New Approaches using Misoprostol for the Management of Postpartum Hemorrhage at the Community Level

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October 2015
Inequities in Access to Services

- Since 1990, 45% reduction in maternal mortality
- Leading single direct cause of maternal death globally: hemorrhage
- Risk of death far higher in resource-poor community settings
- Most cases of postpartum hemorrhage can be prevented or effectively treated

Say et al. 2014

Women & providers need access to essential life-saving health care interventions, regardless of delivery site
International Consensus: Misoprostol for PPH

- WHO Model List of Essential Medicines
  - Prevention of PPH*: 2011
  - Treatment of PPH*: 2015

- WHO, FIGO, ICM & UNCoLSC
  - Recommend misoprostol for PPH care*

- Evidence-Based Regimens
  - Prevention of PPH: 600mcg oral dose (3 tablets)
  - Treatment of PPH: 800mcg sublingual dose (4 tablets)

An important uterotonic option in community settings
Low-cost, easy to use, available in tablet form, stable at room temperature

*where oxytocin (gold standard) is not available or cannot be safely used
WHO PPH Guidelines (2012): Prevention with Misoprostol in the Community

- Support its use by lay health workers if no skilled birth attendant present
- Call for additional research of antenatal distribution of misoprostol to women for self-administration
Self-Administered Misoprostol for PPH Prevention

- **Experience from rural Uganda**
  - Advance distribution of misoprostol given to women to self-use following home deliveries
  - 600 mcg oral misoprostol vs placebo

- **Our research revealed**
  - 97% of women took the study medicine
  - No adverse events
  - High acceptability
  - Evidence of misoprostol (ie study medicine) use in clinics when oxytocin unavailable

**Empowering women to deliver their own care**

# Strategies Using Uterotonics for PPH Management at the Community Level

## Prevention

**Administration after delivery to lower incidence of PPH**

- Effectively reduces average blood loss
- Most popular approach adopted by programs

**Limitations:**

- Unclear if prevention alone “saves lives”
- Does NOT eliminate need for PPH treatment
- Few current misoprostol programs address treatment options for when women fail to respond to prophylaxis (6-16%)

## Treatment

**Administration after PPH diagnosis to stop bleeding**

- Integration into programs has been slower
- Stops bleeding in 20 minutes in 9/10 women*
- Treatment interventions often limited to referral only
- Recognition that treatment options are urgently needed in all settings where women deliver

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Integrating PPH Treatment into Models of Care

- Misoprostol can be of greatest use in settings where:
  - IV oxytocin is not feasible
  - Referral not always possible

- Barriers to using misoprostol in these settings:
  - Unknown safety of misoprostol for treatment following its prophylactic use
  - Concern about capacity of non-physician providers to diagnose & treat PPH
  - Focus on universal prophylaxis
New Approaches to PPH Treatment

Building the evidence base for misoprostol for PPH management & its safe integration into programs at the community level:

1. Treatment as “First Aid” (along with referral)
2. Treatment following Prevention
3. Secondary Prevention / Early Treatment

Considerations: Cost per woman, sustainability, provider training, exposure to side effects, potential for ‘over-use’, reaching women most in need of interventions, acceptability among providers & women, rarity of severe PPH event...
1. Treatment as “First Aid” with Referral

Assess impact of adding misoprostol given to women as ‘first aid’ to standard of care, referral to higher level facility

<table>
<thead>
<tr>
<th>Location</th>
<th>Egypt: El Beheira governorate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Attendant</td>
<td>Midwife or Nurse-Midwife</td>
</tr>
<tr>
<td>Context</td>
<td>Home births or births in Primary Health Units</td>
</tr>
<tr>
<td>Protocol</td>
<td>If PPH diagnosed: Referral + 4 tablets of misoprostol OR of placebo</td>
</tr>
</tbody>
</table>

Our research revealed

- No instances of providers using misoprostol at inappropriate time
- No serious adverse events or maternal deaths associated with misoprostol
- Side effects (shivering): short-lived & easily managed
- Transfer levels low
2. Treatment following Prevention

Key Question
Is it safe to administer a treatment dose of misoprostol for PPH after prophylaxis?
(800mcg SL + 600mcg oral misoprostol)

<table>
<thead>
<tr>
<th>Location</th>
<th>Pakistan: Chitral district (Khyber-Pakhtunkhwa province)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Attendant</td>
<td>Traditional Birth Attendant</td>
</tr>
<tr>
<td>Context</td>
<td>Home births</td>
</tr>
<tr>
<td>Protocol</td>
<td>Prophylactic dose (3 tablets) given by TBA</td>
</tr>
<tr>
<td></td>
<td>If PPH diagnosed, referral + 4 tablets of misoprostol or of placebo (TBA)</td>
</tr>
</tbody>
</table>

Our research revealed
- 800mcg SL misoprostol for treatment + 600 mcg oral misoprostol prophylaxis is safe
- No serious adverse events
- Side effects: transient, easily managed, & acceptable
- Transfers levels low

Similar trial ongoing in Afghanistan (Badakhshan) where prophylactic dose of misoprostol is self-administered.
PPH Diagnosis In Community Deliveries

Marked bedpan ~500ml to trigger diagnosis

Two cloths to help diagnose PPH (~500ml)

Visual estimation of blood loss or other clinical signs or symptoms may also trigger diagnosis in some cases
### 3. Secondary Prevention/Early Treatment

#### Compare Universal Prophylaxis to Secondary Prevention

<table>
<thead>
<tr>
<th>Location</th>
<th>India: Bijapur, Karnataka</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Attendant</td>
<td>Auxiliary Nurse Midwife</td>
</tr>
<tr>
<td>Context</td>
<td>Home births or births at health sub-centres</td>
</tr>
<tr>
<td>Protocol</td>
<td>600mcg oral misoprostol to all women OR 800mcg sublingual misoprostol only to women who bleed ≥ 350mL</td>
</tr>
</tbody>
</table>

- **Innovative early intervention approach:**
  - Uses treatment dose to provide early treatment only to women with above average blood loss

- **Several potential advantages over universal prophylaxis:**
  - Medicates fewer women
  - Reduces cost
  - Improves acceptability (fewer side effects)

- May alleviate concerns about late diagnosis at community level
Our research revealed

- Secondary prevention is no worse than (non inferior to) universal prophylaxis
- Substantially fewer women medicated – 5% compared to 99%
- Providers successfully administered both regimens & easily managed side effects
- Women willing to use misoprostol in future deliveries & recommend to others

Acceptable & feasible alternative strategy to universal prophylaxis

Practical way to address simultaneously prevention & treatment

Equips providers with a timely & fitting strategy to manage bleeding before point of emergency

Read more: Raghavan S et al, 2015, British Journal of Obstetrics & Gynaecology
Misoprostol for primary versus secondary prevention of PPH: a cluster-randomised non-inferiority community trial
What The Evidence Tells Us

- Community providers can be trained to recognize heavy bleeding & to offer misoprostol treatment.
- Low transfer rates highlight importance of treatment options as part of basic EmOC at delivery site.
- Offering misoprostol for PPH treatment at community level is safe – no serious adverse events associated with misoprostol.
- High acceptability, tolerability of side effects.
- Women can be involved in their own care.

800mcg sublingual misoprostol is a safe and effective treatment option at ALL levels of care, irrespective of prophylaxis strategies.
What Next?...

- Clear evidence-based policies and guidelines
  - Integration of misoprostol for PPH indications into national essential medicines lists
  - Development of clinical guidelines

- Train/support health providers & community health workers
  - on appropriate use & administration of misoprostol for PPH.

- Quality assured product
  - Eg European Medicines Agency approval of first misoprostol product (Hemoprostol, Linepharma) for treatment of PPH in low resource settings (2014)

- Public sector engagement
  - Scaled up models of successfully piloted misoprostol service delivery programs
Thank you on behalf of our many partners & collaborators