

## Misoprostol for the Treatment of Postpartum Hemorrhage: Findings from Clinical Research Trials

Gynuity Health Projects has undertaken a significant body of work to evaluate misoprostol for the treatment of postpartum hemorrhage (PPH). This summary describes a series of clinical trials conducted on the use of misoprostol to treat PPH due to uterine atony among women undergoing vaginal delivery.

### MISOPROSTOL AS PRIMARY TREATMENT FOR PPH

In collaboration with partners in five countries (Burkina Faso, Ecuador, Egypt, Turkey and Vietnam), Gynuity conducted two large clinical trials to evaluate the safety, efficacy, and acceptability of sublingual (under the tongue) misoprostol to treat PPH. The studies compared misoprostol to oxytocin, the international standard of care for treating PPH, using a randomized double-blind placebo-controlled study design. One study was conducted at hospitals where women routinely received 10 IU oxytocin in the third stage of labor. In this study, 3% of women were treated for PPH. The other study was conducted in hospitals where women did not receive oxytocin before or during the third stage of labor, resulting in a 10% rate of PPH treatment. In the two studies, more than 40,000 women were consented and screened for PPH; of these, 1,787 were treated with one of two regimens: 800 mcg sublingual misoprostol or 40 IU oxytocin delivered intravenously (IV).

### STUDY FINDINGS

#### *Efficacy*

800 mcg sublingual misoprostol works well to control postpartum bleeding.

In the study where all women received oxytocin prophylaxis:

- Misoprostol and oxytocin were similarly effective in treating PPH.
- Both treatments stopped active bleeding within 20 minutes for nearly 90% of cases.
- Mean measured blood loss, provision of additional uterotonics, blood transfusion, and hysterectomy, and change in postpartum hemoglobin (Hb)  $\geq 2\text{g/dL}$  were similar for both treatments.

In the study where no women received oxytocin prophylaxis:

- Both treatments stopped active bleeding within 20 minutes for at least 90% of women.
- Women treated with oxytocin had a lower mean blood loss, faster time to bleeding cessation and received fewer additional interventions, such as additional uterotonics.
- Postpartum Hb changes of  $\geq 2\text{g/dL}$  were similar for both treatments.

## Safety and acceptability (in both studies)

- Shivering and fever occurred more frequently with misoprostol.
- Among women treated with misoprostol, fever  $\geq 40.0^{\circ}\text{C}$  was commonly observed in one country; all cases were transient, non-life threatening, and did not lead to prolonged hospitalization.
- Women reported both routes of treatment administration (tablets or IV) as acceptable, and most side effects as tolerable.
- Severe adverse events were rare.

## MISOPROSTOL AS ADJUNCT TREATMENT FOR PPH

In collaboration with the Department of Reproductive Health and Research at the World Health Organization (WHO), Gynuity conducted a study of misoprostol as adjunct treatment to conventional uterotonics for PPH treatment. This double-blind, randomized controlled trial was conducted at WHO Collaborating Centers in Argentina, Egypt, South Africa, Thailand, and Vietnam. Women had their third stage of labor managed actively with 10 IU of oxytocin. Consenting women with clinically diagnosed PPH were given conventional uterotonics and, at the same time, either 600 mcg sublingual misoprostol or placebo.

## STUDY FINDINGS

- The data show no benefit of simultaneous administration of misoprostol + standard uterotonics over placebo + standard uterotonics for treatment of PPH.
- Significantly more fever was observed among women given misoprostol + standard uterotonics.

## IMPLICATIONS FOR CLINICAL PRACTICE

- Sublingual misoprostol (800 mcg) is a safe, effective and acceptable alternative first-line treatment for PPH due to uterine atony.
- Misoprostol is easy to administer and may be particularly useful in settings where administration of IV oxytocin is not possible, particularly at lower levels of the health care system.
- Simultaneous administration of misoprostol (600 mcg) to conventional uterotonics for PPH treatment confers no clinical advantage.

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