

Misoprostol and Postpartum Hemorrhage (PPH) Research, April 2007, Version 7

I. PREVENTION

Institution/ principal investigator	Study title	Study locations	Study design	Number of subjects	Study environs	Study objective	Outcomes and notes	Study dates
University of California, San Francisco Michael Varner, MD, and Dr. Suellen Miller, PhD, CNM	Randomized double-masked trial of ZHI BYED 11, a Tibetan traditional medicine, versus misoprostol to prevent postpartum hemorrhage in Lhasa, Tibet	Lhasa, Tibet, China	Randomized, placebo-controlled	848 women expected to be enrolled. .	Maternity hospital	Comparison of misoprostol administered in third stage of labor versus Zhi Byed 11 (ZB11), a Tibetan medicine, administered at beginning of second stage of labor. Secondary objectives: determining the acceptability of giving Tibetan and Western medicine during third-stage labor to pregnant women delivering at Lhasa maternity hospitals and determining if the active management of the third stage of labor reduces the incidence of other pregnancy complications.	Incidence of PPH: blood loss >500 ml.	Ongoing. Feasibility study completed January 2004.
Aga Khan Foundation, Aga Khan University, Aga Khan Health Service, Gynuity Health Projects, and Family Care International Gijs Walraven, Juanita Hatcher, Naushaba Mobeen, Jennifer Blum, Zafar Ahmad, Nadeem Zuberi, Tess Aldrich, Jill Durocher, Beverly Winikoff	A placebo-controlled randomized trial of misoprostol in the management of the third stage of labor in the home delivery setting in rural Pakistan	Chitral District, Pakistan	Randomized, placebo-controlled	1,600 women.	Home births with traditional birth attendants	Misoprostol, 600 mcg oral, vs. placebo for prevention of PPH where injectable oxytocics not available.	Postpartum hemorrhage (blood loss \geq 500 ml); drop in hemoglobin > 2g/dL from pre- to post-delivery. Secondary outcomes: Intermediate and severe PPH (blood loss \geq 750 ml and \geq 1000 ml); mean blood loss; side effects for women; anemia.	Ongoing, July 2005 start date.
University of California at Berkeley, Gonoshastaya Kendra, and Ventures Strategies for Health and Development Martha Campbell, Ndola Prata, and Malcolm Potts	Use of misoprostol to prevent postpartum hemorrhage	Bangladesh	Intervention	1,000 women expected in each intervention and control areas.	Home births assisted by traditional birth attendants (TBAs)	Misoprostol, 600 mcg oral, vs. non-intervention for prevention of PPH.	Postpartum hemorrhage (blood loss \geq 500 ml). Secondary outcomes: side effects; blood loss >1000 ml; need for additional interventions; side effects.	Ongoing.

Principal investigator/ institution	Study title	Study locations	Study design	Number of Subjects	Study environs	Study objective	Outcomes and notes	Study dates
Tigay Health Bureau, Ethiopian Society of Obstetricians and Gynecologists, with support from the Packard Foundation in collaboration with University of California at Berkeley, and Venture Strategies for Health and Development Martha Campbell, Ndola Prata, and Malcolm Potts	Use of misoprostol to prevent postpartum hemorrhage	Ethiopia (four sites)	Intervention	1,000 women per site.	Home births	Misoprostol, 600 mcg oral, vs. non-intervention for prevention of PPH.	Postpartum hemorrhage (blood loss \geq 500 ml). Secondary outcomes: side effects; blood loss >1000 ml; need for additional interventions; side effects.	Starting January 2006.
University of California at Berkeley and Venture Strategies for Health and Development Martha Campbell, Ndola Prata, and Malcolm Potts	Misoprostol for preventing postpartum hemorrhage	Bangladesh	Randomized	3,000 women.	Hospital	Will produce data that will indicate whether or not misoprostol can be safely used where IV oxytocics are not available, and if so, when should it be administered to women (prophylactically or therapeutically).	Measured blood loss; need for additional interventions; hemoglobin levels.	Ongoing.
University of Witwatersrand, South Africa/Effective Care Research Unit/Gynuity Health Projects G.J. Hofmeyr, MD	Misoprostol for preventing postpartum hemorrhage	South Africa, Nigeria, Uganda	Randomized, placebo-controlled	1,200 women.	Hospital	Misoprostol as adjunct prophylaxis. Misoprostol 400 mcg sublingual vs. placebo.	Blood loss \geq 500 mls within one hour after enrollment. Secondary outcomes: blood loss \geq 1,000 mls within one hour after enrollment; mean blood loss after enrollment; blood transfusion; hemoglobin level < 8 g/dL 24 hours after delivery; maternal morbidity and mortality; side effects.	Ongoing, start date August, 2005.

II. TREATMENT

Principal investigator/ institution	Study title	Study locations	Study design	Number of Subjects	Study environs	Study objective	Outcomes and notes	Study dates
World Health Organization/Gynuity Health Projects Jose Villar, Beverly Winkoff, Mariana Widmer, Jennifer Blum, Guillermo Carroli, GJ Hofmeyr, Nguyen Thi Nhu Ngoc, Hany Abdelaleem, Pisake Lumbiganon	Misoprostol for the treatment of postpartum hemorrhage	Argentina, Egypt, South Africa, Thailand, and Vietnam	Randomized, placebo-controlled	1,400 women	Health center/hospital	Misoprostol, 600 mcg sublingual, vs. placebo as adjunct treatment in addition to routine treatment with oxytocin for PPH.	Incidence of PPH: ≥ 500 ml measured blood loss at 60 minutes.	Ongoing.
University of California at Berkeley, Women's Health and Action Research Centre, and Venture Strategies for Health and Development Martha Campbell, Ndola Prata, and Malcolm Potts	Controlling postpartum hemorrhage after home births in Nigeria	Nigeria	Interventional	1,000 women	Home births	Misoprostol, 1,000 mcg rectal, vs. non-intervention as treatment for PPH.	Blood loss; need for additional intervention; referrals.	Ongoing. No dates available.
Aga Khan Foundation, Aga Khan University, Aga Khan Health Service, Gynuity Health Projects, and Family Care International Nadeem F Zuberi, MD	Misoprostol in the treatment of postpartum haemorrhage: a placebo randomized controlled trial in 4 Karachi hospitals	Karachi, Pakistan	Randomized, placebo-controlled	900 women	Hospitals	Misoprostol as adjunct treatment for PPH. Misoprostol 600 mcg sublingual vs. placebo in addition to standard injectable oxytocics	Blood loss ≥ 500 ml after enrolment. Secondary outcomes: mean blood loss, clinical complications (need for blood transfusion, hysterectomy), hemoglobin 12-24 hours after delivery, side effects.	Ongoing.
Gynuity Health Projects/Family Care International Beverly Winikoff, MD, MPH, Jennifer Blum, MPH, Rasha Dabash, MPH, Sheila Raghavan, MSc, Ayisha Diop, MPH, Ilana Dzuba, MHSc,	Misoprostol for the treatment of primary postpartum hemorrhage	Burkina Faso, Ecuador, Egypt, and Vietnam	Randomized, placebo-controlled	1,900 women expected	Hospitals	Misoprostol as a stand alone treatment vs. oxytocin with two separate subgroups (women who did and who did not have oxytocin for prophylaxis or induction/augmentation).	Need for additional treatment after initial PPH treatment; comparison of Misoprostol and oxytocin groups at interim analysis at one year. Secondary outcomes: mean blood loss after PPH treatment; change in hemoglobin from pre-delivery to postpartum; time to bleeding cessation; blood transfusion; side effects; acceptability for women.	Ongoing, July 2005 start date.

III. COMPLETED STUDIES

Principal investigator/ institution	Study title	Study locations	Study design	Number of Subjects	Study environs	Study objective	Outcomes and notes	Study dates
University of Missouri, University of Illinois, Chicago and Jawaharlal Nehru Medical College Richard J. Derman, MD, and B. S. Kodkany. National Institute of Child Health and Human Development grant funded	A Randomized Placebo-Controlled Trial of Oral Misoprostol for Prevention of Postpartum Hemorrhage at Four Primary Health Centers of the Belgaum District, Karnataka India	Belgaum District, Karnataka India	Randomized, double-blind, Placebo-controlled	1,620 women	Births at home or rudimentary subcenters	Misoprostol, 600 mcg oral, given in the third stage of labor after delivery of the baby by auxiliary nurse midwives.	<p>Incidence of PPH: blood loss \geq 500 ml within two hours of delivery. Secondary outcomes: incidence of delayed PPH and secondary infection (lower abdominal pain, fever, and foul discharge); transport to higher-level medical facility; use of uterotonic agents; blood transfusion; surgical intervention; maternal mortality for 42 days. Preliminary data show mean blood loss is <300 ml.</p> <p>Results show that misoprostol significantly reduces PPH \geq 500 ml, using their protocol by 47%. Data are published: Derman et al. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomised controlled trial. <i>The Lancet</i>. 2006;368:1248–1253.</p>	Study completed December 2005.
JHPEIGO/Maternal & Neonatal Health Harshad Sanghvi, MD United States Agency for International Development funded	Safety, Acceptability, Feasibility and Program Effectiveness (SAFE) Demonstration Project of Community-Based Distribution of Misoprostol for Prevention of Postpartum Hemorrhage in Rural Indonesia	Indonesia	Interventional	Intervention area: 1,360 women, comparison area: 495 women	Home births	Safety, acceptability and feasibility of misoprostol, 600 mcg oral, after informed community-based distribution during antenatal period by trained community volunteers.	<p>Incidence of PPH, misoprostol use after birth, acceptability to families, and programmatic feasibility.</p> <p>Preliminary results: women in intervention area were 24% less likely to perceive excessive bleeding, 31% less likely to need emergency referral, and 47% less likely to need emergency referral for PPH.</p> <p>Final report pending.</p>	Study completed. No dates available.

<p>Medical Research Council, UK and Population Council Gijs Walraven, Jennifer Blum, Yusupha Dampha, Maimuna Sowe, Linda Morison, Beverly Winikoff, Nancy Sloan</p>	<p>Misoprostol in the management of the third stage of labour in the home delivery setting in rural Gambia: a randomised controlled trial.</p>	<p>Gambia</p>	<p>Randomized, placebo-controlled</p>	<p>1200 women</p>	<p>Home births</p>	<p>Misoprostol, 600 mcg oral, vs. placebo for prevention of PPH where injectable oxytocics not available.</p>	<p>Postpartum hemorrhage (blood loss ≥ 500 ml; drop in hemoglobin > 2 g/dL from pre-to post-delivery. Secondary outcomes: Intermediate and severe PPH (blood loss ≥ 750 ml and $\geq 1,000$ ml); mean blood loss; side effects for women; anemia.</p> <p>Published: Walraven G., Blum J., Dampha Y., Sowe M., Morison L., Winikoff B., Sloan N. Misoprostol in the management of the third stage of labour in the home delivery setting in rural Gambia; a randomised controlled trial. <i>British Journal of Obstetrics and Gynaecology</i> 2005; 112(9):1277–1283.</p> <p>Conclusion: 600 mcg oral misoprostol is a promising drug to prevent PPH</p>	<p>Study completed.</p>
<p>John Snow International's Healthy Mother Healthy Child Project in collaboration with University of California at Berkeley, funded by United States Agency for International Development, and Venture Strategies for Health and Development Martha Campbell, Ndola Prata, and Malcolm Potts</p>	<p>Misoprostol and active management of the third stage of labor.</p>	<p>Egypt</p>	<p>Pre-post.</p>	<p>2,532 women</p>	<p>Hospital</p>	<p>Comparison of 600 mcg misoprostol oral to current AMTSL practices, including women using ergometrine, oxytocin, a combination of ergometrine and oxytocin, and those not using uterotonics</p>	<p>Measured blood loss, need for additional interventions, and main side effects.</p> <p>Results show use effectiveness of misoprostol was better than the current standard practice. In the study, 2% of women who received misoprostol developed PPH, compared to 6% of those receiving the current practice for the active management of the third stage of labour (crude OR 0.28 CI 0.17-0.47).</p> <p>More information can be accessed at: http://venturestrategies.org/projects/index.php?status=current&id=itpydn_16r4c0</p>	<p>Completed.</p>
<p>University of California at Berkeley Martha Campbell, Ndola Prata, and Malcolm Potts</p>	<p>Controlling postpartum hemorrhage after home births in Tanzania</p>	<p>Tanzania</p>	<p>Interventional</p>	<p>849 women</p>	<p>Home births</p>	<p>Misoprostol, 1,000 mcg rectal, vs. non-intervention as treatment for PPH.</p>	<p>Published in International Journal of Gynaecology and Obstetrics July 2005.</p>	<p>Study completed.</p>