WHO recommendation on use of vaginal misoprostol for induction of labour in the third trimester, in women with a dead or an anomalous fetus

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Recommendation

In the third trimester, in women with a dead or an anomalous fetus, oral or vaginal misoprostol are recommended for induction of labour.

(Low-quality evidence, strong recommendation)

Publication history

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Assessed as up-to-date: February 2011

Remarks

- The doses and regimens recommended for use of misoprostol for induction of labour at term also apply to the above recommendation.
- The participants in the technical consultation considered the risk of tachysystole and hypertonus and uterine rupture to be high during labour induction in women with a fetal anomaly or after fetal death. Hence, the participants noted the importance of close monitoring of the woman once labour is established.
- The participants noted also that the trials included in the systematic review that provided evidence for the above recommendation included women in the second and third trimesters of pregnancy. The participants re-discussed the body of evidence related to misoprostol for induction of labour at term and found it to be applicable to that section also. Hence, the evidence related to induction of labour at term using misoprostol was downgraded for indirectness when applied to termination of pregnancy in women with a fetal anomaly or after intrauterine fetal death.

Background

Induction of labour is defined as the process of artificially stimulating the uterus to start labour.(1) 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. (2-4)

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.(5, 6) 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. (2, 7)

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. (7, 8) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on induction of labour (2011). (9)

A Cochrane systematic review was conducted, on use of misoprostol for induction of labour associated with fetal anomaly or intrauterine fetal death. (10) 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 with a dead or an anomalous fetus in the third trimester (P), does induction of labour vaginal misoprostol (I), compared to no intervention, (C), improve maternal and perinatal outcomes (O)?
Evidence Summary

Labour induction in women carrying an anomalous or dead fetus requiring pregnancy presents a different scenario for clinical management than labour induction in women with a normal live fetus. First, increased uterine contractility leading to fetal distress is no longer a major concern. Second, often induction of labour in women with an anomalous or dead fetus is performed before term, when the uterus may be less responsive to uterotonics than it is at term.

Evidence concerning the use of misoprostol for induction of labour associated with fetal anomaly or intrauterine fetal death is summarized in a systematic review (10) that evaluated several comparisons between various misoprostol preparations on the one hand, and misoprostol and various prostaglandins on the other. Overall, in this review contains few trials with small numbers of participants, which created substantial uncertainty regarding the size of the effect.

Compared with oral misoprostol, vaginal misoprostol was associated with a lower risk of vaginal birth not achieved within 24 hours (six trials, 507 participants, RR 0.37, 95% CI 0.15–0.87) (EB Table 2.10.1). A combination of oral plus vaginal misoprostol did not produce better results than vaginal misoprostol alone (two trials, less than 100 participants), although moderate differences cannot be ruled out due to the small number of studies (EB Table 2.10.7). When the same combination was compared with oral misoprostol alone, there was a reduced risk of women not achieving vaginal birth within 24 hours in those receiving the combined regimen (one trial, 56 participants, RR 0.47; 95% CI 0.23–0.96) (EB Table 2.10.8). The addition of laminaria tent to vaginal misoprostol resulted in no additional benefits (EB Table 2.10.6). One trial reported that a lower cumulative dose of vaginal misoprostol (< 800 ?g) was associated with an increased risk of vaginal birth not being achieved within 24 hours (RR 1.85, 95% CI 1.13–3.03), although there was a lower risk of surgery to evacuate the uterus (RR 0.57, 95% CI 0.33–0.98) (EB Table 2.10.12). In terms of dosing intervals of vaginal misoprostol, no differences were observed between 6-hourly versus 12-hourly dosing (three trials, 416 participants) (EB Table 2.10.2).

Sublingual misoprostol was found to be more effective than vaginal misoprostol for reducing the risk of vaginal birth not achieved within 24 hours (two trials, 202 participants, RR 0.24, 95% CI 0.08–0.74) (EB Table 2.10.9). A similar trend was seen in the comparison with oral misoprostol (two trials, 204 participants, RR 0.22, 95% CI 0.01–4.99) (EB Table 2.10.10). In the same comparison, the induction-to-delivery interval was reduced in women receiving sublingual misoprostol (mean difference 7.17 hours, 95% CI –13.73 to –0.6). No differences were observed in terms of dosing (100 ?g versus 200 ?g, sublingual; one trial, 81 participants) (EB Table 2.10.11). There are limited data on comparisons of vaginal misoprostol with other prostaglandins. In a comparison of vaginal misoprostol versus prostaglandin F2 alpha, women receiving vaginal misoprostol showed a reduced risk of surgical evacuation of the uterus (five trials, 439 participants, RR 0.63, 95% CI 0.41–0.98) (EB Table 2.10.5).

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 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 review:

[Dodd JM, Crowther CA. Misoprostol for induction of labour to terminate pregnancy in the second or third trimester for women with a fetal anomaly or after intrauterine fetal death. Cochrane Database Syst Rev. 2010(4):Cd004901.](#)

**References**


Citation


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