THE USE OF MISOPROSOL IN THE PREVENTION AND MANAGEMENT OF POST PARTUM HEMORRHAGE IN POOR RESOURCES SETTINGIN EBOONYI STATE

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Abstract:

This study examines the use of Misoprosol in the prevention and management of Post Partum Hemorrhage in poor resources settings in Ebonyi State. A survey design was used and the sample size was 526respondents made up of 263 midwives and 263 Public Health Workers drawn from Federal Teaching Hospital Abakaliki, General Hospital and Health Centers across Ebonyi State. The instrument for data collection was 20- item structured questionnaire which was based on the three research questions that guided the study. The reliability index of the instrument was at 0.76 coefficience. The hypothesis was tested at 0.05 alpha level using t-test. The results of the study showed that Hemorrhage is a leading and deadly cause of maternal death in developing countries. The 2012 World Health Organization guidelines for the prevention and management of Post Partum hemorrhage (PPH) recommended oral administration of Misoprosol by Community Health Workers, Traditional birth Attendants and Ante Natal care providers. In view of the above, the paper recommends that Government should make Misoprosol available in all the Hospitals and Health Centers among other things.

Keywords:Misoprosol, Prevention/management and Post partum Hemorrhage.

Introduction:

The lifetime risk of dying from pregnancy or delivery/childbirth ranges from about one in 39 in sub-Sahara Africa to 1:3800 in developed countries (Shelton, et al., 2012). They stated that hemorrhage continues to be a leading cause of maternal death in developing countries and the predominant cause in Africa (34%) and Asia (31%).Post Partum hemorrhage (PPH) is defined as blood loss > 500ml occurs in approximately 6% of deliveries globally and severe PPH (> 1000ml) in an additional 1.8% with variation across regions of the world (Berkele, 2010). PPH is also conceptualized as excessive bleeding into from the genital tract with a perceived blood loss of 5000-1000ml in the absence of clinical signs of cardiovascular instability that deteriorates the patient's conditions, occurring from

the third stage of labour till six weeks post delivery (Lynch, Kieth, Laloonde and Karoshi, 2006). This can occur in the first 24 hours of delivery (early or primary PPH), or after 24 hours but within six weeks of delivery (late or secondary PPH) (Lynch et al, 2006).

Medical intervention of various high-impact effectively prevent PPH. Active management of third stage of labour, using oxytocin as a preferred uterotonic is prominent among them (Marshal and Raynor 2014). Its administration needs the assistance of skilled birth attendant (SBA) and therefore, it is not available to women having unattended home births, either by choice of lack of access to SBAs or distant level of care in community or poor resource setting.

Misoprosol, an oral prostaglandin E_1 analogue that can be administered immediately after delivery offers an important alternative for PPH prevention in low or poor resource settings and at home births where oxytocin is not available or where its use is not possible. It requires no injection, supplies of skilled provider for administration. It does not need refrigeration and hence, can be stored and provided where there is no electricity. These factors enables the programme for the prevention of PPH using misoprosol to achieve potentially high coverage and use especially, by women who reside at a distance from health facility

There is compelling evidence that misoprosol is both safe and effective (Ministry of Health, 2011). This body of evidence led the World Health Organization (WHO) to amend its model list of essential medicine in March, 2011 to include misoprosol for the prevention of PPH in settings where oxytocin is not available or cannot be safely used (Berkely, 2010).

Hence, the 2010 WHO guideline for the prevention and management of PPH recommended oral administration of misoprosol by community health workers (CHWs) including the traditional birth attendants (TBAs) directly by pregnant women for self-administration at home (WHO, 2012). It is noted that this intervention is cost-effective and concluded that the largest gains in prevention against PPH were realized by the poor, the illiterate and those living in remote areas.

HIGHLIGHTS OF MISOPROSOL

The advent of Misoprosol has led to many innovative research as well as controversy. Currently, its role in management of PPH, induction of labour, cervical ripening and termination of pregnancy cannot be over-emphasized.

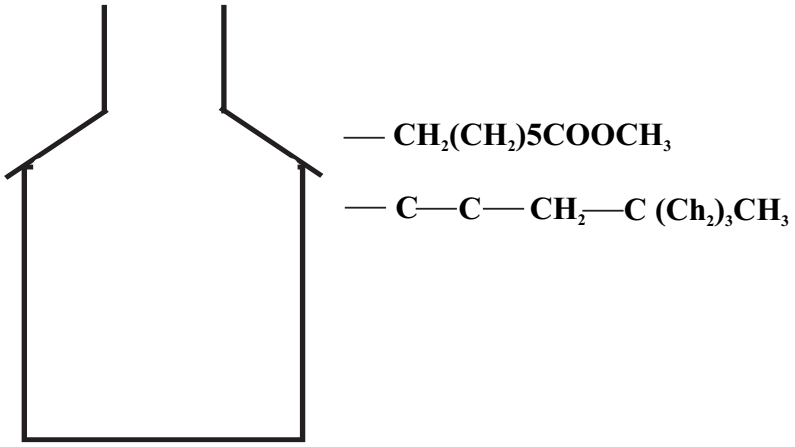
Initially, the drug was approved by the United States Food and Drug Administration (FDA) in 1988 for oral administration for the prevention and treatment of peptic ulcler associated with the use of non-steroidal anti-inflammatory drugs (Lynch et al., 2006). Obstetricians and Gynaecologists have keen interest in it since 1990 and because of its multiple uses; it has been ascribed one of the most important medications in obstetrical practice. As of 2005, its use for pregnant women was not approved by FDA and manufacturers (Lynch et al, 2006).

Concept of Misoprosol

Misoprosol is a synthetic PGE analogue (Lynch et al.,2006).

Its natural one is not orally sustainable and it is not stable in acid media and not suitable for parenteral use because it has a quick degradation in the blood.

The synthetic misoprosol is produced by uttering the chemical structure of the naturally occurring compound in order to make it orally stable and clinically useful. It is manufactured as oral tablet of 200µg. Its chemical formulae is; **$C_{22}H_{3}80_{5}$(+)** methyl (13E-11; 16-dihydroxy-16-methyl-G-O+O-prost-13enoate.



Chemical structure of misoprosol
Source: (Lynch et al., 2006)

Doses, Routes and uses of Misoprosol

400-500µg (rectally, orally): for the prevention of PPH and conduct of 3rd stage of labour.

600µg orally (sublingually): for active management of third stage of labour, PPH.

600µg (intravenously) : for the management of 3rd stage of labour
800µg (vaginally); for the management of PPH (Lynch et al, 2006)

Uses of Misoprosol

Misoprosol in the first trimester

For the first trimester medical termination of pregnancy, misoprosol is used extensively together with mifepristone or methotrexate e.g administration of

600μg of rectal mifepristone followed by 48 hours later by 400μg of oral misoprosol resulted in 91-97% complete abortion (Lynch et al., 2006). The authors opined that misoprosol has been used alone for medical termination of pregnancy with variable efficacy. It can be use as a cervical primary agent before ccervical aspiration or before surgical abortion.

Misoprosol in the second trimester

Indications for termination of pregnancy in second stage include chromosomal and structural fetal abnormalities e.g. on the face. Surgical evaluation of the uterus is being practiced in some centers. Intra-amniotic PGE infusion, oxytocin infusion and vaginal PGE_2 were practiced before the introduction of misoprosol.

Intravaginal misoprosol in the dose of 400 mg every 3 hours is more effective and associated with fewer side effects and shorter drug administration to abortion interval than the aforementioned. Also, vaginal misoprosol can still be used for induction of labour during second trimester between 50 and 80μg.

Misoprosol in the Third Trimester

Misoprosol is cost effective and safe alternative for induction of labour at term (Lynch et al., 2006). It has been found via randomized trials that it is more effective than placebo and other prostaglandins and it is associated with high rate of vaginal delivery within 24 hours, a shorter induction to delivery interval and significantly lower caesarian section (C/S) rates. It is not recommended for induction in cases of previous C/S because it is associated with higher frequency of disruption of previous uterine incision scars compared to 0-2% patients with vaginal birth. Equally, it can still be used for induction of labour after fetal death because there are adverse effects of uterine hyperstimulation on the fetus. The dose 50μg is given every 12 hours but higher dose is given in second trimester and early in the third trimester. Misoprosol is suitable for both prevention and treatment of PPH because of its uterotonic effects. Other uses of misoprosol include: intra-uterine insemination and hysteroscopy and cervical pregnancy though rare.

Advantages of Misoprosol

1. Stable in ambient temperature
2. It has long-shelf life
3. It is of low cost. This made it a central focus of research in obstetrics and gynaecology for 2 years.
4. It is absorbed rapidly via oral route but can still be use buccally (sublingually, rectally, vaginally but not parenterally).

Adverse effects: skull defects, cranial nerve palsies, facial malformations and club defects when used during first trimester of pregnancy (Lynch et al., 2006). Common effects include diarrhea and abdominal cramps, nausea, flatulence, chills, shivering

and fever, all of which are dose-dependent (Lynch et al., 2006). Congenital abnormalities associated with fetal death when used in termination of pregnancy.

Toxic effects: Not yet known as a pregnant woman has tolerated a cumulative dose up to 2200mg administered over a period of 12 hours without any serious effects (Lynch et al., 2006).

Pharmacokinetics, Physiology and Teratogenicity profile of Misoprosol

Khan (2013) defined pharmacokinetics as the movement of a drug into, through, and out of the body- the time course of its absorption while according to the author, physiology of drug e.g misoprosol is the science of the functioning of that drug whereas its teratogenicity is the ability of the drug to produce deformity in the developing embryo or in the individual who has taken such drug.

Misoprosol is absorbed widely and undergoes de-esterification to misoprosol acid which is responsible for its chemical activity and it can be detected in plasma after oral administration, the peak level of misoprosol acid is reached within 1-3 minutes and in plasma state was achieved within 2 days.

The bioavailability of misoprosol is decreased with food or antacids. It is primarily metabolized in the liver and less than 1% of active metabolite is excreted in urine (Lynch et al., 2006). Patients with hepatic disease should receive decreased doses and so also patients with renal diseases requiring dialysis.

Pharmacokinetic studies in pregnant women show that sublingual misoproson use 1st trimester of pregnancy produce early and higher peak plasma concentration than vaginal or rectal misoprosol resulting in early uterine tones (Lynch et al., 2006), e.g. intra-uterine pressure rises on average of 25 minutes after the oral administration and 21 minutes after vaginal administration.

Objectives of the study

Generally, the objective of the study is to find out the uses of Misoprosol in the prevention and management of Post Partum Hemorrhage (PPH) in poor resource setting in Ebonyi State. Specifically the objective of the study is to

1. Find out the condition where Misoprosol is used in the preventive or therapeutic purpose of PPH and its management.
2. Ascertain the choice of Misoprosol over other uterotonic agents in the prevention and management of Post Partum Hemorrhage (PPH) in poor resource settings in Ebonyi State.
3. Identify the roles of midwives in the use of Misorosol over other uterotonic agents in the prevention and management of PPH in poor resource settings in Ebonyi State.

Research questions

1. What are the conditions Misoprosol is used.
2. Why is Misoprosol preferred to other preventive agents.
3. What are the roles of midwives in the administration of Misoprosolfor the

prevention and management of poor partum haemorrhage.(PPH)

Hypothesis: There is no significant difference in the mean ratings of midwives and other public health workers in the use of Misoprosol instead of other uterotonic agents.

Methodology: The research design for the study is descriptive survey design. The sample of the study comprised 526 respondents, made up of 263 midwives and 263 public health workers in Ebonyi State. Structured questionnaire was developed and used for data collection; patterned in form of modified four point Likert rating scale of Strongly agree 4 points, Agree 3points, Disagree 2points and Strongly disagree 1point. The instrument was subjected to face and content validation, which yielded a reliable coefficient of 0.76. Data collected were analysed using mean, standard deviation and t-test statistic of significant difference between sample means. A criterion mean of 2.5 was used for determining the acceptable value for each question.

Results

The presentation of data was done following the research questions and hypothesis that guided the study as follows:

Research Question 1: What are the conditions Misoprosol is used

Table: Mean and Standard deviation rating on the condition, Misoprosol is used

S/N	Items	$\overline{X}$	SD	Decision
1	After a woman delivers a baby in a setting, where it is culturally difficult to measure blood loss	3.02	1.22	Agree
2	where a woman delivers at home for cultural/family reasons.	2.65	1.21	Agree
3	when the clients blood loss is determined before its administration.	2.76	1.20	Agree
4	it is used during conception/early pregnancy.	2.01	1.16	Disagree

From the data in table 1 above, the respondents agreed to the statements on the condition for using Misoprosol, except item 4 with mean response of 2.01 which is below 2.5 acceptable benchmark. This signifies disagreement.

Research Question 2:

Why is Misoprosol preferred to other uterotonic agents in the prevention and management of Post Partum Haemorrhage (PPH) at community base level.

Table 2: Mean and standard deviation ratings on preference of misoprosol to other preventive agents.

S/N.	ITEM	$\overline{X}$	SD	Decision
1.	Proved to be more active in the management of third Stage of labour	2.56	1.28	Agree
2	There is significant reduction in duration of third stage labour using misoprosol.	2.61	1.32	Agree
3	It does not require injection supply unlike other types	3.17	1.42	Agree
4	It does not require skilled health provider (unskilled birth attendants can use it).	3.46	1.44	Agree
5	Illiterate women with minimal training can administer misoprosol effectively.	2.76	1.29	Agree
6	Misoprosol is more adaptable and used at poor resource Setting, and has reduced referrals to health facilities.	3.12	1.40	Agree
7	Rectal misoprosol can control PPH.	2.64	1.56	Agree
8	It reduces the need for additional uterotonic agents during caesarean delivery	2.51	1.61	Agree
9	Misoprosol does not require electricity or refrigerator for storage hence it is the best.	2.81	1.77	Agree

The data in table 2, above reveal that the respondents were unanimous in their agreement on why misoprosol is preferred to any other uterotonic agents in the prevention and management of PPH.

Research Question 3:
What are the role of midwives in the use of Misoprosol for the prevention and management of PPH

Table 3: Mean and standard deviation rating on role of midwives in the use of Misoprosol

S/N	ITEM	$\overline{X}$	SD	DECISION
1	Educate, Traditional Birth Attendants, family members and Friends on the use of misoprosol during pregnancy and labour	3.01	1.38	Agree
2	Carrying out advocacy programme to those involve in delivery of babies at the community level on the risk factors of PPH.	2.84	1.32	Agree
3	Visit client centers to ensure that misoprosol is properly covered in a container and used when needed.	3.16	1.41	Agree
4	Ensure the use of misoprosol is integrated in the curriculum of Midwifery and nursing school.	2.64	1.56	Agree
5	Ensure that every skilled birth attendant will have misoprosol and knows how to administer it.	2.71	1.26	Agree
6	Distribute Misoprosol to health centers	1.15	1.18	Disagree

The data in table 3 show that out of the six items, only the 6th item has a mean of 1.15 and SD of 1.18. This implies that the respondents disagreed with the item while they agreed with the other five items with mean range of 2.64 to 3.16.

Hypothesis 1
There is no significant difference in the mean ratings of midwives and other public health workers in the use of Misoprosol instead of other uterotonic agents.

Table: 4
Result of t-test analysis of difference in the mean ratings of midwives and other Public Health Workers on the use of Misoprosol

Respondent	Number	Mean	SD	DF	Tcal	Tcrit	Decision
Midwives	263	2.61	1.18	524	1.31	1.96	Null Hypothesis Accepted
Other Health Workers	263	2.61	1.18				

No significance, at 0.05 level of significance in table 4, the calculated-t (1.31), is less than the critical-t (1.96), thus leading to acceptance of the null hypothesis that there is no significant difference in the mean ratings of the midwives and other Health Workers in the use of Misoprosol instead of other Uterotonic agents.

Discussion

The data analyzed revealed that, the conditions Misoprosol is used include, after a woman delivers a baby in a setting where it is culturally difficult to measure the blood loss. This is in agreement with Lynch, Keith, Laoude and Keroshi (2006), who stated that, a prophylactic dose of 600 misoprosol is given after delivery of the baby in settings where it is culturally difficult to measure the blood loss after delivery and in places where for cultural or other reasons, women deliver at home etc. it was also discovered that Misoprol is preferred to other Uterotonic agents because it proves more active in the reduction in duration of third stage labour, and can be used in poor setting among the illiterate women with a minimal training. This is in conformity with the assertion of Lynch et al (2006), Berkeley (2010), Sheldom, Blum, and Winkoff (2012),that the use of Misoprosol especially the oral one is effective and can significantly reduces the duration of third stage of labour. It does not require injection, skilled provider or refrigerator, hence there is no need for electricity. That is why it is mostly preferred and used than injectable oxytocin and ergometrrine. The result of the analysis also identified the roles of the Midwives in the use of Misoprosol to include; educating the traditional birth attendants, carrying out advocacy programmes at community level for rural women on the risk factor of PPH, ensuring that Miisoprosol is available and kept at the correct temperature among other thing.

Lynch et al (2006) identification of the roles of the Midwives which agreed with the findings of this study that the Midwives should expose all the people involved in the delivery of babies at the community level about the risk factors of PPH. Also visit client's homes/ centers to ensure that Misoprosol is properly covered in a container and used when needed, etc.

The hypothesis tested showed no significant difference between the mean ratings of Midwives and other health workers on the use of Misoprosol instead of other Uterotonic agents. This implied that both the midwives and public health workers preferred to use Misoprosol, which means it is better and more effective than the other agents

Conclusion:

It is of primary important to prevent or manage Post Partum Hemorrhage (PPH) at a primary or secondary levels occurring at low-resources setting (community level). In any programme embarked to reduce maternal mortality to its barest minimum with misoprosol (Lynch et al, 2006). Mostly the deliveries in developing countries occur at poor resource setting/home in the presence of unskilled birth attendants.

Currently, the vital nature, safety and efficiency of the use of misoprosol are well established in many hospital settings. However, the most significant impact of misoprosol is felt at low-resource setting at a household level, where most deliveries take place (Lynch et al, 2006). Some studies have tested such technology in home

births and all of them produced encouraging results. Therefore, the use of misoprosol in the prevention and management of Post Partum Hemorrhage (PPH) in poor-resource setting should be advocated for since it will take all women many decades to receive skilled care (attention at delivery) in their homes. Equally, misoprosol has the potential to control Post Partum Hemorrhage (PPH) and reduce maternal mortality at community- based level. No wonder the World Health Organization (WHO) has added it in its list of essential medicines as its use for home birth is a strategy to achieve a greater protection from Post Partum Hemorrhage (PPH).

Recommendations

The following recommendations were made based on the pertinent issues discussed in this study:

1. There should be appropriate dissemination of information about the use of misoprosol in the prevention and management of Post Partum Hemorrhage (PPH) PPH especially in poor- resource settings in Ebonyi State.
2. The midwives should embrace health visits to respective homes where babies are delivered to ensure the adequate use of misoprosol.
3. The use of misoprosol should be limited to people that know how to use it with particular attention paid to the route and dosage of administration.
4. The Government should make it available for use at the community level.
5. The drug should not be distributed by any lay health workers rather by trained health workers or ANC provider or TBAs and community health workers and other community health personnel such as family planning, field workers or community drug keepers who have been trained.
6. Programmes that educate women and families for self- administration of misoprosol appears to be safe because it leads to low rate of erroneous early administration.

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