WHO recommendation on the use of oral misoprostol for labour augmentation

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Recommendation

The use of oral misoprostol for labour augmentation is not recommended.

(Strong recommendation, very low-quality evidence)

Publication history

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Remarks

- The GDG noted that there is no clear evidence that the potential benefits of oral misoprostol, compared to intravenous oxytocin, for labour augmentation outweigh its potential harms.

- The GDG concluded that oral misoprostol is unlikely to be a safe substitute to oxytocin for labour augmentation where skilled attendants are available. The group also noted that settings where skilled birth attendants are not available (and where misoprostol could have been useful in this regard) are also likely to lack the resources to manage complications that could arise in women undergoing augmentation.

- The GDG considers the dosage regimens used in the primary studies as not evidence based with potential for serious harms, given the high rate of uterine hyperstimulation with fetal heart rate changes. The group put its emphasis on the implications of such adverse effects for maternal and infant outcomes, particularly in low-resource settings, and therefore strengthened the recommendation.

- Further pharmacological effects of orally ingested misoprostol, if found detrimental to the health of the mother or her baby during the course of labour, cannot be prevented by termination of the therapy as is possible with oxytocin infusion.
**Background**

Difficult labour (or dystocia) is characterized by abnormally slow labour progress arising from inefficient uterine contractions, abnormal fetal presentation or position, inadequate bony pelvis or abnormalities of the pelvic soft tissues of the mother. (1, 2) Evidence suggests that up to one third of first-time mothers experience delay in the first stage of labour. (3)

Augmentation of labour is the process of stimulating the uterus to increase the frequency, duration and intensity of contractions after the onset of spontaneous labour. It has commonly been used to treat delayed labour when uterine contractions are assessed to be insufficiently strong or inappropriately coordinated to dilate the cervix. Labour augmentation has traditionally been performed with the use of intravenous oxytocin infusion and/or artificial rupture of amniotic membranes (amniotomy). The procedure aims to shorten labour in order to prevent complications relating to undue prolongation, and to avert caesarean section. There is evidence that a significant proportion of women with uncomplicated pregnancies are subjected to routine augmentation of labour with oxytocin. (4)

While augmentation of labour may be beneficial in preventing prolonged labour, its inappropriate use may cause harm. Augmentation with synthetic oxytocin may result in uterine hyperstimulation, with adverse effects such as fetal asphyxia and uterine rupture, and thus increase the risk of a cascade of interventions during labour and delivery. (5)

**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. (6) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on augmentation of labour (2014). (7)

A Cochrane systematic review was conducted, on use of the partograph as a monitoring tool to identify when intervention becomes indicated during labour. (8) 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 on augmentation of labour in September 2013, 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.

Further information on procedures for developing this recommendation are available here.

**Recommendation question**

For this recommendation, we aimed to answer the following question:
In pregnant women in labour (P), does the use of oral misoprostol for labour augmentation (I), compared to no or other interventions (C), improve maternal and perinatal outcomes (O)?

Evidence Summary

Evidence was drawn from a Cochrane systematic review that included two trials, each examining a different comparison. (8) Women in both trials were all in spontaneous labour requiring augmentation. The trials were conducted in Taiwan and the USA.

The trial in Taiwan, China (231 women) compared titrated oral misoprostol with IV oxytocin for labour augmentation. Women in the misoprostol group were randomized to receive an initial dose of 20 micrograms (mcg) of misoprostol (in 20 ml of water) repeated every hour up to four hours, after which the dose was increased to 40 mcg per hour up to a maximum cumulative dose of 1600 mcg. All but three of the women randomized received the intended treatment.

In the trial in the USA, women were randomized to receive either oral misoprostol or usual care (IV oxytocin). In this trial, lower doses of misoprostol were achieved by cutting up 100 mcg tablets. Women were initially given 75 mcg of oral misoprostol, which was repeated after four hours provided no adverse effects were observed. There was considerable deviation from protocol in this trial although analysis was by intention to treat: in the misoprostol group 136/176 (77.3%) received the trial drug, while in the oxytocin group 143/174 (82.2%) women received the control drug as intended.

Findings for the two trials were not pooled in view of the different misoprostol regimens.

Titrated oral misoprostol versus oxytocin: maternal outcomes

- For the misoprostol group on the 20 mcg per hour regimen, overall there was no evidence of differences between groups for most critical and important maternal outcomes.

- Mode of delivery was similar in the misoprostol and oxytocin groups; most of the women in both groups gave birth vaginally within 24 hours of the commencement of augmentation (RR 1.02, 95% CI 0.93 to 1.11). Similar numbers of women (approximately 80% in both groups) had given birth vaginally within 12 hours of augmentation (RR 0.91, 95% CI 0.80 to 1.03). There was no significant difference between groups in terms of the number of women undergoing caesarean section (RR 0.88, 95% CI 0.42 to 1.85). Rates of “failure to progress” were similar in the two groups (RR 0.80, 95% CI 0.36 to 1.77).

- Few women (two in each group) had uterine hyperstimulation with fetal heart rate changes (RR 0.96, 95% CI 0.14 to 6.68). No women were identified with hypertonus, but more women in the oxytocin group were reported to have tachysystole: 7/118 in the misoprostol group versus 17/113 in the oxytocin group (RR 0.39, 95% CI 0.17 to 0.91).

- Maternal side-effects (including pyrexia, shivering, nausea and vomiting) were reported, but there were very few events in either group.

- For the 75-mcg dosage regimen, there was no evidence of differences between groups for most maternal outcomes.

- There were no significant differences between women in the misoprostol and oxytocin groups for rate of caesarean section for fetal distress (RR 1.58, 95% CI 0.53 to 4.74), caesarean section for prolonged labour (RR 0.84, 95% CI 0.39 to 1.82), or caesarean section for any indication (RR 1.04, 95% CI 0.57 to 1.92). Few women had forceps delivery (RR 1.98, 95% CI 0.37 to 10.66) and the overall rate of spontaneous vaginal birth was very similar in both groups (RR 0.98, 95% CI 0.91 to 1.06).
More than a quarter of women in both groups were reported to have uterine hyperstimulation with fetal heart rate changes and, although the rate was higher in the misoprostol group, the difference between the groups was not statistically significant (RR 1.26, 95% CI 0.88 to 1.80). Uterine hyperstimulation over a 10-minute period (without fetal heart rate changes) was reported for more than 60% of women in both groups; more women in the misoprostol group (approximately 75% versus 64%) were reported to have hyperstimulation of labour (RR 1.17, 95% CI 1.02 to 1.35). The number of women with tachysystole over a 20-minute observation period was reported to be similar in both groups (RR 1.21, 95% CI 0.84 to 1.72).

Most of the women in both groups had epidural analgesia (RR 0.92, 95% CI 0.84 to 1.01). Maternal blood transfusion for hypovolemia was reported, and no difference between groups was identified (RR 2.97, 95% CI 0.61 to 14.49). Rates of chorioamnionitis were similar for the women in both groups (RR 0.87, 95% CI 0.55 to 1.37).

**Titrated oral misoprostol versus oxytocin: infant outcomes**

- For the 20-mcg dosage regimen, few important infant outcomes were reported.
- There were no babies with Apgar scores < 7 at five minutes in either group. There were few admissions to NICU, and no significant difference between groups (RR 2.39, 95% CI 0.47 to 12.09).
- For the 75-mcg dosage regimen, Apgar score of < 4 at five minutes was reported: there were no events in either group. Only one baby was admitted to NICU. There was no significant difference between groups for umbilical cord artery pH of < 7.1 (RR 0.74, 95% CI 0.17 to 3.26). Other critical and important neonatal outcomes were not reported.

Further information and considerations related to this recommendation can be found in the WHO guidelines, available at: [http://apps.who.int/iris/bitstream/handle/10665/112826/WHO_RHR_14.15_eng...](http://apps.who.int/iris/bitstream/handle/10665/112826/WHO_RHR_14.15_eng...)

**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 augmentation 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 did not identify further research priorities on this topic.
Related Links

WHO recommendations for augmentation of labour (2014) –full document and evidence tables

Supporting systematic review:


References


Citation


Published on RHL (https://extranet.who.int/rhl)

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