Questions raised over use of misoprostol to prevent postpartum haemorrhage in poor countries

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The World Health Organization should reconsider its approval of misoprostol to prevent postpartum haemorrhaging in poorer countries, says a review of the evidence.1

The review concluded that the evidence to support the use of misoprostol in low and middle income countries in home and community settings where parenteral uterotonics were not available was “at best weak and inconclusive.”

Most maternal deaths relating to pregnancy and childbirth occur in lower income countries, and a quarter of deaths are associated with postpartum haemorrhage, defined as blood loss of more than 500 mL after a vaginal delivery.2

Anaemia is the main risk factor for postpartum haemorrhage and can be treated easily if diagnosed. But in lower income countries without antenatal screening for anaemia WHO guidelines recommend that skilled birth attendants perform active management of the third stage of labour. This consists of three interventions: prophylactic administration of a uterotonic drug, where oxytocin is the drug of choice followed by ergometrine/methylergometrine; early cord clamping and cutting; and controlled cord traction.3

Oxytocin and ergometrine preparations are heat sensitive and usually require intravenous or intramuscular administration. Where skilled birth attendants are not available or the delivery is at home or in a community clinic, misoprostol, another uterotonic, tends to be used because it is stable and can be given orally, or as a vaginal or rectal preparation.

In May 2011, WHO’s Essential Medicines List approved the inclusion of misoprostol for the prevention of primary postpartum haemorrhage in settings where parenteral uterotonics are not available or feasible. The decision was based on the evidence from four randomised controlled trials, which were among those reviewed by the latest analysis.

The UK researchers, led by Allyson Pollock at the Centre for Primary Care and Public Health at Queen Mary University of London, identified 172 studies assessing the effectiveness of misoprostol for preventing primary postpartum haemorrhage in home and community settings in low and middle income countries. Of these, only six fulfilled the inclusion criteria. Three of the six compared misoprostol with active management of the third stage of labour, two with expectant management of labour, and one with birth attendants being allowed to choose management practice.

The three studies comparing misoprostol with active management of the third stage of labour showed no significant differences in overall incidence of postpartum haemorrhage, although one study showed a significant decrease in severe haemorrhage using misoprostol. One study of expectant management and one on the choice of management by birth attendants found significant decreases in incidence of postpartum haemorrhage with misoprostol.

The researchers, however, criticised the reliability of the results because all the studies except one excluded women at highest risk of postpartum haemorrhage and there was inconsistent management of women in the control arms, including types of uterotonics.

The incidence of postpartum haemorrhage fell in both the control and intervention groups in two of the papers that informed the WHO decision to approve misoprostol, the researchers pointed out, suggesting that “factors other than misoprostol use are crucial.”

They added that the outcomes of all four studies included in the WHO assessment might have been influenced by the skills of the birth attendants caring for the women, who “were able to assess antenatal complications, manage uncomplicated labour, and detect obstetric complications.

“In many areas there is limited access to personnel with these skills, and therefore women cannot be assessed for their suitability for misoprostol,” they said.

“WHO should rethink its recent decision to include misoprostol on the Essential Medicines List,” they concluded.

Andrew Weeks, professor of international maternal health at the University of Liverpool, who has researched the use of misoprostol himself, disagreed. “WHO have been the most cautious of all and far more cautious than many people would have wanted,” he said.

Weeks, who is a member of the International Federation of Gynecology and Obstetrics guidelines committee on use of misoprostol in low income settings and was initially undecided about misoprostol himself, said that ,as more studies have been published, people who were enthusiastic about misoprostol from the outset had been proven right.

He said he found the Journal of the Royal Society of Medicine’s paper “intriguing” and its conclusions “bizarre.” Every research paper could be criticised in some way especially when conducted in low resource settings, but three of the six studies assessed were “top quality” double-blind randomised placebo control trials.
“They are saying this evidence isn’t enough,” Weeks said. “How many more [trials] are they wanting to do?”

Changes to the WHO Essential Medicines List are made by a panel that meets every two years. The next meeting will be held in early 2013. A spokesman for WHO said: “WHO is the secretariat for the panel and welcomes the submission of applications—for medicines to be added, deleted, or modified.”

Misoprostol is currently licensed for postpartum haemorrhage prevention in India, Bangladesh, Nepal, Ghana, Kenya, Mozambique, Nigeria, Sudan, Tanzania, Uganda, Zambia, Somaliland, Pakistan, and Sierra Leone.

In situations where skilled birth attendants are unavailable, WHO guidelines advocate misoprostol use for postpartum haemorrhage prevention while the International Confederation of Midwives and the International Federation of Gynaecology and Obstetrics suggest using misoprostol in all situations where oxytocin is not available.