesis.

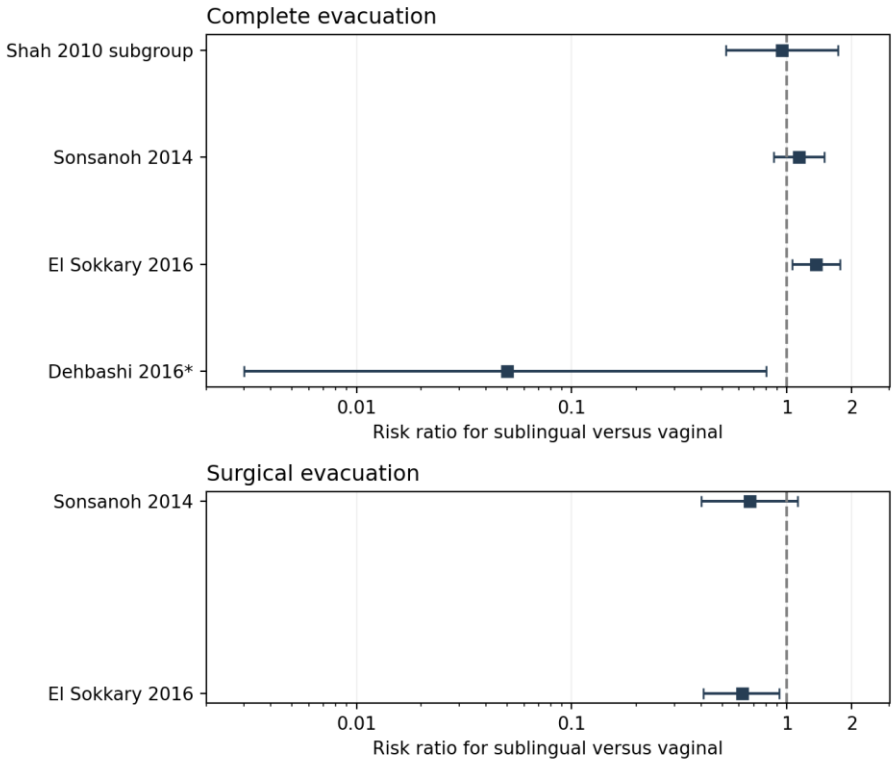
Table 3 Effectiveness outcomes

Outcome and study	Sublingual	Vaginal	Effect with 95% CI
Complete evacuation Shah subgroup	11/22	10/19	RR 0.95 (0.52–1.73)
Sonsanoh	41/60	36/60	RR 1.14 (0.87–1.49)
El Sokkary	56/80	41/80	RR 1.37 (1.06–1.77)

Dehbashi	0/27	9/25	RR 0.05 (0.003–0.80)*
Surgery Sonsanoh	16/60	24/60	RR 0.67 (0.40–1.12)
El Sokkary	24/80	39/80	RR 0.62 (0.41–0.92)
Expulsion time Sonsanoh	12.6 ± 3.9 h n=51	21.1 ± 10.2 h n=50	MD −8.5 h (−11.5 to −5.5)
El Sokkary	12.6 ± 3.1 h n=80	9.0 ± 1.6 h n=80	MD +3.6 h (2.8–4.4)

* Continuity corrected display estimate using 0.5 in all four cells; original counts shown. Dehbashi denominators remain disputed. Tang arm level counts were unverified and are not included. Timing denominators differ from randomized totals; El Sokkary timing denominator is retained as supplied and is uncertain.

Figure 2 Study specific risk ratios without pooled estimates



Squares show the extracted RR; horizontal lines show 95% CIs on a logarithmic scale. RR >1 favors sublingual treatment for complete evacuation but indicates more surgery for surgical evacuation. No summary diamond or weighting is shown. * Dehbashi uses a continuity corrected display estimate and disputed denominators.

Adverse Effects

Adverse effects were reported inconsistently. Sonsanoh recorded nausea in 6/60 versus 7/60, diarrhoea in 4/60 versus 3/60, fever in 7/60 versus 4/60 and abdominal pain in 27/60 versus 19/60. Heavy bleeding occurred in 12/60 versus 3/60, RR 4.00 (95% CI 1.19–13.48); this finding was based on few events and a history based assessment. El Sokkary recorded nausea in 44/80 versus 32/80, hyperpyrexia in 12/80 versus 4/80 and severe pain in 20/80 versus 16/80. Its inconsistent diarrhoea figures were not used.

Dehbashi reported nausea or vomiting in 6/27 versus 0/25, diarrhoea in 6/27 versus 5/25 and abdominal pain in 1/27 versus 0/25, with the same unresolved denominators. In Shah's mixed gestational age population, unpleasant taste occurred in 15/25 versus 1/25 and nausea in 5/25 versus 1/25. These whole trial findings are contextual and cannot establish first trimester specific risks. The extraction did not support dependable comparisons of transfusion, infection, hospital readmission or other serious adverse events. Table 4

distinguishes eligible trial data from mixed population information.

Table 4 Adverse effects

Effect	Sonsanoh	El Sokkary	Dehbashi	Shah overall
Nausea	6/60 vs 7/60	44/80 vs 32/80	6/27 vs 0/25 (nausea or vomiting)	5/25 vs 1/25
Diarrhoea	4/60 vs 3/60	Inconsistent within report	6/27 vs 5/25	Not reported
Fever	7/60 vs 4/60	12/80 vs 4/80 (hyperpyrexia)	Not reported	Not reported
Abdominal pain	27/60 vs 19/60	20/80 vs 16/80 (severe pain)	1/27 vs 0/25	Not reported
Heavy bleeding	12/60 vs 3/60	Not reported	Not reported	Not reported
Shivering or rigor	Not reported	Not reported	Not reported	6/25 vs 4/25
Unpleasant taste	Not reported	Not reported	Not reported	15/25 vs 1/25

Values are SL versus V, n/N. Shah overall includes pregnancies beyond the first trimester and is contextual only. Dehbashi denominators remain disputed. Not reported means unavailable in the supplied extraction, not zero events. Diarrhoea in El Sokkary is withheld because the report is internally inconsistent.

Certainty of Evidence

The supplied provisional GRADE assessment rated complete evacuation and time to expulsion as very low certainty, and surgical evacuation and heavy bleeding as low certainty. Reasons included risk of bias, inconsistent effects, nonuniform assessment intervals and imprecision. For time to expulsion, the 261 participants represent the reported outcome denominators, not the combined number randomized. The ratings in Table 6 should be interpreted as provisional assessments of the extracted dataset rather than definitive ratings of the complete literature.

Table 6 Provisional certainty of evidence

Outcome	Trials and participants	Findings	Certainty and limitations
Complete evacuation	4; 361	No pooled effect; RRs 0.05–1.37	Very low; risk of bias, inconsistency, differing assessment intervals
Surgical evacuation	2; 280	RRs 0.67 and 0.62	Low; risk of bias and imprecision
Time to expulsion	2; 261 outcome observations	MDs −8.5 h and +3.6 h	Very low; inconsistency and risk of bias
Heavy bleeding	1; 120	RR 4.00 (1.19–13.48)	Low; few events and history based measurement

Certainty ratings are the source document's provisional GRADE judgments. No pooled absolute effect is available. Participant totals use extracted analysis denominators and do not imply complete randomized follow-up.

DISCUSSION

Principal Findings

The current evidence does not demonstrate a consistent advantage of either administration route for complete evacuation. Two trials showed similar point estimates with wide confidence intervals; one high risk trial favored sublingual treatment and another high risk trial strongly favored vaginal treatment. These findings cannot be reconciled by considering administration route alone. Dose, repeat schedules, assessment time, thresholds for surgery and trial integrity all affect what each result measures.

A possible reduction in surgical evacuation with sublingual treatment was observed in two trials. However, this observation rests on 280 analyzed participants, includes one trial with unexplained postrandomization losses and does not establish a reliable overall treatment effect.

Expulsion time estimates were also inconsistent and were based on different analysis populations. Selecting only participants who expelled after treatment may change the meaning of the comparison because expulsion itself can be affected by the intervention.

Outcome Definitions and Clinical Interpretation

Complete evacuation is sensitive to the interval allowed for treatment to work. A trial that initiates surgery soon after the final dose may report lower medical success than one allowing several days of observation. Ultrasound thresholds also differed: an endometrial interface below 15 mm in El Sokkary and an endometrium below 10 mm without residue in Dehbashi. These endpoints are not interchangeable with absence of surgery until return of menses. A pooled result across these definitions could obscure differences in management decisions as well as biological treatment response.

Tolerability may influence treatment acceptability even when evacuation rates are similar. The extracted adverse effect data suggest possible increases in selected symptoms with sublingual administration, including heavy bleeding in one trial. The record is too inconsistent to quantify a general safety advantage for either route. In particular, history based heavy bleeding cannot be interpreted as a demonstrated increase in transfusion or life threatening hemorrhage. Unreported serious outcomes should not be represented as equivalent between treatments.

The findings apply to the misoprostol only regimens studied. They do not determine the comparative performance of routes when used with mifepristone, establish an optimal dosing schedule, or support extrapolation to second trimester miscarriage. This manuscript is an evidence synthesis rather than a treatment guideline. Patient preferences and clinical circumstances remain relevant, but the current data do not justify a firm route preference on effectiveness grounds.

Strengths and limitations

The synthesis preserves study level event counts, assessment intervals and regimen details rather than hiding their differences within an overall estimate. It distinguishes first trimester subgroup data from whole trial mixed gestational age data and exposes denominator conflicts, attrition and inconsistent adverse effect reporting. Keeping unverified data outside numerical estimates prevents greater precision from being implied than the evidence supports.

The principal limitation is incomplete identification of eligible evidence. Reproducible database searches were not completed, eight reports remain awaiting classification and potentially eligible published trials may therefore be missing. Targeted bibliographic checks performed while drafting do not repair that limitation. A comprehensive systematic review cannot be claimed from this record alone. Extraction and risk of bias assessment were performed by one reviewer, increasing vulnerability to selection, transcription and judgment errors.

The included trials also have important limitations. Two were rated at high risk of bias, gestational age limits were incompletely documented for two, and Shah's eligible subgroup was small. Dehbashi's denominator conflict prevents a stable estimate. El Sokkary's unexplained reduction from randomized to analyzed participants undermines interpretation. Sparse and heterogeneous adverse effect reporting prevents a complete benefit–harm assessment. Provisional GRADE ratings depend on this incomplete dataset, and absence of a common primary time point limits quantitative synthesis.

Implications for Research

The most useful further evidence would compare routes under a clearly specified dosing schedule with standardized definitions of complete evacuation and prespecified assessment intervals. Trials should report allocation concealment, all randomized participants, rescue treatment, reasons for surgery and serious adverse events. Reporting both early response and later avoidance of surgery would separate speed of expulsion from ultimate treatment success. For the present review, completion of evidence identification and independent verification is necessary before interpreting the manuscript as a completed comprehensive systematic review.

CONCLUSION

The currently extracted randomized evidence provides low or very low certainty information about sublingual versus vaginal misoprostol alone for first trimester missed miscarriage. Complete evacuation and expulsion time findings are inconsistent. Two trials suggest less surgical evacuation with sublingual treatment, while some adverse effects may be

more frequent. Differences in treatment regimens, outcome timing, trial quality and unresolved data discrepancies preclude a definitive conclusion about route superiority. This fully written manuscript describes the available synthesis, but the underlying review process remains preliminary.

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