WHO recommendation on use of low doses of vaginal prostaglandins for induction of labour

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Recommendation

Low doses of vaginal prostaglandins are recommended for induction of labour.

(Moderate-quality evidence, strong recommendation)

Publication history

First published: February 2011

Updated: prioritized for updating in 2018

Assessed as up-to-date: February 2011

Remarks

- Prostaglandin preparations other than misoprostol are expensive and may not be a priority for implementation, especially in low- and middle-income countries.
- When prostaglandins are used, close monitoring of the woman and fetus should begin immediately after administration of the drug.

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)

Cochrane systematic reviews were conducted, on use of prostaglandins other than misoprostol for induction of labour. (10-13) 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 in women with previous caesarean section using misoprostol (I), compared to no intervention, (C), improve maternal and perinatal outcomes (O)?

**Evidence Summary**

Four systematic reviews (10-13) summarize the evidence related to the use of prostaglandins other than
misoprostol for induction of labour. In these reviews, various preparations of prostaglandin E2 and prostaglandin F2 alpha have been evaluated.

Overall, prostaglandin E2 (all regimens) preparations were more effective than placebo for induction of labour at term (EB Table 2.6.1). There was a reduced risk of vaginal births not achieved within 24 hours (two trials, 384 participants, RR 0.19, 95% CI 0.14–0.25) and fewer caesarean births (34 trials, 6399 participants, RR 0.89, 95% CI 0.79–1.00). A higher risk of uterine hyperstimulation with fetal heart rate changes was observed (14 trials, 1259 participants, RR 4.14, 95% CI 1.93–8.9), but without additional adverse maternal and perinatal priority outcomes (Apgar score, admission to a neonatal intensive care unit, perinatal death and serious maternal morbidity or death).

Direct comparisons between intracervical prostaglandin E2 and intra-vaginal prostaglandin E2 were made in 28 studies (3781 participants) and the results were in the favour of the latter (EB Table 2.8.2). Although similar in terms of other priority outcomes, intracervical prostaglanidns have been associated with an increased risk of vaginal birth not achieved within 24 hours (eleven studies, 2200 participants, RR 1.26, 95% CI 1.12–1.41). There is limited evidence from randomized controlled trials (three trials, 113 participants) on oral versus intra-cervical prostaglandins (EB Table 2.7.3) and oral versus vaginal prostaglandins (EB Table 2.7.4); no differences were found between the two types of intervention.

The comparison between oxytocin alone and vaginal prostaglandins favoured the prostaglandins (EB Table 2.1.3): oxytocin alone was associated with an increased risk of vaginal birth not achieved within 24 hours (three trials, 260 participants, RR 1.77, 95% CI 1.31–2.38); comparisons involving other priority outcomes, which were made in 26 trials involving 4514 participants, showed similar results.

Vaginal prostaglandin E2 gel has been compared with vaginal prostaglandin E2 tablets and, overall, both formulations were found to have similar effects (five trials, 881 participants evaluated for five priority outcomes) (EB Table 2.6.4). Vaginal prostaglandin E2 gel has also been compared with vaginal prostaglandin E2 suppository/pessary (EB Table 2.6.5). In this comparison, the gel was associated with less uterine hyperstimulation (two trials, 159 participants, RR 0.16, 95% CI 0.03–0.87) and there was no statistically significant difference between the gel and suppository/pessary in terms of the risk of caesarean section (two trials, 159 participants, RR 0.65, 95% CI 0.38–1.11) and Apgar score less than seven at 5 minutes of life (one trial, 69 participants, RR 0.21, 95% CI 0.01–4.13). There was limited, low-quality evidence showing no statistically significant differences between controlled-release prostaglandin E2 and other prostaglandin E2 formulations (eight trials, 929 participants, five priority outcomes evaluated).

Low-dose prostaglandin E2 has been compared with its high-dose counterpart in seven trials (EB Table 2.6.8). The use of lower doses may present comparative advantages over the higher doses: (i) lower risk of uterine hyperstimulation with fetal heart rate changes (two trials, 140 participants, RR 0.18, 95%, CI 0.03–0.99); (ii) similar risk of caesarean section (seven trials, 1466 participants, RR 1.07, 95% CI 0.8–1.42) and Apgar score less than seven at 5 minutes of life (three trials, 1064, RR 0.51, 95% CI 0.2–1.31); and (iii) a trend towards reduced risk of admission to a neonatal intensive care unit (one trial, 955 participants, RR 0.51, 95%, CI 0.24–1.09).

**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?
- In under-resourced settings with weak health systems and staff shortages, how can effective monitoring of women be ensured during induction of labour?

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


Citation