WHO recommendation on use of oral misoprostol for induction of labour

10 February 2011

**Recommendation**

Oral misoprostol (25 ?g, 2-hourly) is recommended for induction of labour. *(Moderate-quality evidence, strong recommendation)*

**Publication history**

**First published:** February 2011

**Updated:** No updated planned

**Assessed as up-to-date:** February 2011

**Remarks**

- The recommendation refers to women with a non-scarred uterus.
- The participants in the technical consultation noted the importance of closer monitoring of the mother and her fetus starting immediately after the administration of misoprostol. The participants noted also that labour induction with misoprostol in women with previous caesarean section had not been included as a priority topic in the process of scoping for the present guidelines. However, the participants felt that it was important to address this issue in these guidelines. The participants noted too that one randomized controlled trial (1) was interrupted at the early recruitment stage due to safety concerns (i.e. occurrence of uterine rupture) and that there were observational studies showing mixed results. The participants placed high value on safety and agreed not to recommend the use of misoprostol for induction of labour in women with a scarred uterus. The panel noted that a method with a low risk of uterine hyperstimulation (e.g. balloon catheter) may be preferred in women with a scarred uterus.

**Background**

Induction of labour is defined as the process of artificially stimulating the uterus to start labour.(2) It is usually performed by administering oxytocin or prostaglandins to the pregnant woman or by manually rupturing the amniotic membranes. Over the past several decades, the incidence of labour induction for shortening the duration of pregnancy has continued to rise. In developed countries, the proportion of infants
delivered at term following induction of labour can be as high as one in four deliveries. (3-5)

Over the years, various professional societies have recommended the use of induction of labour in circumstances in which the risks of waiting for the onset of spontaneous labour are judged by clinicians to be greater than the risks associated with shortening the duration of pregnancy by induction. These circumstances generally include gestational age of 41 completed weeks or more prelabour rupture of amniotic membranes, hypertensive disorders, maternal medical complications, fetal death, fetal growth restriction, chorioamnionitis, multiple pregnancy, vaginal bleeding and other complications.

Although currently available guidelines do not recommend this, induction of labour is increasingly being used at the request of pregnant women to shorten the duration of pregnancy or to time the birth of the baby according to the convenience of the mother and/or health-care workers.(6, 7) During induction of labour, the woman has restricted mobility and the procedure itself can cause discomfort to her. To avoid potential risks associated with the procedure, the woman and her baby need to be monitored closely. This can strain the limited health-care resources in under-resourced settings. In addition, the intervention affects the natural process of pregnancy and labour and may be associated with increased risks of complications, especially bleeding, caesarean section, uterine hyperstimulation and rupture and other adverse outcomes. (3, 8)

Methods

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, guided by the GRADE approach.(8, 9) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on induction of labour (2011).(10)

Cochrane systematic reviews were conducted, on use of oral misoprostol for induction of labour. (11-13) In the review, randomized controlled trials relevant to the key question were screened by review authors, and data on relevant outcomes and comparisons were extracted. Evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgments for each outcome, and the estimated risks.

WHO convened a Guideline Development Group (GDG) meeting on recommendations induction of labour in April 2010, where this recommendation was developed. The GDG comprised of a group of independent experts, who used the evidence profiles to assess evidence on effects on the pre-specified outcomes. GDG members discussed the balance between desirable and undesirable effects, overall quality of supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity, to formulate the recommendation. Remarks were added to clarify the recommendation, and aid implementation.

Recommendation question

For this recommendation, we aimed to answer the following question:

- in pregnant women at or beyond term (P), does induction of labour using oral misoprostol (I), compared to no intervention, (C), improve maternal and perinatal outcomes (O)?

Evidence Summary

Evidence on misoprostol for induction of labour at term was derived from three systematic reviews (11-13)
which include a large number of randomized controlled trials. Historically, most trials have studied the vaginal route of administration for misoprostol use in induction of labour. However, owing to concerns about the risk of uterine hyperstimulation with vaginal misoprostol, more recent trials have focused on lower vaginal misoprostol doses and the oral route for misoprostol administration.

**A. Vaginal misoprostol**

Compared with either placebo or expectant management, vaginal misoprostol was associated with a reduced risk of not achieving vaginal birth within 24 hours of labour induction (five trials, 769 participants, RR 0.51, 95% CI 0.37–0.71) (EB Table 2.3.1).

Compared with intravenous oxytocin alone (EB Table 2.3.4), vaginal misoprostol was associated with a reduced risk of vaginal birth not achieved within 24 hours (nine trials, 1200 participants, RR 0.62, 95% CI 0.43–0.9), fewer caesarean sections (25 trials, 3074 participants, RR 0.76, 95% CI 0.60–0.96) and fewer infants with Apgar score below seven at 5 minutes of life (13 trials, 1906 participants, RR 0.56, 95% CI 0.34–0.92).

Compared with other prostaglandins (EB Tables 2.3.2 and 2.3.3), vaginal misoprostol was associated with a reduced risk of vaginal birth not achieved within 24 hours (vaginal and intracervical prostaglandins), fewer caesarean sections (vaginal prostaglandins), and increased risk of uterine hyperstimulation with fetal heart rate changes, but without increased risk of other priority outcomes (vaginal and intracervical prostaglandins). Compared with higher doses of vaginal misoprostol, lower doses (25 ?g, 6-hourly) were associated with a reduced risk of uterine hyperstimulation with fetal heart rate changes (16 trials, 2540 participants, RR 0.51, 95% CI 0.37–0.69). The risk of vaginal birth not being achieved within 24 hours was similar with both higher and lower doses (EB Table 2.3.5).

**B. Oral misoprostol**

Compared with placebo or expectant management, oral misoprostol lowered the risk not only of vaginal birth not achieved within 24 hours (one study, 96 participants, RR 0.16, 95% CI 0.05–0.49), but also of caesarean births (six trials, 629 participants, RR 0.61, 95% CI 0.41–0.93) (EB Table 2.4.1). Comparisons between oral misoprostol and intravenous oxytocin (eight trials, 1026 participants) showed the two to be similar with regard to the risk of priority outcomes (EB Table 2.4.2).

Oral misoprostol was more effective than intracervical prostaglandins in achieving vaginal birth within 24 hours (three trials, 452 women, RR: 0.78, 95%, CI 0.63–0.97) (EB Table 2.4.4). The comparison between oral misoprostol and vaginal prostaglandins favoured oral misoprostol: a reduced risk of caesarean births was observed (12 trials, 4350 participants, RR 0.87, 95% CI 0.78–0.97) without any increase in the risks of adverse maternal and perinatal outcomes (EB Table 2.4.5). Lower doses of oral misoprostol (up to 50 ?g) were associated with similar outcomes compared with higher doses (100 ?g) (EB Table 2.4.6). Most trials that had compared vaginal prostaglandins with oral misoprostol had studied dosages of 20–25 ?g, 2-hourly (EB Table 2.4.6); oral misoprostol was associated with a reduction in caesarean section rates.

**C. Oral misoprostol versus vaginal misoprostol**

Priority outcomes have been evaluated in direct comparisons between oral and vaginal misoprostol in 25 trials involving 5096 women (EB Table 2.4.3). Oral and vaginal misoprostol were similar with regard to all but one of the priority outcomes: compared with vaginal misoprostol, oral misoprostol was associated with a lower risk of Apgar score being less than seven at 5 minutes of life (14 trials, 3270 participants, 94 events, RR 0.65, 95% CI 0.44–0.97).

**D. Oral or vaginal misoprostol versus sublingual/buccal misoprostol**

Vaginal misoprostol has been compared with sublingual/buccal misoprostol in nine trials with 2385 participants. These trials indicate that vaginal and sublingual/buccal misoprostol are similar with regard to
all the priority outcomes (EB Table 2.5.1). Data on oral versus sublingual/buccal misoprostol are limited and no firm conclusions can be drawn from them (EB Table 2.5.2).

Implementation considerations

- The successful introduction of this recommendation into national programmes and health-care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. The adaptation and implementation processes may include the development or revision of existing national guidelines or protocols based on this recommendation.
- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.
- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations (including, for example, the availability of induction agents and monitoring capacity), and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
- In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.

Research implications

The GDG identified that further research on the following high-priority questions is needed:

- What is the best regimen for oral misoprostol that would give superior results to those achieved with vaginal misoprostol 25 ?g?
- What risks (for both the mother and the fetus) are associated with induction of labour and, in terms of those risks, how does induction of labour compare with elective caesarean section? What is the role of caesarean section in the management of women in whom induction of labour has failed?

Related Links

WHO recommendations on induction of labour (2011) – full document and evidence tables

Pregnancy, Childbirth, Postpartum and Newborn Care: A guide for essential practice

Managing Complications in Pregnancy and Childbirth: A guide for midwives and doctors (2nd ed)

Supporting systematic reviews:


References


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