Medical methods for first trimester abortion

14 March 2016

Key findings

The review assessed different medical methods (single, combination of drugs) and route of administration for first trimester abortions.

Key findings from this review are:

- Combined medical abortion regimens appear more effective than single method.
- In the combined regimen, mifepristone dose of 200mg does not significantly decrease the method effectiveness.
- Administration of vaginal misoprostol is more effective than oral misoprostol and has fewer side effects than sublingual or buccal administration.

Evidence included in this review

Fifty-eight trials were included in this review, which can be grouped into the following methods:

- combined regimen mifepristone/prostaglandin (comparing doses of mifepristone, doses of prostaglandin, type of prostaglandin, timing of prostaglandin, and route of administration for misoprostol; single versus split or continuous dose of prostaglandin, mifepristone alone versus mifepristone/prostaglandin);
- prostaglandin alone (comparing to combined regimen, route of administration)
- combined regimen methotrexate/prostaglandin (comparing timing of prostaglandin, route of methotrexate, dose of methotrexate, and route of misoprostol administration)
- tamoxifen versus methotrexate (combined with prostaglandin); and
- combined regimen mifepristone/prostaglandin versus mifepristone/prostaglandin plus tamoxifen.

Women undergoing first trimester medical abortions were included in the trials.

Quality assessment

The GRADE approach was not used. Risk of bias in the included studies was assessed. Thirty-five trials scored adequate concealment, and in 23 trials allocation was unclear.

Clinical implications

Combination of mifepristone/misoprostol appears to be a safe and effective method of abortion during the first trimester (up to 63 days). Reducing the dosage of mifepristone from 600mg to 200mg does not appear to reduce the effectiveness. It should be noted that trials included did not address medical abortion carried
out in settings where it is difficult for women to receive follow-up care, or there is no system for referral in case of an emergency.

**Further research**

Further trials are required to compare methotrexate/prostaglandin combined methods with the standard regimen of mifepristone/prostaglandin. To understand which methods are preferable for women (due to side-effects and bleeding patterns) and acceptable in different settings, further research in this area is required.

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**Cochrane review**


**Abstract**

Surgical abortion by vacuum aspiration or dilatation and curettage has been the method of choice for early pregnancy termination since the 1960s. Medical abortion became an alternative method of first trimester pregnancy termination with the availability of prostaglandins in the early 1970s and anti-progesterones in the 1980s. The most widely researched drugs are prostaglandins (PGs) alone, mifepristone alone, methotrexate alone, mifepristone with prostaglandins and methotrexate with prostaglandins.

To compare different medical methods for first trimester abortion.

The Cochrane Controlled Trials Register, MEDLINE and Popline were systematically searched. Reference lists of retrieved papers were also searched. Experts in WHO/HRP were contacted.

Types of studies
Randomised controlled trials comparing different medical methods for abortion during first trimester (e.g. single drug, combination) were considered. Trials were assessed and included if they had adequate concealment of allocation, randomisation procedure and follow-up. Women, pregnant during the first trimester, undergoing medical abortion were the participants. The outcomes were mortality, failure to achieve complete abortion, surgical evacuation, ongoing pregnancy at follow-up, time until passing of conceptus, blood transfusion, side effects and women's dissatisfaction with the procedure.

Two reviewers independently selected trials for inclusion from the results of the search strategy described previously. The selection of trials for inclusion in the review was performed independently by two reviewers after employing the search strategy described previously. Trials under consideration were evaluated for appropriateness for inclusion and methodological quality without consideration of their results. Data were processed using Revman software.

Fifty-eight trials were included in the review. The effectiveness outcomes below refer to 'failure to achieve complete abortion' with the intended method unless otherwise stated. 1) Combined regimen mifepristone/prostaglandin: Mifepristone 600 mg compared to 200 mg shows similar effectiveness in achieving complete abortion (4 trials, RR 1.07, 95% CI 0.87 to 1.32). Misoprostol administered orally is less effective (more failures) than the vaginal route (RR 3.00, 95% CI 1.44 to 6.24) and may be associated with more frequent side effects such as nausea and diarrhoea. Sublingual and buccal routes were similarly effective compared to the vaginal route, but had higher rates of side effects. 2) Mifepristone alone is less effective when compared to the combined regimen mifepristone/prostaglandin (RR 3.76 95% CI 2.30 to 6.15). 3) Five trials compared prostaglandin alone to the combined regimen (mifepristone/prostaglandin).
All but one reported higher effectiveness with the combined regimen. The results of these studies could not be combined but the RR of failure with prostaglandin alone is reportedly between 1.4 to 3.75 with the 95% confidence intervals indicating statistical significance. 4) In one trial comparing gemeprost 0.5 mg with misoprostol 800 mcg, misoprostol was more effective (failure with gemeprost: RR 2.86, 95% CI 1.14 to 7.18). 5) There was no difference in effectiveness with use of a divided dose compared to a single dose of prostaglandin. 6) Combined regimen methotrexate/prostaglandin demonstrates similar rates of failure to complete abortion when comparing intramuscular to oral methotrexate administration (RR 2.04, 95% CI 0.51 to 8.07). Similarly, day 3 vs. day 5 administration of prostaglandin following methotrexate administration showed no significant differences (RR 0.72, 95% CI 0.36 to 1.43). One trial compared the effect of tamoxifen vs. methotrexate and no statistically significant differences were observed in effectiveness between the groups.

Safe and effective medical abortion methods are available. Combined regimens are more effective than single agents. In the combined regimen, the dose of mifepristone can be lowered to 200 mg without significantly decreasing the method effectiveness. Vaginal misoprostol is more effective than oral administration, and has less side effects than sublingual or buccal. Some results are limited by the small numbers of participants on which they are based. Almost all trials were conducted in settings with good access to emergency services, which may limit the generalizability of these results.


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