Does cervical preparation before outpatient hysteroscopy reduce women's pain experience?
A systematic review
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CRD summary
The authors concluded there was no evidence to recommend routine administration of mifepristone or misoprostol to women before out-patient hysteroscopy. Cervical priming with vaginal prostaglandins could be considered for postmenopausal women if using hysteroscopic systems greater than 5mm in diameter. Reliability of the conclusion should be interpreted carefully due to limited evidence and possible biases in the review process.

Authors' objectives
To compare the effect on pain and need for cervical dilatation following various methods of cervical preparation in women who underwent out-patient hysteroscopy.

Searching
MEDLINE, EMBASE, CINAHL and The Cochrane Library were searched from inception to February 2010. Search terms were reported and there were no language restrictions. The reference lists of relevant articles were scanned to locate further studies. The Journal of Minimally Invasive Gynaecology (formerly Journal of the American Association of Gynaecologic Laparoscopists) and Gynaecological Surgery were handsearched for publications between 2000 and 2010. The authors did not search for unpublished material.

Study selection
Eligible for inclusion were randomised controlled trials that reported on pain following cervical preparation in women prior to diagnostic or operative out-patient hysteroscopy. Cervical preparation had to be compared with no intervention or placebo. Additional outcomes of interest were prevalence and extent of cervical dilatation, and adverse events (bleeding, gastrointestinal symptoms, abdominal pain and failed procedures).

The included trials evaluated an anti-progestogen (mifepristone 200mg, 30 hours prior to surgery) or prostaglandins (misoprostol 200 to 400μg given between four and 24 hours prior to surgery). Most drugs were administrated vaginally. Pre- and post-menopausal women were included. Most trials used the visual analogue scale to assess pain and results were reported in various formats. Several methods were used to assess cervical dilation.

Two reviewers independently carried out the study selection. Disagreements were resolved by consensus.

Assessment of study quality
Trial quality was assessed using Cochrane criteria which covered random sequence generation, allocation concealment, blinding of patients and clinicians, blinding of outcome assessment (patient pain scores, dilation assessment by clinicians), whether incomplete outcome data were addressed, selective reporting and other biases. Trials were scored low, high or unclear.

One reviewer carried out the quality assessment.

Data extraction
Data were extracted on mean/median and p-values for the various outcomes of interest. For adverse events (nausea, diarrhoea, vaginal bleeding, cervical lacerations and failed procedures), data were collected to calculate odds ratios and 95% confidence intervals (CI).

One reviewer carried out the data extraction. Authors were contacted for further information, where possible.

Methods of synthesis
Meta-analysis was conducted only for adverse events, using the fixed-effect Peto method. Statistical heterogeneity was assessed using I² and X². Due to clinical heterogeneity, other outcomes were synthesised narratively. Subgroup results
were presented according to menopausal status.

**Results of the review**

Six trials were included (468 patients). Four trials were considered to have been high quality.

In pre-menopausal women, mifepristone had no effect on pain (one trial), and results for misoprostol compared with placebo were mixed in two other trials. In postmenopausal women, pain following hysteroscopy was significantly reduced with misoprostol, but there was no difference between groups during clamping of the cervix or endometrial biopsy (one trial). In studies that contained pre- and post-menopausal women, significant reductions in pain were reported after hysteroscopy when misoprostol was compared with no intervention (one trial) and after cervical dilatation to 6mm when misoprostol was compared with placebo (one trial). The result after cervical dilatation remained significant in post-menopausal women only. There were no significant differences between groups specifically in relation to need for dilatation of the cervix following priming versus placebo (three trials). Statistically significant differences were found in one further trial for the amount of force needed for dilation above 6mm (pre- and post-menopausal women) and in another trial for required dilation above 6mm (premenopausal women).

There were no significant differences between groups for nausea (two trials; $I^2=0\%$); diarrhoea (two trials; $I^2=0\%$); vaginal bleeding (four trials; $I^2=78\%$); cervical laceration (three trials; $I^2=19\%$); or failed procedures (two trials; $I^2=72\%$).

**Authors’ conclusions**

There was no evidence to recommend the routine administration of mifepristone or misoprostol to women before outpatient hysteroscopy. Cervical priming with vaginal prostaglandins could be considered in postmenopausal women if using hysteroscopic systems greater than 5mm in diameter.

**CRD commentary**

The review question was clear and supported by potentially replicable inclusion criteria. A range of data sources were accessed to identify relevant studies, and steps were taken to minimise language bias. Publication bias was possible (acknowledged by the authors). The selection of studies was conducted with attempts to minimise reviewer error and bias, but similar steps were not taken for the processes of data extraction or quality assessment. An appropriate quality assessment tool was applied, and the results of this were integrated to the discussion of results. Study details were provided.

Substantial statistical heterogeneity in some of the adverse events meta-analyses suggested that a fixed-effect model might not have been appropriate. However, the authors justified the Peto method on the basis of rarity of events. The authors’ conclusion reflects the limited evidence presented (a few heterogenous studies with small sample sizes), but its reliability should be interpreted carefully considering possible biases in the review process.

**Implications of the review for practice and research**

**Practice:** The authors did not state any further implications for practice.

**Research:** The authors stated that a future individual patient data meta-analysis was needed to explore the use of cervical priming agents in populations with different menopausal status. A well-designed clinical trial was also needed to enable further subgroup analysis in relation to women with previous caesarian section or loop biopsy, and with those who were nulliparous or postmenopausal. Future trials should use technologies that were clinically relevant to modern practice.

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