

Misoprostol for the Prevention of Postpartum Hemorrhage: Findings from Clinical Research Trial in Chitral, Pakistan

From 2005 to 2008, the Aga Khan University, Karachi, Aga Khan Health Service, Pakistan, and Gynuity Health Projects carried out a community-based study in Chitral district, North-West Frontier Province, Pakistan to examine the efficacy and safety of misoprostol for prevention of postpartum hemorrhage (PPH) during home births. The double-blinded, randomized-controlled trial enrolled nearly 1,400 women to test whether 600 mcg oral misoprostol reduces the incidence of PPH when administered by trained traditional birth attendants (TBAs) during the third stage of labor. The study was undertaken in remote, mountainous villages where the majority of deliveries are conducted by TBAs at the home, and access to emergency maternal health care services is limited.

Women with pregnancy complications or who planned to deliver at a health center were not eligible to participate in the study. Consenting women delivering at home with a trained TBA were randomized to receive either 600 mcg oral misoprostol or matching placebo. The main study hypotheses were that misoprostol would reduce the rate of PPH (≥ 500 ml), and decrease the drop in hemoglobin from pre- to post-delivery, when compared to a placebo.

Trained TBAs, Lady Health Visitors (LHVs), and Community Health Nurses (CHNs) based at 17 primary-care facilities within the Aga Khan Health Services network provided care during delivery, oversaw data collection, and ensured protocol compliance. LHVs and CHNs were responsible for consenting pregnant women, conducting interviews during antenatal care visits, and measuring blood loss and hemoglobin levels. TBAs conducted deliveries, administered the study medication, collected blood loss, and observed women for side effects for one hour. Study benefits included prompt detection of severe PPH due to standardized blood collection, improved postpartum care, early recognition of anemia, and stronger linkages between TBAs and primary care health facilities.

STUDY FINDINGS

Primary outcomes

- Oral misoprostol reduced the rate of PPH ($\geq 500\text{ml}$) by 24% compared with placebo.
- Women receiving misoprostol had a smaller drop in hemoglobin ($>2\text{g/dL}$) from pre- to post-delivery, compared with placebo.

Side effects and safety

- Shivering and chills were reported in 1 of every 9 women who received misoprostol and 1 of every 20 women given placebo.
- Seven cases of fever were detected in each of the study groups; all other side effects were minimal.
- Referrals for higher level of care during the immediate postpartum period were similar following administration of misoprostol (2.4%) or placebo (1.8%).
- No maternal deaths or severe adverse events occurred among women participating in this trial.

IMPLICATIONS

- Based on the results of this and previous community-based studies, oral misoprostol (600mcg) is safe and effective, and could be used routinely for PPH prevention in low-resource settings where injectable oxytocin is not available or not feasible.
- Misoprostol is easy to use and administer, and traditional birth attendants can be trained in its appropriate use for prevention of PPH. Careful monitoring and evaluation should accompany any widespread introduction of this drug.

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