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Misoprostol: Saving Women's Lives in Pakistan

A Fact Sheet for Healthcare Providers

Pakistan has the highest Maternal Mortality Ratio (MMR) in South Asia, at 276/100,000 live births (PDHS, 2012-13). Nearly 16,000 women die of pregnancy and childbirth-related complications each year, i.e., a maternal death occurs every 30 minutes. Post-Partum Haemorrhage (PPH) and post abortion complications are among the common reasons for women dying during pregnancy and childbirth. PPH is the leading cause of maternal death (27%), with over 5,000 women dying each year in Pakistan (PDHS 2006-07). Abortion contributes to 11% of the MMR (Jafarey, 1992) in hospital-based studies, while the Pakistan Demographic and Health Survey (PDHS 2006-07) reports it at 5.6%. Most of the women who die are in the prime of their lives, live in rural areas and have no skilled attendance at birth (PDHS, 2006-07).

One effective strategy to address and prevent these maternal deaths is the use of Misoprostol, a simple, easy to administer medicine that has been included in the World Health Organisation's List of Essential Medicines. Recently, due to efforts made by the National Committee of Maternal and Neonatal Health and other organizations such as Mercy Corps, Misoprostol has been included in the Provincial Essential Medicines Lists of Pakistan. Due to its proven effectiveness, the WHO and other recognised technical and professional bodies have recommended its use, especially in low resource settings. Misoprostol is low cost, and can be administered orally, sublingually, vaginally and rectally.

What You Need to Do

- Train all Skilled Birth Attendants (SBAs) in the correct use of Misoprostol
- Support training of TBAs in the correct use of Misoprostol for prevention of PPH in the home setting
- Train LHWs on the role of Misoprostol in the prevention and treatment of PPH so that they can raise awareness about this among the communities where they work
- Train LHWs on advance distribution of Misoprostol to pregnant women in the eighth month of pregnancy for use during childbirth to prevent PPH
- Senior healthcare providers should train all cadres of SBAs in the correct use of Misoprostol for different reproductive health indications according to their level and skill
- Healthcare Providers should use evidence-based protocols for correct use of Misoprostol for reproductive health indications

Maternal deaths...

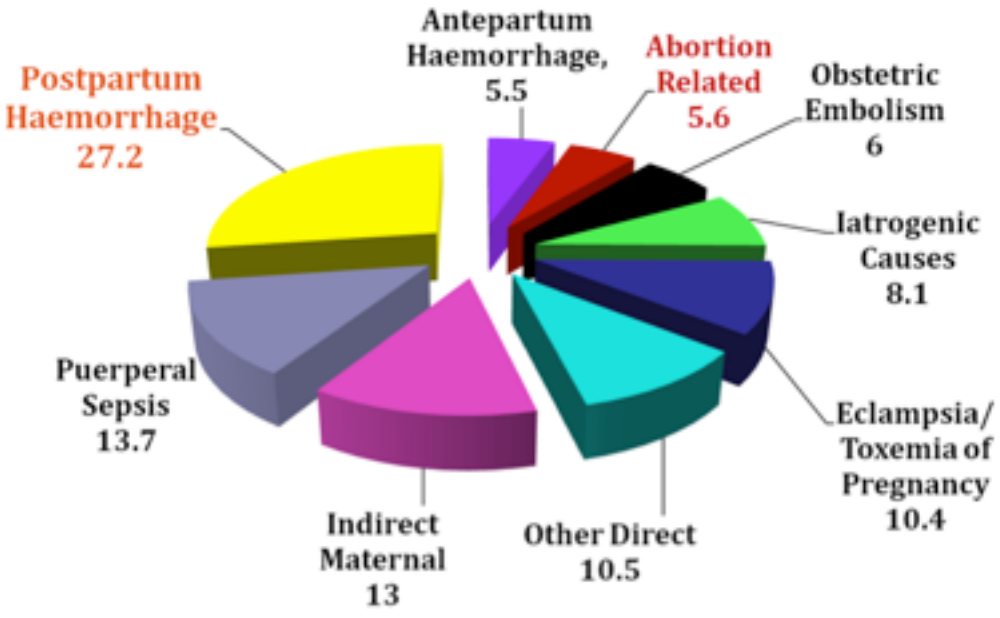
- Are mostly PREVENTABLE
- Are reflective of women's status in society
- Are indicative of the quality of health care services
- Affect families, communities, nations adversely

Post-partum Haemorrhage and Complications of Abortion

PPH, i.e., excessive blood loss after childbirth is, in 70-90% of cases, due to failure of the uterus to contract (Atony). Uterotonic medicines (Oxytocin, Ergometrine, Misoprostol) help the uterus to contract and reduce blood loss after childbirth, thereby preventing PPH.

Among other major causes of maternal death is complications arising from abortion. The incidence of abortion in Pakistan is about 900,000 per year with 200,000 women reporting to hospitals with complications (The Population Council, 2004). This incidence is believed to be significantly under-reported due to the stigma attached to abortion. Mid-level health care providers and TBAs are mostly responsible for the high levels of morbidity and mortality associated with abortions (Zaidi, 2009), and complications such as haemorrhage, infection and injury to internal organs are mainly due to lack of skills and unhygienic conditions. Therefore, training healthcare providers on the use of Misoprostol is a cost-effective way of saving women's lives.

Causes of Maternal Death



Misoprostol

All women should receive a uterotonic during the third stage of labour to prevent PPH. Oxytocin given by injection is the uterotonic of choice. However, effective administration of oxytocin may present a challenge, particularly in low resource settings. Oxytocin requires administration by a trained provider, since it needs to be given by intramuscular/intravenous injection. It has to be refrigerated to maintain efficacy.

The need for refrigeration is not only in the provider's clinic; the cold chain has to be maintained from point of manufacture to wherever it will eventually be used. In a country such as Pakistan, the majority of the population resides in remote rural areas and temperatures are often high in summer. There are frequent power breakdowns, and even if this is not the case, refrigeration for storage or for transportation may not be available or providers may not be aware of the need for proper storage. Therefore, in settings where giving oxytocin is not feasible or where it is not available, Misoprostol, a synthetic analogue of Prostaglandin E2, has emerged as an alternative uterotonic.

Misoprostol is also useful for treating abortion-related complications. It is an alternative to Dilatation and Curettage (D&C), which, while still in practice, is recommended (by WHO) to be replaced by vacuum aspiration techniques or medications such as Misoprostol.

Safety Profile

Misoprostol has been available in the market under the brand name Cytotec for the treatment and prevention of gastric ulcers since 1985. Millions of individuals have used it in over 80 countries worldwide including Pakistan.

Misoprostol:

- Has an excellent safety profile
- Is extremely effective
- Has minimal, if any, side effects
- Is ideal for prophylaxis and treatment of PPH because it is:
  - Inexpensive;
  - Stable at room temperature. No need for refrigeration;
  - Administered in tablet form, with no need for injections; and
  - Unskilled providers (TBAs) can be easily trained in its use.

Reproductive Health Indications of Misoprostol

- Prevention and Treatment of PPH
- Treatment of incomplete and missed abortion
- Legal/therapeutic indications for termination of pregnancy
- Cervical ripening prior to procedures such as hysteroscopy, insertion of Intra Uterine Contraceptive Device (IUCD), endometrial sampling, etc.
- Induction of labour

Misoprostol: Routes of Administration

Route	Onset of Action	Time to Peak Concentration	Duration of action
Oral	8 Minutes	30 Minutes	2 Hours
Sublingual	11 Minutes	30 Minutes	3 Hours
Vaginal	20 Minutes	75 Minutes	4 Hours
Rectal	10 Minutes	20-65 Minutes	4 Hours

Note: Bioavailability varies between each route, thus the correct dose MUST be used for the route chosen

Side effects

Misoprostol is generally well tolerated. Side effects include shivering, nausea, vomiting, diarrhoea and fever. These are usually transient, generally well tolerated and require symptomatic management in most cases. It has no significant effects on lungs or blood vessels so can be used in asthmatics.

Contraindications

None, unless previous known allergy to prostaglandins.

Efficacy

- When used for PPH prevention, it can reduce incidence of up to half the initial rate; it also reduces the need for additional interventions and number of referrals.
- When used to treat abortion-related complications, Misoprostol is:
  - 95-100% effective in treatment of incomplete abortion
  - 80-90% effective for treatment of missed abortion between 4-12 weeks gestation
  - 90-100% effective for treatment of missed abortion between 12-24 weeks gestation

Advantages of Misoprostol over Oxytocin

	Misoprostol	Oxytocin	Ergometrine
Stability	Heat Stable	Not heat stable	Not heat stable
Storage	Stable at room temperature	Requires refrigeration at 2-8℃	Requires refrigeration at 2-8℃ and storage in dark closed containers
Administration	Skilled provider not necessary	Requires skilled provider	Requires skilled provider
Route of administration	Tablets can be given orally, vaginally and rectally	Needs to be administered by intramuscular/ intravascular injection	Needs to be administered by intramuscular/ intravascular injection
Suitable for home births	Yes	No	No
Serious side effects	No	No	Yes

Misoprostol: Recommended Indications and Dosage 2012

(Check for updates at www.figo.org)

Indications	Dosages
	Pregnancy - First Trimester
Missed Abortion	800 ug vaginal*x 3 hourly (maximum 2 doses) or 600 ug sublingual** x 3 hourly (maximum 2 doses)
Incomplete Abortion***	600 ug oral single dose or 400 ug sublingual single dose
Therapeutic/Legal Induced Abortion	800 ug vaginal x 3 hourly (maximum 3 doses within 12 hours) or 800 ug sublingual x 3 hourly (maximum 3 doses within 12 hours)
Cervical Ripening Pre Instrumentation	400 ug vaginal 3 hours before procedure or 400 ug sublingual 2-3 hours before procedure
Pregnancy - Second Trimester (Care with previous uterine scar and caesarean section)	
	Intrauterine Foetal Death
13-17 weeks	200 ug vaginal x 6 hourly (maximum 4 doses)
18-26 weeks	100 ug vaginal x 6 hourly (maximum 4 doses) (use half the dose if previous C-Section)
	Therapeutic Legal Induced Abortion
13-26 weeks	400 mcg vaginal x 3 hourly (maximum 5 doses) (use half the dose if previous C-Section)
Pregnancy - Third Trimester (use correct dose- overdose can lead to complications)	
	Intrauterine Foetal Death
27-43 weeks	25 ug vaginal x 6 hourly Or 25 ug oral x 2 hourly (Do not use if previous caesarean section)
	Live Foetus
Induction of labour	25 ug vaginal x 6 hourly Or 25 ug oral x 2 hourly (Do not use if previous caesarean section)
	Post-Partum
Prevention of PPH	600 ug oral single dose
Treatment of PPH	800 ug sublingual single dose

* Vaginal – inserted deep into the vaginal vault. Tablets do not need to be moistened

**Sublingual – place under the tongue. If not completely dissolved in 30 minutes, swallow the remainder
*** Leave to work for 1-2 weeks unless excessive bleeding or infection
ug= microgramme

WHO and Misoprostol

In May 2011, the World Health Organisation moved Misoprostol from its Complementary List to the Core Model List of Essential Medicines for prevention of PPH. WHO stated that: "….[N]ew evidence submitted showed that Misoprostol can be safely administered to women to prevent PPH by TBAs or assistants trained to use the products at home deliveries (2011)."

The WHO also added Misoprostol to its List of Essential Medicines in March 2009 for treatment of incomplete and missed abortion. It was added to the WHO Complementary List in 2005 for termination of pregnancy (together with Mifepristone; where legally permitted and culturally appropriate) as well as for induction of labour.

As for its use by women themselves, a study in Pakistan has shown that it is feasible for rural women to self administer with a little guidance and information. WHO and FIGO suggest further research before recommending self-administration.

"… in home births without a skilled attendant, Misoprostol may be the only technology available to control PPH." - International Federation of Gynaecology and Obstetrics (FIGO), the International Confederation of Midwives (ICM), etc.

Action Needed to Promote Use of Misoprostol for Prevention and Treatment of PPH, and Prevention and Treatment of Post Abortion Complications

- Senior healthcare providers should train all cadres of Skilled Birth Attendants (SBAs) in the correct use of Misoprostol for different reproductive health indications according to their level and skill.
- Healthcare Providers should use evidence-based protocols for correct use of Misoprostol for reproductive health indications.
- SBAs should support training of Traditional Birth Attendants (TBAs) in the correct use of Misoprostol for prevention of PPH in the home setting.

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