Low-dose oral misoprostol for induction of labor: a systematic review
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CRD summary
This review assessed the effects of low-dose oral misoprostol compared with dinoprostone, vaginal misoprostol and oxytocin for labour induction in women with a viable foetus and found it to be at least as effective as both vaginal misoprostol and vaginal dinoprostone. Although aspects of the review were unclear, it was of a sufficient standard and the conclusion may be reliable.

Authors' objectives
To estimate the efficacy and safety of low-dose oral misoprostol compared with dinoprostone, vaginal misoprostol and oxytocin for labour induction in women with a viable foetus.

Searching
MEDLINE, EMBASE and Cochrane Pregnancy and Birth Group Trials Register were searched, without language restrictions, from inception to January 2008. Search terms were reported. References of retrieved articles were searched to identify further additional relevant articles.

Study selection
Randomised controlled trials were assessed as eligible for inclusion if participants were women between 32 and 42 weeks of gestation (irrespective of membrane or cervical status) who underwent labour induction and were assigned either 25μg or less of oral misoprostol (treatment group) or vaginal dinoprostone, vaginal misoprostol or oxytocin (comparator group). The most common comparison in the included studies was 20μg oral misoprostol administered every two hours compared with 2mg of dinoprostone (two doses administered every six hours). Other studies compared oral misoprostol with vaginal misoprostol or oxytocin; doses and regimens varied between studies. Study locations included South Africa, Australia, China, India, USA, Switzerland and UK. Where reported, maximum Bishop scores ranged from 5 to 7. One small study comprised women who had previously had artificial or spontaneous rupture of membranes.

Two reviewers independently assessed studies for inclusion. Disagreements were resolved by consensus with a third reviewer.

Assessment of study quality
Study quality was assessed using the Jadad scale with criteria of randomisation and adequacy of method, double blinding, adequacy of allocation concealment, description of loss-to-follow-up and exclusions. Each study was assigned a quality score of up to 5 points. Studies that achieved 2 or fewer points out of 5 were considered to be of poor quality.

Data extraction
Data were extracted to calculate risk ratios (RRs) with 95% confidence intervals (CIs) for a range of primary and secondary outcomes. Primary outcomes included: those who did not achieve vaginal delivery within 24 hours, caesarean delivery rate and uterine hyperstimulation with foetal heart rate changes. Secondary outcomes included: need for oxytocin augmentation; epidural use; presence of meconium-stained amniotic fluid; Apgar scores of less than 7 at five minutes; admission to neonatal intensive care units; neonatal morbidity; perinatal mortality; serious maternal morbidity; maternal adverse effects; postpartum haemorrhage; maternal death; and maternal satisfaction.

Methods of synthesis
Where data allowed, data were pooled for each of the primary and secondary outcomes using the Mantel-Haenszel method. I² tests were conducted to assess heterogeneity. If I² was greater than 50%, results were pooled using a random-effects method instead. Data were analysed on an intention-to-treat basis. A funnel plot was planned if sufficient included studies were identified, but they were not.
Results of the review
Nine studies included in review (n=3,344 calculated from tables in paper and n=2,937 reported in paper, range 30 to 741 participants). Three achieved the maximum Jadad quality score of 5 points; six achieved 3 points.

Comparison between oral misoprostol and dinoprostone: There was a statistically significant reduction in the risk of women who required caesarean section in women who received oral misoprostol (RR 0.82, 95% CI 0.71 to 0.96, I²=6%; five studies). There were no statistically significant differences for all other primary and secondary outcomes.

Comparison between oral and vaginal misoprostol: There was a statistically significant difference in the rates of the primary outcome uterine hyperstimulation with foetal heart rate changes (RR 0.19, 95% CI 0.08 to 0.46, I²=48%; two studies) that favoured oral over vaginal misoprostol. This was also true for the secondary outcome uterine hyperstimulation without foetal heart rate changes (RR 0.36, 95% CI 0.22 to 0.59, I²=0%; two studies). No statistically significant differences were reported for all other outcomes. Maternal outcome results were not reported.

No statistically significant differences were reported between groups in the two studies that compared oral misoprostol with oxytocin therapy.

Heterogeneity assessed with the I² statistic varied between 0% and 92%. For all of the statistically significant outcomes I² was under 50%, and so judged not to be significant.

No studies had a quality score of less than 3 out of 5, so a planned sensitivity analysis to investigate heterogeneity that stratifying results by study quality was not conducted.

Authors’ conclusions
Low-dose oral misoprostol solution administered every two hours seemed at least as effective as vaginal dinoprostone and vaginal misoprostol, with lower rates of caesarean delivery (dinoprostone) and uterine hyperstimulation (misoprostol).

CRD commentary
This review addressed a clear review question with relevant inclusion and exclusion criteria. The number of reviewers involved at data extraction and validity assessment stages of the review were not clearly reported, so the possibility of error and biases at these stages could not be ruled out. The study selection and data extraction stages of the review all appeared well conducted and reported. The authors did not state whether they searched for unpublished studies and so the possibility of publication bias could not be ruled out. Language restrictions at the search and study inclusion stages were not reported and so language bias could not be ruled out. Details of primary studies appeared appropriate and clear enough to allow readers to assess the appropriateness of the treatment groupings and comparisons made. The method of data synthesis appeared appropriate and clearly presented, although the large number of secondary outcomes considered increased the possibility of spurious associations being identified.

Although the review was generally well conducted, reporting of some aspects of the review process was unclear and the reliability of the conclusions may be affected by publication bias.

Implications of the review for practice and research
Practice: The authors stated that oral misoprostol solution appeared the optimal choice for induction of labour. A commercial oral preparation would improve dosage accuracy and was likely to be popular.

Research: No implications were stated for research.

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