Comparison of sublingual versus vaginal misoprostol for second-trimester pregnancy termination: a meta-analysis

CRD summary
The review concluded that sublingual and vaginal misoprostol were safe and effective for mid-trimester pregnancy termination. The review was generally well conducted, but potential trial quality issues, small number of trials for some outcomes and notable variation limit the reliability of the pooled results.

Authors’ objectives
To determine the efficacy and safety of vaginal versus sublingual misoprostol for mid-trimester pregnancy termination.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to June 2010 without language restrictions. Search terms were reported. Reference lists of retrieved articles were searched.

Study selection
Randomised controlled trials (RCTs) in women with a gestational time of 13 to 28 weeks that reported the primary outcome of successful second-trimester abortion (including complete and incomplete abortion) within 24 hours of misoprostol or the secondary outcomes of successful abortion within 48 hours, induction-to-abortion interval from the start of treatment to expulsion of foetus were eligible for inclusion. Trials that used both routes of administration in the same patient were excluded, as were trials that combined misoprostol with mifepristone or any other prostaglandin analogue.

Two reviewers independently performed study selection. Consensus was achieved by discussion.

Assessment of study quality
Trial quality was assessed using the Jadad criteria of randomisation, blinding, allocation concealment and loss to follow-up to give a maximum score out of five. Poor-quality trials (score zero to 1) were excluded from the review.

The authors did not state how many reviewers performed validity assessment.

Data extraction
Categorical data were extracted and used to calculate risk ratios (RRs) and odds ratios (ORs), together with 95% confidence intervals (CIs). Continuous data were extracted and used to calculate mean differences and 95% CIs.

Two reviewers independently performed data extraction. Consensus was achieved by discussion.

Methods of synthesis
A random-effect meta-analysis was used to calculate pooled risk ratios, weighted mean differences (WMDs) and odds ratios, together with 95% confidence intervals. Trials were analysed for dose separately (less than 400µg versus 400µg).

Statistical heterogeneity was assessed using $I^2$ and $X^2$.

Sensitivity analysis excluded individual trials. Subgroup analysis was conducted by parity (nulliparous versus multiparous women), placental retention, side-effects and route of intervention administered.

Publication bias was assessed using funnel plots and Begg and Mazumdar test.
Results of the review

Six RCTs (1,429 participants) were included in the review. Quality assessment using the Jadad scale indicated that trials were of moderate quality: five trials scored 3 and one trial scored 2 points. Most trials were unblinded. Trial sample size ranged from 49 to 681 participants.

Dose of less than 400ug (three trials, 251 participants): There was no significant difference in efficacy at 24 hours between the two routes of administration (I²=91.3%). Compared with vaginal misoprostol, sublingual misoprostol had statistically significantly longer induction to delivery time (WMD, -6.18, 95% CI -9.88 to -2.49, I²=75.7%).

Dose of 400ug (three trials, 1,178 participants): There was no significant difference in abortion efficacy at 24 hours (I²=41.3%), but there was a statistically significantly greater abortion efficacy at 48 hours with vaginal misoprostol (RR 0.96, 95% CI 0.93 to 0.99, I²=0%) compared with sublingual. The subgroup of nulliparous women demonstrated statistically significantly greater abortion efficacy at 24 hours with vaginal misoprostol compared with sublingual misoprostol (RR 0.78, 95% CI 0.71 to 0.87, I²=0%).

A higher proportion of women preferred the sublingual route compared with the vaginal route (RR 2.4, 95% CI 1.92 to 3.00). There was no statistically significant difference in adverse events, except that fever was more common in the vaginal group. Sensitivity analysis did not significantly alter the results. There was no evidence of publication bias. Other subgroup analyses were presented in the review.

Authors' conclusions

Sublingual and vaginal misoprostol were safe and effective for mid-trimester pregnancy termination.

CRD commentary

Inclusion criteria for the review were clearly defined and several relevant data sources were searched without language restrictions. Publication bias was assessed and was not detected, although the reliability of the assessment with less than 10 trials was questionable. Attempts were made to reduce reviewer error and bias during study selection and data extraction, but the authors did not state if the same methods were used for quality assessment.

Quality assessment indicated that the trials were of moderate quality; only one trial blinded participants to the intervention, which may have introduced bias into the analysis. Trials were combined using appropriate statistical methods. Statistical heterogeneity was assessed and explored. The authors acknowledged that some of the outcomes had only a few trials with usable data and there was notable statistical heterogeneity in several of the analyses.

The review was generally well conducted, but potential trial quality issues, small number of trials for some outcomes and statistical heterogeneity limit the reliability of the pooled results.

Implications of the review for practice and research

Practice: The authors stated that the differences between the two routes probably did not have clinical consequences.

Research: The authors stated that further research was required to determine the efficacy, safety and optimal doses of sublingual and vaginal misoprostol for second-trimester medical abortion.

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