INTRODUCTION OF MISOPROSTOL INTO THE NIGERIAN MARKET: CHALLENGES

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INTRODUCTION

- Nigeria has one of the highest maternal mortality ratios in the world.
- The national average for MMR is 1000/100,000 live births (with wide regional disparities)
- The major causes of deaths are post partum haemorrhage (PPH) (20-30%), eclampsia (23%), sepsis (17%) and unsafe abortion (25-40%).
- Uterine atony accounts for over 70% of deaths from PPH.
- All of these causes of maternal deaths are preventable.

POST PARTUM HAEMORRHAGE (PPH)

Definition

- Blood loss after birth in excess of 500ml or of such magnitude as to alter the haemodynamic state of the mother irrespective of the quantity of blood loss.

Types of PPH

- Primary–within the first 24hrs of delivery.
- Secondary- after the first 24hrs and within the first 6 wks of delivery.

Risk Factors for PPH

- Uterine atony.
- Little or no access to proper & emergency medical services.
- Lack of skilled health providers.
- Delay due to inefficient transport system.
- High incidence of pre-existing anaemia.
- Significant risk factors for PPH were: prolonged second and third stages of labour, non-use of oxytocics after delivery, grand multiparity, previous PPH and primigravidity (1).

Contribution of Various Obstetric Causes of PPH in Nigeria

- Uterine atony (85% - 90%) – Failure of the uterus to contract after delivery;
- Genital tract trauma(10%) – vaginal, cervical and perineal lacerations, etc; and
- Clotting defects (2%).

Complications of Postpartum Hemorrhage

- Orthostatic hypotension;
- Anemia and fatigue, which may make maternal care of the newborn more difficult;
- Postpartum anaemia which increases the risk of postpartum depression;
- Blood transfusion with its associated risks may be necessary;
- In the most severe cases, haemorrhagic shock may lead to anterior pituitary ischemia with delay or failure of lactation (i.e. postpartum pituitary necrosis); and
- Maternal death

PREVENTION OF PPH

Active Management of the Third Stage of labour (AMTSL): This includes administration of uterotonics (oxytocics) within 1 minute of birth , early cord clamping & cutting and controlled traction to deliver the placenta (with counter-traction on the uterus).

Prevention of PPH Using Uterotonic Drugs

- Administration of oxytocin immediately after childbirth is probably the single most important intervention to prevent PPH.
- A woman receiving a uterotonic delivers placenta faster & less likely to require manual removal of placenta.

Challenges Associated With the Use of Traditional Oxytocic Drugs (Oxytocin and Ergometrine)

- Cost – training of health workers for safe administration/accessories;
- Storage – oxytocin and ergot derivatives are thermolabile & must be refrigerated to remain effective;
- Safe handling – parenteral administration requires skilled personnel ;
- Safety – Ergot derivatives are contraindicated in hypertensive women and can cause severe headache, convulsion & even death;
- Risk of water intoxication from rapid infusion with oxytocin due to its antidiuretic

properties;

- ❖ Association of intrapartum oxytocin with neonatal jaundice; and
- ❖ Presence of many fake & substandard brands in the market because of their popularity.

THE WAY FORWARD?

Misoprostol: The Life-Saving Prostaglandin Analogue

- ❖ Misoprostol is an E_1 prostaglandin analogue:
  - o It binds selectively to EP2/EP3 receptors of the myometrium - uterotonic property;
  - o It has a fast onset of action – peak plasma levels of misoprostol acid achieved within 12 (± 3) minutes;
  - o It is thermostable and remains effective even in tropical climate;
  - o It is relatively affordable; and
  - o It has multiple routes of administration including:
    - ▪ Rectal
    - ▪ Vaginal
    - ▪ Buccal /sublingual - rapid onset.
- ❖ Pharmacokinetics:

o Bioavailability: it is extensively absorbed.

o Metabolism: de-esterified to misoprostol acid, then to prostaglandin-F analogues.

o Half life: 20–40 minutes.

o Excretion: renal (80%) and faecal (15%).

o Mean plasma concentrations of misoprostol acid is reached within a short time with oral, rectal, and vaginal administration (2).

o Rectal misoprostol may have a higher bioavailability in the third stage of labour , because the rectal mucosa is moister and thus enhances absorption. When misoprostol 600 µg is administered in the third stage of labour, peak levels higher than those noted above are achieved by both the oral and rectal route (3).

- ❖ Benefits of Using Misoprostol

o Incidence of manual removal of placenta is less than with other oxytocic agents due to their different uterotonic effects. Ergometrine induces tonic uterine contractions while misoprostol induces rhythmic uterine contractions (4).

Ergometrine versus Misoprostol (5, 6)

- ❖ The use of syntometrine is contraindicated in hypertensive patients as ergometrine stimulates vasoconstriction and causes hypertension.
- ❖ In pre-eclamptic patients, it may cause headaches, convulsion and even death.
- ❖ Misoprostol does not cause hypertension and is associated with a 55–60% reduction in the incidence of hypertension when compared with syntometrine. Misoprostol is also a potent vasodilator. Its vasodilatory effects appears to involve arterioles, pre-capillary sphincters and post capillary venules, leading to a decrease in the total peripheral resistance and a consequent fall in blood pressure. It reduces the mean arterial pressure and systemic vascular resistance and has a modest and transient antihypertensive effect in patients with essential hypertension. Thus Misoprostol is a suitable oxytocic agent in hypertensive and pre-eclamptic women undergoing vaginal delivery while ergometrine is contraindicated in women with pregnancy-induced hypertension (7).

Dosage

- ❖ For prevention of PPH: 600 µg (3 tablets) to be taken orally.
- ❖ For treatment of PPH: 1000 µg (5 tablets) to be taken orally/administered rectally.

Side Effects

- ❖ Misoprostol-related pyrexia (usually 38-39°C). No treatment other than paracetamol is needed;
- ❖ Shivering; and
- ❖ Headache

A toxic dose has not been established. Cumulative doses of up to 2,200 µg every 12 hours have been administered without serious side effects. Unlike PGE_2 and PGF_{2a}, Misoprostol does not cause bronchospasm and thus poses no theoretical risk in asthmatics (8).

CONCLUSION

Misoprostol:

- ▪ Is uterospecific;
- ▪ Is stable at ambient temperature - No need for special storage;
- ▪ Effective – stops PPH in minutes;
- ▪ Has versatile routes of administration - can be administered orally, bucally, sublingually and rectally;
- ▪ Main oxytocic agent in hypertensive and pre-eclamptic women - most suitable and safe for women with high BP in pregnancy;
- ▪ Approved and vailable in Nigeria – Listed in the WHO essential drug list.

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