WHO recommendation on the uterotonic drug of choice for the prevention of postpartum haemorrhage in settings where skilled birth attendants are not present and oxytocin is unavailable

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Recommendation

In settings where skilled birth attendants are not present and oxytocin is unavailable, the administration of misoprostol (600 µg PO) by community health care workers and lay health workers is recommended for the prevention of postpartum haemorrhage.

(Strong recommendation, moderate-quality evidence)

Publication history

First published: September 2012

Updated: updated planned for 2018

Assessed as up-to-date: September 2012

Remarks

- Misoprostol (600 µg PO) was regarded by the GDG as an effective drug for the prevention of PPH. However, the GDG considered the relative benefits of oxytocin compared to misoprostol in preventing blood loss, as well as the increased adverse effects of misoprostol compared to oxytocin.
- The recommendations concerning alternative uterotonics should not detract from the objective of making oxytocin as widely accessible as possible.
- In view of past concerns regarding the community-level distribution of misoprostol and the potential for serious consequences of administration before birth, the GDG places emphasis on training persons administering misoprostol and monitoring community distribution interventions with scientifically sound methods and appropriate indicators.

Background

Postpartum haemorrhage (PPH) is defined as blood loss of 500ml or more within 24 hours after birth. PPH is
the primary cause of nearly one-fifth of all maternal deaths globally. Most of these deaths occur during the first 24 hours after birth. The majority could be prevented through the use of prophylactic uterotonics during the third stage of labour, and by timely and appropriate management.

It is generally assumed that by preventing and treating PPH, most PPH-associated deaths could be avoided. The prevention and treatment of PPH are therefore vital steps towards improving the health care of women during childbirth and the achievement of the Millennium Development Goals. To reach these objectives, health workers in developing countries should be given access to appropriate medications and be trained in procedures relevant to the management of PPH. Countries also need evidence-based guidance to inform their health policies and improve their health outcomes.

Methods

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, based on the GRADE approach. (1, 2) Outcomes used for this recommendation were the prioritized outcomes from the WHO recommendations on prevention and treatment of postpartum haemorrhage (2012).(3)

One systematic review provided evidence. (4). 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 in March 2012. This group of independent experts 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, magnitude of effect, balance of benefits versus disadvantages, resource usage, and feasibility, 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:

- For all women giving birth in settings where skilled birth attendant and oxytocin are unavailable (P), does other uterotonic drug administration during the third stage of labour (I) compared to placebo, or no treatment (C) improve maternal outcomes, including postpartum haemorrhage prevention (O)?

Evidence Summary

A Cochrane systematic review found no randomized controlled trials which provided direct evidence about this topic (4).

The GDG therefore reviewed the literature using a more inclusive search strategy that included non-randomized and other observational studies (5-15).
Effectiveness of oral misoprostol only in the reduction of postpartum blood loss

Evidence for the contribution of oral misoprostol only in the reduction of postpartum blood loss came mostly from one randomized controlled trial conducted in rural India (5). In this trial, 600 µg of oral misoprostol was compared with placebo in the context of the expectant management of the third stage of labour. Misoprostol was administered by auxiliary nurse-midwives who assisted with deliveries at primary health facilities and in homes. An overall reduction was reported in: blood loss (mean difference in total blood loss: -48 ml) (95% CI -63.81 ml to -32.19 ml), PPH (blood loss >500 ml) 149 events (RR 0.53; 95% CI 0.39 to 0.74), and severe PPH (blood loss >1000 ml) 12 events (RR 0.2; 95% CI 0.04 to 0.91). However, firm conclusions cannot be drawn from this evidence as the trial reported too few events related to the impact of misoprostol in severe health outcomes, including severe PPH. (Moderate-quality evidence) As noted, these deliveries were assisted by auxiliary nurse-midwives at primary health facilities or in homes and the use of misoprostol was supervised by these health professionals.

Caution should be exercised when extrapolating data provided by this trial to deliveries that are not assisted by skilled birth attendants, either at home or when the use of misoprostol is unsupervised. (Very-low-quality evidence)

Evidence of a similar very-low quality was provided by other studies (6-10). In addition, a non-randomized cluster trial evaluated the use, at a community level, of a supervised 400 µg dose of misoprostol during the third stage of labour (11). In this study, a reduced risk of self-reported PPH (RR 0.29, 95% CI 0.18 to 0.48) was found. (Very-low-quality evidence).

Feasibility of advanced distribution of misoprostol

Non-randomized and other observational studies (12,13) suggest that the community distribution of misoprostol during pregnancy is strongly associated with an increased use of misoprostol during the third stage of labour. (Moderate-quality evidence).

Effect of community distribution of misoprostol on health outcomes

A Cochrane systematic review identified no randomized controlled trials providing direct evidence on the effect of the community distribution of misoprostol on health outcomes (4). Non-randomized trials and other observational studies which evaluated the use of the community distribution of misoprostol did not evaluate the effect on health outcomes or failed to demonstrate any benefit (12,13). Some model-derived data and model-based simulations suggest that the community distribution of misoprostol could potentially contribute to a reduction in the burden of PPH in settings of low coverage of skilled birth attendants (14,15). However, the primary sources of evidence and the assumptions informing the development of this modelling impacted on the quality of the evidence generated. For example, in the models developed by Pagel (14), a trial conducted in rural India (5) is the main source of data regarding the effectiveness of misoprostol for reducing PPH through community distribution. However, in this trial, 25 auxiliary nurse midwives undertook the deliveries, administered the study drug, and measured blood loss. (Overall, the quality of evidence was low or very low, mostly due to indirectness.).

Further information on evidence supporting this recommendation are available here.

Implementation considerations
The successful introduction of evidence-based policies related to the prevention and management of PPH into national programmes and health care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. These processes may include the development or revision of national guidelines or protocols based on this recommendation.

The recommendation should be adapted into locally-appropriate documents and tools that are able to meet the specific needs of each country and health service. Modifications to the recommendation, where necessary, should be justified in an explicit and transparent manner.

An enabling environment should be created for the use of this recommendation, including changes in the behaviour of health care practitioners to enable the use of evidence-based practices.

Local professional societies may play important roles in this process and an all-inclusive and participatory process should be encouraged.

**Research implications**

The GDG identified these research priorities related to this recommendation:

- In settings where the use of injectable uterotonics is not feasible, what are the effects of antenatal distribution of misoprostol to pregnant women for self-administration during the third stage of labour?
- What is the minimum effective dose of misoprostol for the prevention of PPH?
- Should misoprostol be used in addition to oxytocin for PPH prevention?

**Related Links**

WHO recommendations on prevention and treatment of postpartum haemorrhage (2012) - [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)**

**VIDEO: Active management of third stage of labour**

Education material for teachers of midwifery. Managing postpartum haemorrhage.

**Links to supporting evidence:**


References
