

EVALUATING FACTORS ASSOCIATED WITH FAILED INDUCTION OF LABOUR IN PATIENTS UNDERGOING INDUCTION WITH TITRATED ORAL MISOPROSTOL AT HARARE HOSPITAL MATERNITY

BY

DR BISMARK MATEVEKE R0021130

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Abbreviations

BC	Before Christ
BMI	Body mass index
CTG	Cardiotocograph
EDLIZ	Essential Drugs List and Standard Treatment Guidelines in Zimbabwe
IOL	Induction of labour
IUD	Intrauterine death
JREC	Joint research and ethics committee
MPA	Misoprostol acid
MRCZ	Medical research council of Zimbabwe
MU	Montevedio units
NSAID	Non steroidal anti inflammatory drug
PIH	Pregnancy induced hypertension
RCOG	Royal College of obstetricians and gynecologists
TVS	Transvaginal ultrasound
UK	United Kingdom
US FDA	United States Food and Drug Administration

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1.1 INTRODUCTION

Induction of labour is the artificial stimulation of uterine contractions before the spontaneous onset of labour, in order to achieve vaginal birth, when the risks of continuation of the pregnancy outweigh the benefits. This is usually preceded by a process of cervical ripening involving softening, thinning, and partial dilatation of the cervix¹. The rates of labour induction vary widely with a reported 25% incidence in developed countries, the rates for developing countries being generally lower. The WHO global survey on maternal and perinatal health showed an overall rate of induction of labour of 9.6% with the highest rates being found in Asian and Latin American countries (Sri Lanka 35.5%) and the lowest rates in African countries (Niger 1.4%)². In 2004 and 2005, 1 in 5 deliveries in the UK was as a result of induction of labour³. In the United States the rates of labour induction have increased from 10.9% of all pregnancies in 1989 to 20.6% in 2003. At Harare Hospital Maternity the rate of induction of labour is reported at around 7% to 10%²⁶.

Induction of labour based solely on maternal request, to shorten pregnancy duration and time the birth of the baby, with no associated fetal or maternal medical indications, has been reported in developed countries⁴.

Induction of labour can be achieved through various non pharmacological (mechanical) and pharmacological methods. The mechanical methods include use of a traction catheter (balloon), extra amniotic saline infusion, osmotic dilators like hygroscopic laminaria and amniotomy .There is however insufficient evidence to assess their effectiveness against placebo or no treatment but they tend to be associated with a lower risk of uterine hyperstimulation, fetal heart rate abnormalities and incidence of caesarean section compared with pharmacological methods. Pharmacological methods include the use of

oxytocin and prostaglandins mainly, though there are other novel approaches employing mifepristone, relaxin, and oestrogen and nitric oxide donors like glyceryl trinitrate. Misoprostol is now being widely used *off label* for cervical ripening and induction off labour due to its low cost, availability and uterotonic activity. New label for use of misoprostol in pregnancy for inducing uterine contractions was approved by U.S FDA in 2002.

Many different routes of administration (rectal, vaginal, sublingual and oral) have been evaluated. The oral route has been the subject of many trials and different regimes have been employed. The WHO recommends a dose of 25microgrammes orally every 2hours (doses between 20 to 50 microgrammes accepted as safe)². At Harare Hospital Maternity unit the recommended labour induction regime which had been in use since the introduction of oral misoprostol is tabled below:

Table1: Harare hospital maternity oral misoprostol regime (during the study period).

PARITY	LOADING DOSE	HOURLY DOSE
Para O	30ml [*]	20ml [*]
Para 1 and 2	20ml [*]	15ml [*]
Para 4(with caution)	15ml [*]	15ml*

200microgrammes misoprostol dissolved in 200ml saline to make a 1microgrammes/ml solution

The doses are stopped when contractions start.

At Parirenyatwa Hospital Mbuya Nehanda Maternity Home, different titrated oral misoprostol regimes for labour induction were employed between the different obstetric firms with the initial bolus 1mg/ml solution ranging from 30ml to 100 ml orally followed by hourly 20ml to 50ml solutions until the start of contractions. This was then harmonised for

all obstetric firms to a regime starting with an initial bolus of 50mcg then subsequently 25mcg hourly orally regardless of parity with caution being taken for para 4(and above).

The sixth essential medicines list and standard treatment guidelines for Zimbabwe (*EDLIZ*) 2011 edition recommends oral misoprostol 25microgrammes every 4hours to a maximum of 6 doses for labour induction⁵. Currently the labour ward manual for central, provincial and district hospitals was released in 2013 (published 2012) and came up with the following recommendations for labour induction with oral misoprostol:

- Single dose should not exceed more than 50microgrammes
- Regime a) give 50microgrammes orally swallowed with some water every 4hours (maximum 4 doses)
- Regime b) give 20mls of a 1microgrammes/ml solution(200mg tablet dissolved in 200mls sterile water or tap water) every 2hours up to a maximum of 200microgrammes
- For suspected fetal macrosomia, or parity 3 and above, and multiple pregnancy use
 25ml every 4hours

These recommendations have since been adopted at both central hospitals⁶.

Vaginal prostaglandin E_2 (tablet or gel) is the recommended gold standard for induction of labour, unless otherwise contraindicated, in the UK. Misoprostol is only offered as a method of induction to women with intrauterine fetal demise or in the context of a clinical trial^{3,7}.

In this study we evaluated factors associated with failed induction in women whose labour was artificially induced with titrated oral misoprostol after 37 completed weeks of gestation

or more including post term pregnancies. This was done before the implementation of the current guidelines mentioned above.

RESEARCH QUESTION

What are the factors associated with failed induction in patients induced with titrated oral

Misoprostol at 37 completed weeks or more of gestation?

OBJECTIVES <u>Primary</u>

 To asses factors associated with failed induction in patients induced with oral Misoprostol at 37 completed weeks of gestation or more (including post term pregnancies).

Secondary

- To calculate rates of failed induction after oral Misoprostol at Harare maternity
- To determine rates of Caesarean section for failed induction
- To determine the frequency of common complications after oral Misoprostol.

LITERATURE REVIEW 4.1 Historical reviews

Several pharmacological methods have been employed to try and induce labour dating as far back as 600 BC. In 1582 it was described that delivery could be hastened by administering spurs of the secale cornutum (fungus) from which ergot alkaloids were derived. As a result of the inability to ensure adequate dosage, frequent uterine ruptures resulted and by 1828 its use during delivery was stopped with use being reserved for the management of post partum hemorrhage. In 1932, Dudley and Moir isolated egormetrine. In the 19TH century quinine was also used for the same purpose. In 1948 Theobald and associates described their use of a posterior pituitary extract, oxytocin, for labour induction by intravenous infusion however it was not until 1953 that Vincent Du Vigneaud synthesised oxytocin for which he won a Nobel Prize for chemistry. The term *prostaglandin* was coined in 1935 by von Euler based on the belief that its presence in semen originated predominantly from the prostate gland (seminal vesicles later demonstrated to be the source). By 1968 prostaglandins were synthesised in the laboratory⁸. The commonest indication for induction of labour all this time was for intrauterine fetal death. This has however changed within the last 50 years with prolonged pregnancy and hypertensive complications being the number one reasons for induction of labour.

4.2 Anatomy and physiology of labour

The uterine cervix acts as a barrier to parturition and cervical status prior to induction is predictive of induction success in both nulliparous and multiparous women⁹. It is composed largely of fibrous connective tissue made up of extra cellular matrix of collagen (70% type1 and 30% type 2), elastin, proteoglycans, and cellular portion composed of smooth muscle,

fibroblasts, epithelium and blood vessels¹⁰. Cervical ripening describes a process characterised by softening, thinning (effacing), and dilatation of the cervix resulting from the breakdown of the extracellular matrix components under hormonal influence and prostaglandin action. Methods of inducing labour are aimed at initiating and accelerating this physiologic process. Garret in 1960 coined the terms *ripe* or *unripe* to describe the state of the cervix as predictive of labour onset within 48hours of amniotomy¹¹.

4.3 Induction of labour

Induction of labour is the process of artificially stimulating uterine contractions in order to achieve a vaginal birth and is initiated when the benefits of carrying out a vaginal delivery outweigh the potential fetal and maternal risks associated with the continuation of the pregnancy¹. The indications can be classified into maternal, fetal or social reasons.

Maternal indications include hypertension in pregnancy at term, prolonged pregnancy, premature rupture of membranes ≥ 34 weeks, abruptio placentae and other maternal medical complications. Fetal indications include intrauterine fetal death and chorioamnionitis. Induction may also be done for logistic reasons like distance from hospital or psychosocial reasons. Induction of labour may also be done for maternal request or convenience.

Risks associated with induction of labour include an increase in the incidence of operative vaginal delivery and caesarean delivery, excessive uterine activity with resultant uterine rupture or none reassuring fetal heart rate pattern, postpartum haemorrhage and risk of iatrogenic prematurity¹. The contraindications to labour induction are the same as those for spontaneous labour and vaginal delivery and are summarised below³:

Maternal contraindications

- Previous classical or multiple caesarean section
- Infections e.g. active genital herpes
- Major placenta previa
- Any other contraindication to vaginal delivery

Fetal contraindications

- Malpresentations
- Severe fetal compromise (preterminal CTG or severe doppler anomalies)
- Cord prolapse
- Vasa previa

There has been no general consensus or standardised criteria on the definition of failed labour induction with variable end points having been described. These include caesarean delivery, failed vaginal delivery within a specified time, and failed achievement of active labour within a specified time¹². The Royal College of Obstetricians and Gynaecologists (RCOG) defines failed induction of labour as labour that fails to start after one cycle of treatment⁷. Monique G.L and Dwight J.R reviewed available data on labour induction and extensively evaluated Friedman's publications on labour progress, they then proposed to define failed labour induction as the inability to achieve cervical dilatation of 4cm and 90% effacement or at least 5cm (regardless of effacement) after a minimum of 12-18 hours of membrane rupture and oxytocin administration (with a goal of 250MU or 5 contractions in 10 minutes)¹³. This study however has limitations because it was purely based on observational data. The following table summarises some of the definitions used for failed labour induction from several randomised clinical trials¹³:

DEFINITION	SOURCE
Failure to achieve dilation >4 cm after trial of oxytocin to a	Wing and Paul
maximum of 20 MU/min	
Failure to enter the active phase (not specifically defined) of	Ngai et al, Hoffman
labour within 12 h after IOL was begun	and Fawcus
Failure to enter the active phase of labor (Bishop score <8)	Shetty et al
after 24 h of IOL	
Adequate (>200MU) contractions for 2 h without cervical	Lo et al
change	
Failed induction: painful, regular contractions with cervical	Meyer et al
change were not achieved and the patient was delivered by	
caesarean with failed induction as the sole indication	
Failure to deliver within 24 h of induction	Fisher et al

Table2: Definition of failed induction used in clinical trials¹³.

In this study we will employ a definition for failed labour induction based on RCOG guidelines: failure to achieve vaginal delivery within 24hours of completing one cycle of titrated oral Misoprostol solution.

In a critical analysis of factors predicting labour induction success, Joan Crane in 2006 individually assessed a variety of maternal and fetal factors as well as biochemical markers in order to evaluate their impact on prediction of successful labour induction. Transvaginal ultrasound of the cervix was also evaluated. Maternal factors assessed included parity, height, weight, and body mass index; fetal factors included birth weight and gestational age, position of the vertex and the biochemical markers were fetal fibronnectin and insulin like growth factor binding protein-1. Successful induction was associated with higher parity, younger maternal age, low BMI, and lower birth weight. A persistent occipitoposterior position is associated with an increased chance of failure. Transvaginal ultrasound and biochemical markers were not shown to be superior to Bishop Score in prediction of a successful induction¹⁴.

In 2012, an Australian study assessing risk factors for failed induction in nulliparous women found maternal height (short stature), cervical dilatation and maternal age as independent risk factors. The investigators also came to the conclusion that it was not possible to arrive at an algorithm that obstetricians could use to identify those women at high risk of failure. Dinoprostone, traction catheter and oxytocin were used for induction in this study¹⁵.

Joan Crane in a Canadian study in 2004 to identify independent risk factors for successful labour induction with oral or vaginal misoprostol concluded that maternal height weight and parity as well as birth weight and some individual components of the bishop score were independently associated with labour induction success¹⁶.

After failed induction of labour options for further management include the following³:

- Expectant management: perform a CTG and ultrasound scan for liquor volume; if both are normal then based on patient's choice she can await spontaneous labour within the next 72 hours. A decision for repeat induction or caesarean section is then discussed with the patient.
- Repeat induction of labour: perform CTG and ultrasound scan, if both are reassuring then repeat induction with the same prostaglandin regime or alternative after 48hours. Mechanical methods (traction catheter) may also be considered.
- Caesarean delivery: for women not willing for expectant management or repeat attempt at induction or non reassuring CTG or ultrasound scan.

At Harare Hospital Maternity the majority of women with failed induction are usually offered a repeat cycle of oral misoprostol (or a switch to vaginal misoprostol) after which emergency caesarean delivery is offered if induction fails or if there is evidence of a non reassuring fetal heart rate.

4.4 Preinduction cervical assessments

The Bishop score is a scoring system for assessing cervical status prior to induction of labour and its components are consistency, cervical dilatation, effacement, cervical length, and position. Other documented preinduction cervical assessment methods include transvaginal ultrasound (TVS) cervical length measurements and fetal fibronnectin assay in vaginal secretions.

After evaluating 1000 women undergoing elective induction of labour, Bishop in 1955 noted that cervical dilatation, effacement, and station correlated with labour duration and in 1964 he developed a scoring system for prelabour cervical assessment and women with a score of 9 or more had a successful induction^{9,17}. Several modifications have been proposed for the scoring system. The following table summarises the modified Bishop scoring system:

	FACTOR				
SCORE	Dilatation(cm)	Effacement	Station	Cervical	Cervical
		(%)		consistency	position
0	closed	0-30	-3	firm	posterior
1	1-2	40-50	-2	medium	midposition
2	3-4	60-70	-1	soft	anterior
3	5	>80	+1, +2	_	-

Table 3: Modified Bishop scoring system.

Courtesy of Williams Textbook of Obstetrics

A score of 5 or less represents an unfavourable cervix and is associated with double the risk of caesarean delivery and a score of 6 or more indicates a ripe cervix and if it is 9 or more, the probability of vaginal delivery after induction is similar to that after spontaneous labour¹. Crane et al In 2004 evaluated 784 women undergoing induction with Misoprostol and found that cervical dilatation was the most important predictor of successful induction followed by station and effacement, cervical consistency was the least useful element¹⁹. The major pitfalls with use of the Bishop scoring system is that in the main, it is very subjective since one cannot precisely measure cervical length by digital examination and determination of consistency or position cannot be quantified or standardised²⁰.

Several comparative trials between Bishop score, transvaginal ultrasound (TVS) cervical length measurements, and fetal fibronnectin assays have produced conflicting results with

earlier studies showing superiority of Bishop Score over TVS, and majority of recent studies finding TVS for cervical length to be a better predictor than any bishop score parameter. Fetal fibronnectin assay does not however seem to be of any significant advantage in prediction of successful induction of labour^{1,21,22}.

4.5 Misoprostol and labour induction

Misoprostol (15 deoxy-16hydroxy-16methyl PgE₁) is a synthetic analogue of prostaglandin E_1 used widely *off label* as one of the pharmacological methods for achieving favourable Bishop scores and stimulation of uterine contractions. It is a methyl esther of prostaglandin E_1 additionally methylated at carbon 16.

Initially developed for treatment and prevention of peptic ulcers it has now found wide use in obstetrics and gynaecology due to its uterotonic and cervical ripening properties. Compared with other prostaglandin preparations, it is generally cheap, widely available and stable at room temperature and has few documented side effects.

It causes cervical ripening through eventual activation of collagenases and also its effects on dermatan sulphate, hyaluronic acid and water composition of the cervix with resultant destruction of the structural collagen network of the cervix, hence softening. Uterine contractions are stimulated through its selective binding to EP-2EP-3 prostanoid receptors leading to myometrial stimulation and the hormonal enhancement of gap junctions facilitating coordinated myometrial contractions and through its effect of increasing myometrial sensitivity to oxytocin¹.

It also has antisecretory and protective properties promoting healing of gastric and duodenal ulcers and it can protect against NSAID associated ulcers.

4.6 Pharmacology of Misoprostol

Pharmacokinetic properties of Misoprostol have been studied including the differences between the various routes of administration.

After oral administration it undergoes rapid and almost complete absorption from the gastrointestinal system, however there is subsequent extensive first pass metabolism by deesterification to Misoprostol acid (MPA). MPA is the biologically active metabolite, and undergoes further metabolism through beta and omega oxidation in various body tissues. Excretion is via the kidney (60%) and faeces (40%). Compared to the vaginal route for administration the oral route is associated with a more rapid increase in plasma concentration, shorter time to peak concentration (about 30 minutes), and a more rapid decline in plasma concentrations thereafter^{23,24}. The area under the curve (bioavailability) is however higher with the vaginal route. After oral administration, there is a rapid increase in uterine tone with a mean time of 8 minutes, which subsequently decreases after 1 to 2 hours and abates. To induce regular uterine contractions a sustained plasma level of Misoprostol is required and this can be achieved by administering repeated doses as needed. In contrast, after vaginal administration the time to peak concentration is longer and regular uterine contractions appear after 1 to 2 hours lasting up to 4hours^{23,24}.

Reported significant side effects of oral Misoprostol are very few with diarrhoea being the most frequent. It is however self limiting. Others include nausea and vomiting, and hyperpyrexia with fever and chills. Uterine rupture especially in women with previous uterine scar is especially worrisome. Misoprostol has however not been shown to be teratogenic, fetotoxic or embryo toxic with the few reported fetal structural anomalies being most likely due to ischaemic effects of uterine contractions after Misoprostol

administration in the first trimester^{23,24}. Also reported is an increase in meconeum staining of the liquor after misoprostol administration.

4.7 Evidence for use of Misoprostol as an induction agent

Several studies have looked at the effectiveness of the different routes of administration of Misoprostol for achieving favourable bishop scores or inducing uterine contractions.

Zvandasara P et al randomised 164 pregnant women with singleton foetuses in cephalic presentation to induction of labour with titrated oral Misoprostol or vaginal Misoprostol. The main indication for induction was post term pregnancy followed by hypertension, and the mean drug dose for the oral misoprostol group was 28microgrammes. The success rate after induction with oral misoprostol was 89% (90% with vaginal misoprostol). They concluded that there was no superiority of vaginal misoprostol over oral misoprostol and that oral Misoprostol was very safe to use even in resource poor countries where monitoring is poor²⁵.

Kundodyiwa and others evaluated the safety of low dose oral Misoprostol in comparison to PGE₂, vaginal Misoprostol, and oxytocin for induction of labour through an electronic database search of pubmed, MEDLINE, EMBASE and the Cochrane library. Low dose oral Misoprostol in doses of 20microgrammes every 2hours was found to be as equally effective but associated with reduced incidence of caesarean delivery and uterine hyperstimulation.

Majoko et al, in 2002, in a case series reported a possible dose depended risk of complications, especially uterine rupture, with use of Misoprostol for labour induction and made recommendations for obstetricians to employ doses up to a maximum of 50microgrammes together with close patient monitoring²⁶. In a subsequent randomised

controlled trial comparing high dose (100microgrammes) vs low dose (50microgrammes) Misoprostol, Majoko et al found no benefit with use of higher doses but increased harm from uterine rupture and increased neonatal morbidity²⁷.

Alfirevic and Weeks did a cochrane database search of randomised clinical trials comparing oral Misoprostol to other methods. They concluded that oral Misoprostol is more effective than placebo and is as effective as vaginal Misoprostol for induction of labour and results in fewer caesarean deliveries than vaginal dinoprostone. They recommended oral Misoprostol over vaginal Misoprostol as it is associated with lower rates of hyperstimulation and lower apgar scores as well as being more acceptable to women. Doses of 20-25microgrammes orally in solution every 2hours were noted to be optimal and associated with a reduced risk of adverse outcomes²⁸. The search reviewed 56 trials with a total of 1590 participants.

A randomised clinical trial comparing oral misoprostol with vaginal dinoprostone by Hofmeyr and Alfirevic noted a reduced risk of uterine hyperstimulation in the oral Misoprostol group with, however, a slower response to induction if fetal membranes were not ruptured or when the cervix was no favorable was noted²⁹.

For women with premature rupture of membranes at term, Ngai et al as well as Mozurkewich et al found oral Misoprostol to be as effective as oxytocin, with no evidence of superiority of Misoprostol over oxytocin with regards to mode of delivery or time from induction to delivery^{30,31}

RESEARCH METHODS 5.1 Study design

A prospective cohort study was conducted on pregnant women presenting for induction of labour at 37 completed weeks gestation or greater including those with prolonged pregnancy. Study participants were followed up from time of induction till discharge from hospital.

5.2 Study population

Pregnant women at 37 completed weeks gestation or greater with singleton foetuses in cephalic presentation, including those with prolonged pregnancy, admitted for labour induction were selected for the study. Both Primi para and multi para were considered for selection.

5.3 Study factors

The following study factors were evaluated: general demographic data, parity, gestational age, BMI, bishop score, membrane status before induction (ruptured or unruptured), birth weight, apgar score at 5 minutes, total dose of misoprostol used to achieve a successful induction, outcome of induction and type of delivery.

5.4 Outcome measures

The main outcome measure was the ability to achieve vaginal delivery during the first 24hours of completing one cycle of titrated oral misoprostol. Secondary outcome measures were caesarean delivery, repeat induction of labour, and uterine rupture.

5.5 Inclusion criteria

Pregnant women with indication for induction of labour at 37 completed weeks gestation or more (including those with prolonged pregnancy) were informed on the study details, including risks associated with induction of labour, those who consented were included in the study.

5.6 Exclusion criteria

The following categories of women were excluded from the study

- Women with a previous uterine scar
- Women with multifetal gestation
- Those with non cephalic fetal presentations
- Those women with contraindications to vaginal delivery e.g. cephalopelvic disproportion
- Women with known sensitivity to misoprostol
- Women who did not consent to involvement in the study

5.7 Sample size calculation

The sample size was calculated using stata 12. Using induction success rate of 89% reported by Zvandasara P et al as the proportion of pregnant women who will be successfully induced

by misoprostol in our study population, postulating the rate to be 80% with alpha=0.05 (two-sided) and 90% power we calculated the sample size to be 157 women.

5.8 Study procedures

Pregnant mothers admitted into the antenatal ward and sanctioned for induction of labour for the various reasons by their responsible obstetric teams were recruited into the study if they met the inclusion criteria. They were then followed up from the time of induction up to delivery. Neither the principal investigator nor his assistants interfered in any way or influenced the subsequent management of these patients. Assistance to the principal investigator was provided by the nurse in charge of the antenatal ward and the team of midwives working in antenatal ward, labour ward and postnatal ward.

Once selected for the study, each patient would go through the process of informed consent and signed the consent form. Relevant maternal history and demographic data was collected and filled onto a data sheet. A thorough physical examination (including BMI, obstetric examination and bishop score assessment) was performed and the induction procedure started by the midwives on duty that day. A 200microgrammes tablet of misoprostol was dissolved in 200ml of fresh water to make a 1microgrammes/ml solution. Aliquots of between 15 to 30mls were given hourly according to the induction regimen. This would then be stopped once labour pains started and the patients would then be sent to labour ward.

Intrapartum management of the patients was done by the obstetric team on duty that day and patients were sent to the postnatal ward once delivered. There the principal investigator would follow them up and consolidate information on delivery outcomes and

outcome for the neonate. Caesarean section was done for any arising emergencies during labour.

Those who failed to enter into labour or did not deliver within 24hours of completing the induction process were followed up every day to evaluate their subsequent management, until delivery (caesarean section or otherwise) and routine postnatal follow up was done as before.

The maternity booklet, misoprostol induction chart, and delivery registers were used to assist with consolidation of the study information.

An analysis was then carried out to evaluate study factors between a cohort of women in whom the induction was successful or in whom the induction failed using IBM SPSS Statistics version 21 with assistance from a statistician.

5.9 Ethical considerations

Study participants were furnished with information leaflets informing them about the study in English and Shona languages including risks and benefits to them. Written Informed consent was obtained and those who did not wish to take part were excluded and were not penalised. Issues of confidentiality were discussed with the participants and the information was provided in written format on each consent form (sample of which is provided in the annexe). Ethical approval was sought from Harare hospital institutional ethics board, the joint research and ethics committee (JREC) and the medical research council of Zimbabwe (MRCZ).

RESULTS

One hundred and seventy one (171) pregnant women were included in the study. Two (2) women were then removed after realizing that they did not meet the inclusion criteria as one had gestational age less the 37 weeks and the other delivered a breech which was missed during preinduction evaluation. The final number of women available for analysis was one hundred and sixty nine (169).

6.1 Demographic data

The median age was 24 with age range from 16years to 42years.ninety six percent of participants were married, with 85% having reached ordinary level education. The majority were not employed (69.6%) and 3% were students (secondary or tertiary level). Table 4 shows the distribution of demographic characteristics.

DEMOGRAPHIC	FREQUENCY	PERCENTAGE	
CHARACTERISTIC			
AGE			
<20yrs	26	15.5	
20yrs-<25yrs	60	35.7	
25yrs-30yrs	37	22.0	
30yrs-35yrs	30	17.9	
>35yrs	15	8.9	
EDUCATIONAL LEVEL			
Primary level	7	4.2	

Ordinary level	142	84.5		
Advanced level	14	8.3		
Tertiary level	5	3.0		
EMPLOYMENT				
Housewife	117	69.6		
Formally employed	23	13.7		
Self employed	23	13.7		
student	5	3.0		

6.2 Indications for induction

The commonest indications for induction were hypertension in pregnancy (38.1%), followed by prolonged pregnancy (33.9%). One questionnaire did not have information on the indication for induction. Only one patient was induced for intrauterine fetal demise. Table 5 shows the different indications for induction and their relative frequencies.

INDICATION FOR	FREQUENCY	PERCENTAGES (%)
INDUCTION		
Hypertension in pregnancy	64	38.1
Prelabour rupture of	27	16.1
membranes		
Prolonged pregnancy	57	33.9
other	20	11.9

6.3 Cervical status

Of the 169 participants, 152 (i.e. 89.9%) had an unfavorable Bishop score of \leq 5, and only 17 (i.e. 10.1%) had a favorable Bishop score of \geq 6.

6.4 Parity

Nulli parous women constituted the bulk of study participants at 40.8%, women with either one or two children combined together to make up the highest proportion of study participants at 42%. Only 6.5% of the participants had more than 3 children

6.5 State of fetal membranes.

Thirty one (31) women had ruptured membranes at induction of labour; the majority of the women (138) had intact fetal membranes.

Table 6: Fetal membrane status and induction outcome

STATE OF FETAL	OUTCOME OF INDUCTION		TOTAL	PROPORTION
MEMBRANES	failed	successful		FAILED (%)
ruptured	2	29	31	6.5%
unruptured	40	98	138	29.0%

6.6 Birth weights

All babies had birth weights taken and the mean birth weight was 3078g.

Figure 1: Histogram showing birth weight



6.7 Outcome of induction

Of the 169 women induced with misoprostol in the study, 75.1% (127) had a successful induction and 24.9% (42) had a failed induction. The median delivery time was 16.7 hours (95% CI: 14.67 hours; 17.67 hours). The median dose of misoprostol used was 170 microgrammes (95% CI: 165microgrammes; 180microgrammes), with a range from 20 microgrammes to 215microgrammes.After repeat induction with oral misoprostol, cumulative success of induction increases modestly to 81%. This is increased further to 84% if those women who received per vaginal cytotec are also included.

Of all the women 88.8% had a normal vaginal delivery, 10.7% had caesarian section, and 0.5% had operative vaginal delivery (vacuum).

Of the 169 babies delivered 103 were male (60.9%), and 66 were female (39.1%). A total of 24 babies were admitted to neonatal unit and the reasons for admission in order of frequency were low apgar scores (34.8%), birth weight > 4000g (26.1%), unspecified (26.1%), low birth weight (8.7%) and meconeum aspiration syndrome(4.3%).

When induction failed, the majority of women underwent repeat induction with oral misoprostol using the same regime (45.2%), others had repeat induction with per vaginal misoprostol (11.9%), or caesarian section (23.9%) or were managed expectantly (19%).



Figure 2: Frequency of interventions following induction failure

Only one patient experienced potentially fatal complication of uterine rupture and ended up with a hysterectomy. There were no reported cases of uterine hypertonus and only 12 (7.1%) cases of fetal distress in labour. There were no reported cases of minor side effects like nausea, vomiting, diarrhea or fever.

None of the study participants had membrane sweeping done routinely at 38 to 39 weeks gestation and only 12 (7.1%) had an early pregnancy dating ultrasound scan done before 20 weeks of gestation. 13 (7.7%) reported history of a previous labour induction in prior pregnancies.

6.8 Materno-fetal factors and failed induction with oral misoprostol

Multivariate analysis using Cox-regression model of all materno-fetal indicators and the total dose of misoprostol used was performed using SPSS statistics version 21. Only maternal body mass index and the total dose of misoprostol used were significantly associated with outcome of induction using this model.





The mean BMI of study participants was 31.07kg/m² (95% CI: 30.29kg/m²; 31,97kg/m²) with a range of 18.94kg/m² to 44.92kg/m². A total of 8 readings were recorded as missing. 52.1%

of the women had BMI> 30kg/m². The outcome of induction differed by BMI category (log rank test; Pvalue=0.026). BMI was significantly associated with the outcome of induction, hazard ratio: 0.952 (95% CI: 0.923; 0.982.

The total dose of misoprostol used was significantly associated with the outcome of induction, hazard ratio: 0.981 (95% CI: 0.977; 0.985).

Parity, maternal age, bishop score and birth weight were not found to be significantly associated with outcome of induction. The table below shows the Cox-regression for the association with outcome of induction, with Pvalues, for all the maternal and fetal factors evaluated in the study.

Table 7: Statistical significance of association	between	materno-fetal	factors
and outcome of induction			

variable	P value
ВМІ	0.026
Total dose of misoprostol	<0.001
Age	0.576
Parity	0.565
Indication for induction	0.520
State of fetal membranes	0.168
Birth weight	0.390
Bishop score	0.218

Univariate analysis (unadjusted estimates) using the log rank test for equality of survival functions was performed for BMI, Bishop Score and parity and noted that BMI category was indeed associated with outcome of induction (chi square 7.3; P value=0.026) as well as

bishop score category (chi square 17.72; P value<0.001). Parity was not shown to be associated with outcome of induction (chi square 2.04; P value=0.565).

Discussion

The general demographic characteristics of the study participants shows that the majority of the women undergoing induction of labour are young married girls in their early second generation of life and coming with their first or second pregnancy. They are generally unemployed and having completed or at least attended some secondary education (mostly up to ordinary level certificate). The study did not however address issues related to the pregnancy booking status with, HIV status and other important components of antenatal care.

Harare hospital maternity generally caters for women hailing from the high density suburbs of Harare and some referrals from outside the city of Harare. These are women in general coming from low socioeconomic backgrounds with inadequate access to basic health care needs as a result of financial constraints, putting them at risks of pregnancy complications.

These findings are indeed in keeping with the results obtained by the Zimbabwe demographic and health survey released in 2010 whose highlights included an up to 60% unemployment rate among Zimbabwean women, and the high literacy rates (up to 94% of women attained some form of secondary education)³².

The study showed that induction failed in 24.9% of women induced with titrated oral misoprostol, meaning that about 1 in 4 women induced with our Harare hospital regime end up with a failed induction. A local study comparing effectiveness of oral misoprostol and vaginal misoprostol showed that 11% of women failed on titrated oral misoprostol regime²⁵. Analysis of the cohort of women with failed labour induction showed that 19(45.2%) had a repeat induction with oral misoprostol and of these 10 succeeded in achieving vaginal

delivery within 24hours of completing the cycle. This reduces the failure rate to 19% after two inductions. This is further reduced to 16% if the women who had per vaginal misoprostol instead, are included together with those who had oral misoprostol.

Various studies on induction of labour in general (not limited to oral misoprostol) show varying failure rates up to as high as 25% percent in one study. The high failure rate in this study could be explained by the fact that the definition for failed induction was somewhat restrictive as anyone managing to deliver vaginally after the stipulated 24hours was considered as a failed induction (even if vaginal delivery occurred within 48hours).

Some patients despite getting into active labour within the stipulated 24hours ended up with caesarian sections for compelling reasons during labour e.g. fetal distress or a non reassuring fetal heart rate tracing. They were also included in the cohort of failed inductions for the sole reason of failing to attain an important end point to induction of labour- vaginal delivery.

Other factors that may have contributed include effectiveness of the misoprostol drug itself since in most instances the drug was out of stock and patients had to source it privately on their own putting them at risk of buying fake or cheap imitations.

Whether the regime employed for induction is inferior to other standard regimes recommended by the WHO or others is not clear but it is actually more dose dense in terms dosing frequency compared to these other regimes^{2,5,6,7}. The study did not evaluate the adherence to the regime protocol in terms dosing frequency, timing and when to stop administering the misoprostol as this may also contribute to failures if not adhered to.

Offering a repeat induction with the same regime or different regime, if indicated, does indeed help to reduce failures as shown in this study.

Both routine early obstetric ultrasound scan (<20 weeks) for dating with membrane sweeping starting at 38 or 41 weeks gestation has been shown to prevent post term pregnancies thus reducing inductions of labour for prolonged pregnancy. Membrane sweeping doubles the rate of labour onset within the next 48hours hence decreasing the frequency of pregnancy going beyond 41 weeks of gestation and need for formal induction³³.Compared to no ultrasound scan, a routine early pregnancy ultrasound scan (<20 weeks) was shown to be associated with a reduction in post term pregnancies by affording accurate gestational age assessment³⁴. None of the study participants had membrane sweeping offered and only 7.1% had an ultrasound scan done in early pregnancy.

Hypertensive disease in pregnancy (including chronic hypertension, pregnancy induced hypertension and preeclampsia) was the commonest indication for labour induction closely followed by prolonged pregnancy. The commonest indication for labour induction in America is preeclampsia and post dates³⁵. Prolonged pregnancy is the commonest indication in France and one study in Latin America showed premature rupture of membranes to be the commonest indication³⁶.

Only 1 patient was induced for intrauterine fetal demise. It was however discovered that most of the women with IUD's were erroneously being excluded from the study cohort for supposedly not meeting the inclusion criteria because they had an IUD. This was never part of the exclusion criteria and regrettably barred inclusion of these women from this study.

Whether their inclusion would have an impact on the primary and secondary outcomes remains unknown.

Most of the women who had a failed induction ended up with a repeat induction with oral misoprostol (45.2%), with caesarian section for failed induction being done for 23.9%. It was the second commonest intervention. 19.0% ended delivering without any intervention. Induction with vaginal misoprostol insertion was the least common intervention. There are no laid down standard criteria for options to follow once induction of labour has failed³. When to repeat the induction process or which intervention to offer patients generally varied between the obstetric teams managing the patients. Some patients were subjected to long periods of waiting before any intervention was given, going as long five days for some. When induction failed over a weekend most patients had to wait for a Monday when normal duties resume for them to be reviewed by the responsible teams as the on call team would mostly be occupied with work in labour ward.

Expectant management of failed labour induction seemed to be occurring in the 19.4% of the women who delivered without any intervention but however, this was never offered formally as an option as this intervention came through incidentally through spontaneous labour onset before any intervention was offered. One patient was actually offered caesarian delivery after induction for severe preeclampsia failed, she vehemently refused this intervention despite adequate counseling and requested discharge from hospital. She then presented in labour seven days later and proceeded to an uneventful vaginal delivery of a healthy bay.

This scenario calls for the need for an audit of the management of failed labour induction in order to formulate a protocol to harmonise management of these patients thus preventing

potential adverse outcomes or unnecessary caesarian deliveries. If clinically indicated, this study has shown that indeed repeat induction does improve overall success rates. The essential guide to common obstetric and gynecological conditions in Zimbabwe does not say anything on management of failed labour induction.

In keeping with most studies that proved the safety and efficacy of oral misoprostol for labour induction, only one patient had a uterine rupture after which a hysterectomy was done, 7.1% developed fetal distress and there was no documented evidence of uterine hypertonus in all the patients^{25,26,27,28,29}. Some studies document an increase in meconeum staining of the liquor with use of misoprostol, however only 4.3% percent of delivered babies in this study had a diagnosis of meconeum aspiration syndrome and it is not clear whether the 34.4% of babies admitted in neonatal unit with low apgar scores were born in a meconeum environment²⁷.

The one uterine rupture recorded occurred in a 26 year old para 1 gravida 2 at 38 weeks of gestation who had been induced for hypertension in pregnancy. She had a BMI of 44.9kg/m². A total dose of 165 microgrammes of misoprostol was used for induction. Intrapartum, she was in active phase for close to 6hrs with no decent of the fetal head, a caesarian section was due to be done for failed progress and fetal bradycardia upon where a traumatic uterine rupture was noted. A total hysterectomy was done. She delivered a fresh still birth with weight of 3600g. There was no recorded use of oxytocin intrapartum.

In this study, the only factors shown to be significantly associated with outcome of induction were the body mass index of the mother and the total dose of misoprostol used. Univariate analysis showed bishop score category to be significantly associated with induction outcome. In contrast to most studies published on induction of labour and factors affecting

success rates, we did not find any significant association between maternal age, parity and birth weight with the outcome of induction. The fact that the mean BMI for the study population was 31kg/m² and the fact that a large proportion of women had a BMI>30 shows that obesity in pregnancy within our pregnant population is prevalent and deserves the necessary recognition in order to alleviate potential adverse outcomes associated with obesity in pregnancy including failed induction as demonstrated in this study.

There was significant correlation between the Bishop Score category and outcome of induction with oral misoprostol after univariate analysiss. This means that preinduction cervical assessment in the setting of induction with misoprostol is necessary even though misoprostol does induce both cervical ripening and uterine contractions. Compared to women with ruptured membranes, those who had induction of labour with unruptured membranes had higher induction failure rates (2% vs 29%). These results are in keeping with findings from other studies including a South African study by Hofmeyr and Alfirevic which showed a slower rate of response to induction in women with intact membranes and unfavorable cervix.

Those women who had an induction for hypertension in pregnancy had the highest number of failed inductions possibly due to the fact that most of them had an unfavorable Bishop score and they generally tend to be nulliparous. However regression analysis did not show any significant correlation between indication for induction and outcome of induction.

8.1 Limitations to the study

- Lack of adequate funding for the project resulted in the inability to ensure constant supply of misoprostol for the study from reputable suppliers to counter the constant stock outs by the main pharmacy at Harare hospital. It also resulted in failure to evaluate transvaginal ultrasound for cervical length as a predictor of successful induction
- 2. The principal investigator could not personally be involved in all the day to day study formalities due to other commitments. This resulted in some avoidable study let downs including the exclusion of women with IUD's, and missing BMI's due to incomplete recording of weight and height etc
- 3. The study methods failed to give a comparison of the Harare hospital regime versus standard e.g. the WHO recommended dosing schedule as a way of evaluating induction failure
- 4. An evaluation of the management of failed labour induction was not fully captured and spelled out in the data collection tools hence the need for a formal audit of these interventions
- 5. The system of labour induction with misoprostol was not incorporated into the evaluation tools so that an audit of how the medications were given, dosing schedules, when to stop, whether saline of fresh water was used etc could not be projected during analysis. This was a major setback as these issues may have indirectly contributed to the failures.

8.2 Recommendations

- Routine sweeping of membranes weekly starting at 38 weeks as it has been shown to be safe, not associated with increased infection rates or caesarian delivery rates.
- 2. Routine early trimester ultrasound for all antenatal patients
- The setting up of standard treatment guidelines for the management of failed induction of labour.
- 4. Determination of Bishop Score, and maternal BMI before labour induction as predictors of the likely outcome of induction with misoprostol.

8.3 Conclusion

In conclusion, failed induction of labour when using a titrated solution of oral misoprostol at Harare maternity occurred in 24.9% of women. Repeat induction if indicated reduces failure rates to as low as 16%. Only maternal BMI, the total dose of misoprostol used and bishop score were significantly associated with the outcome of induction. There are no standard treatment guidelines for the management of a failed labour induction.

Appendix 1

Study questionnaire

Evaluation of factors associated with failed induction of labour in patients undergoing induction with oral misoprostol at Harare hospital maternity.

Identification code:

Indicate the appropriate response with an 'x' or fill in the require response where required

A] SOCIO-DEMOGRAHIC DATA

Age			
Educational level			
Marital status	single	married	divorced
Employment			

B] MATERNAL CHARACTERISTICS

- 1. Parity:
- 2. Gravida:
- 3. Estimated gestational age(in completed weeks):
- 4. Was membrane sweeping done?:
- 5. Indication for induction:
- 6. Was a dating USS done before 20 weeks gestation?:
- 7. Was the patient induced in previous pregnancies?:
- 8. Maternal weight(kg): maternal height(m): BMI(kg/m²)
- 9. Membrane status: ruptured/unruptured
- 10. Cervical status:

Dilatation(cm)			position	station of
	effacement/length(cm)	consistency		presenting
				part

• Bishop score:

<u>C] FETAL CHARACTERISTICS</u>

- 1. Fetal viability: ALIVE/IUD
- 2. Birth weight:
- 3. Apgar score:
- 4. Sex: MALE/FEMALE
- 5. Was baby admitted to NNU? YES/NO
- 6. Reason for admission to NNU

D] INDUCTION FACTORS

- 1. Time at start of induction:
- **2.** Time of delivery:
 - i. Induction to delivery interval(hrs min):
- 3. Total dose of misoprostol used:
- **4.** Outcome of induction

Successful	failed	action taken if induction failed

5. Type of delivery:

NVD	vacuum/forceps	cesarean section	indication for
	vacuum, ioreeps		

C/S

6. Reported complications:

Uterine hyperstimulation YES/NO

Uterine rupture YES/NO

Fetal distress YES/NO

Appendix 2

SUBJECT INFORMED CONSENT (ENGLISH)

<u>**Protocol Title:**</u> factors associated with failed induction of labour in patients undergoing induction with titrated oral misoprostol at Harare hospital maternity

Name Of Reaearcher: Dr Bismark Mateveke

Phone number: +263773 379 494 EMAIL ADRESS: bmateveke@gmail.com

Project description

This is a study to find out the reasons why some people fail to deliver normally after labour pains are induced by drinking a drug called *misoprostol*. These women will be 37 weeks pregnant or more including those who have gone past their due date to give birth.

Your rights

Before you decide whether or not to volunteer for this study, you must understand its purpose, how it may help you, and any risks to you. This process is called informed consent.

Purpose of the research study

This study will try to find out if certain factors increase the rates of failed delivery of your baby after labour pains are induced with the drug *misoprostol*. These factors include mother's height, weight, age, number of children you already have, the state of your cervix (mouth of the uterus), number of weeks you have been pregnant, and the amount of *misoprostol* that will be given. The frequency of reported side effects and complications after taking the drug *misoprostol* will also be assessed.

Procedures involved in the study

This study will be carried out at Harare Hospital. When you get admitted into antenatal ward (ward for women who have not yet given birth) for inducing labour pains because your doctors feel that you would benefit from having to give birth than to continue with the risks of carrying on with the pregnancy (high blood pressure for example), you will be asked to participate in this study.

The doctor will explain the study to you. If you agree to participate you will be asked to sign this consent form. You will then be asked to provide some information about yourself and the pregnancy; you will undergo a thorough examination including assessment of your baby and your cervix (mouth of the uterus). You will be given *misoprostol* to drink. This medicine will trigger labour pains. This drug is a tablet that will be dissolved in water and you will be drinking part of the water every hour until you start feeling pains.

Once labour pains start you will be sent to the labour ward (ward for women with labour pains waiting to give birth). In the labour ward you will be closely monitored by the team of doctors and nurses on duty that day. The monitoring will include routine monitoring of your labour and your baby, and vaginal examinations to asses by how much your cervix is open (cervical dilatation).

After you have given birth will be transferred to the postnatal ward (ward for women who have given birth). In the postnatal ward you will be asked to provide information on the outcome of your delivery and the birth weight of your baby. Your maternity booklet will be used to obtain most of this information.

A caesarean section (giving birth by having an operation) will be done for any problems that may arise during the process of inducing labour pains or delivery.

Discomforts and risks

Vaginal examination will be done initially to assess how much your cervix is open and repeated routinely for monitoring progress of labour. This may be associated with some degree of discomfort.

Complications of inducing labour pains include increased risk of excessive labour pains or contractions of your uterus. In very rare occasions the uterus can be torn apart. Sometimes the baby can get tired (non reassuring fetal heart). Sometimes the medicine may fail to trigger labour pains requiring us to either repeat the process or to do an emergency operation to deliver your baby. The drug *misoprostol* may cause nausea and vomiting, shivering and fever, but these side effects are mild and can go away on their own.

Potential benefits

The results from this study will help to improve the doctor's ability to select women who are suitable to start labour pains with the drug *misoprostol*. This will help to reduce the number of women who will fail to give birth normally. This will ultimately reduce the number of operations done to deliver babies thus reducing hospital costs.

There will be no monetary benefits for you if you take part in this study.

Study withdrawal

You may choose to enter the study or withdraw from the study at anytime without loss of benefits entitled to you

Confidentiality of records

None of the information will identify you by name. You will be identified by a unique study identification number. All data will be collected and analyzed according to these numbers. The coded identification numbers and all records will be locked in a filing cabinet. Any links of participant's identification numbers to other identifying information will be stored separately in a locked cabinet with limited access. Every effort will be made to keep your information confidential

Problems/questions

Please ask questions about this research or consent now. If you have any questions in future ask the principal investigator, Dr Bismark Mateveke on this phone number- 0773 379 494.

For questions about your rights as a research participant, contact:

The Chairperson of the Joint Parirenyatwa College of Health Sciences Ethics Research Committee on telephone number 263 4 731000 extension 2240, or the Medical Research Council of Zimbabwe on 263 4 791792.

Authorisation

I have read this paper about this study or it was read to me. I understand the possible risks and benefits of this study. I know being in this study is voluntary. I choose to be in this study: I know I can stop being in the study and I will not lose any benefits entitled to me. I will get a copy of this consent form

Client's Signature	Date
Client's Name	Date
Researcher's Signature	Date
Witness' Signature	Date

Appendix 3

CONSENT FORM (SHONA) Gwaro retenderano reari kuongororwa mutsvakurudzo

<u>Musoro wetsvakurudzo</u>: factors associated with failed induction of labour in patients undergoing induction with titrated oral misoprostol at Harare hospital maternity

Zita remutsvakurudzi: Dr Bismark Mateveke

Nhamba dzenhare: +263773 379 494 Kero yeimeri: bmateveke@gmail.com

Tsananguro yetsvakurudzo

Iyi itsvakurudzo yekutsvaka zvikonzero zvinoita kuti vamwe vanhu vatadze kupona zvakanaka kana varwadziswa nemushonga wekunwa unonzi *misoprostol*. Vanhukadzi ava ndevanenge vava nemasvondo anosvika kana kupfuura makumi matatu nemanomwe vakazvitakura, kusanganisira avo vanenge vapfuura nguva yavaitarisirwa kupona.

Kodzero dzenyu

Musati masarudza kupinda kana kusapinda mutsvakurudzo iyi, munofanirwa kunzwisisa chinangwa chayo, kuti ingakubatsirai sei uye njodzi chero dzipi zvadzo dzingakuwirai. Urongwa uhwu hunonzi tenderano nemunhu.

Chinangwa chetsvakurudzo

Tsvakurudzo ino ichaedza kunzwisisa kana pane zvikonzero zvinowedzera kukundikana kwemadzimai kupona vana zvakanaka mushure mekurwadziswa nemushonga we*misoprostol*. Zvikonzero izvi zvinosanganisira urefu, uremu nezera raamai, uwandu hwevana vamava nahwo, mamiriro emuromo wechibereko chenyu, uwandu hwemasvondo apfuura makazvitakura neuwandu hwemushonga we*misoprostol* hwamuchapiwa. Kuchaongororwawo uwandu hwematambudziko anenge aitika mushure mekunwa mushonga we*misoprostol*.

Zvichaitwa mutsvakurudzo

Tsvakurudzo ino ichaitwa pachipatara cheHarare. Pamuchaiswa muwadhi yevakazvitakura nechinangwa chekuti murwadziswe (kana vanachiremba venyu vakafunga kuti zvinobatsira

kuti mupone pachinhambo chekuramba makatarisana nenjodzi dzine chekuita nekuzvitakura (semuenzaniso, bhiipii)), muchakumbirwa kuti mupinde mutsvakurudzo iyi.

Chiremba vachakutsanangurirai zvine chekuita netsvakurudzo iyi. Kana muchibvuma kupinda mutsvakurudzo muchakumbirwa kusaina gwaro retenderano rino. Muchakumbirwawo kupa ruzivo ruri maererano nemi semunhu uye ruri maererano nenhumbu yenyu. Muchaitwa ongororo dzakawanda, kusanganisira ongororo yemwana wenyu neyemuromo wechibereko. Muchapiwa mushonga we*misoprostol* kuti munwe. Mushonga uyu unoita kuti munzwe marwadzo ekuda kupona. Mushonga uyu ipiritsi rinonyungudiswa mumvura uye muchange muchinwa mvura iyi paawa imwe neimwe kusvikira matanga kunzwa kurwadziwa.

Kana marwadzo ekupona atanga, muchaendeswa kuwadhi yevakazvitakura vanenge vorwadziwa uye vamirira kupona. Muwadhi iyi muchaongororwa zvakanyanya nechikwata chanachiremba nanamukoti vanenge vari pabasa zuva iroro. Ongororo idzi dzinosanganisira kuongorora marwadzo enyu nemwana wenyu uyewo kuongorora sikarudzi nechinangwa chekuona kuti muromo wechibereko chenyu washama zvakadii.

Kana mapona muchaendeswa kuwadhi yevanenge vapona. Muwadhi iyi muchakumbirwa kupa ruzivo ruri maererano nekupona kwenyu neuremu hwemwana wenyu paazvarwa. Gwaro rekuzvitakura kwenyu ndiro richashandiswa kuwana ruzivo rwakawanda.

Kana pakaita matambudziko chero api zvawo pakurwadziswa kana kuti pakupona, muchapona kuburikidza nekuchekwa.

Kusagadzikana nenjodzi

Ongororo yesikarudzi ichatanga kuitwa nechinangwa chekuona kuti muromo wechibereko wakashama zvakadii uye ongororo dzicharamba dzichiitwa kuitira kuona kuti kupona kwaswedera zvakadii. Izvi zvinogona kukonzera kusagadzikana.

Matambudziko ane chekuita nekurwadziswa pakupona anosanganisira njodzi yekurwadziwa zvakanyanya kana kudzoka kwechibereko. Nenguva dziri kure chose, chibereko chinogona kutsemuka. Dzimwe nguva mwana anogona kuneta zvekutadza kufema. Dzimwe nguva mushonga unogona kutadza kuvamba marwadzo ekupona, izvo zvinozoita kuti titange patsva kukupai mushonga wemarwadzo kana kuti kukuchekai kuti tiburitse mwana wenyu mudumbu. Mushonga we*misoprostol* unogona kukonzera kuda kurutsa nekurutsa, kubvunda nekutonhorwa, asi zvose izvi zvinenge zvisina kunyanyoipa uye zvinogona kupera zvega.

Zvakanaka zvinogona kuwanikwa

Zvichabuda mutsvakurudzo iyi zvichabatsira kuvandudza basa rachiremba rekusarudza madzimai akakodzera kurwadziswa nemushonga we*misoprostol*. Izvi zvichaderedza uwandu hwevanhukadzi vanokundikana kupona zvakanaka. Izvi zvichaderedzawo uwandu hwevachachekwa senzira yekuburitsa vana mudumbu, izvo zvinoderedzawo miripo yemuchipatara.

Hapana mari yamuchabhadharwa kuburikidza nekupinda mutsvakurudzo iyi.

Kubuda mutsvakurudzo

Munogona kusarudza kupinda kana kubuda mutsvakurudzo chero nguva ipi zvayo pasina kurasikirwa nezvakanaka zvamunofanirwa kuwana.

Kuchengetedzwa pakavanzika kwemagwaro

Hapana ruzivo ruchakunangai nezita renyu. Muchazikanwa nenhamba yetsvakurudzo. Ruzivo rwose ruchaunganidzwa nekuongororwa kuchishandiswa manhamba aya. Manhamba anenge akaiswa rupawo aya nemagwaro ose achachengeterwa panokiyiwa. Zvimwe zvose zvinobatanidza manhamba emunhu anenge ari mutsvakurudzo nerumwe ruzivo rwakanangana nemunhu uyu zvichachengeterwa pakasiyana, panokiyiwa uye panogona kusvikwa nevanhu vashomashoma. Rizivo rune chekuita nemi ruchachengetedzwa pakavanzika nepose panogoneka.

Matambudziko/mibvunzo

Munokumbirwa kuti mubvunze mibvunzo maererano netsvakurudzo ino kana gwaro retenderano rino ikozvino. Kana mukazoita mibvunzo chero ipi zvayo mune ramangwana, bvunzai mutsvakurudzi mukuru, Dr Bismark Mateveke panhamba dzenhare idzi - 0773 379 494.

Kana mune mibvunzo ine chekuita nekodzero dzenyu semunhu ari mutsvakurudzo, zivisai:

Sachigaro we *Joint Parirenyatwa College of Health Sciences Ethics Research Committee* panhamba dzenhare dzinoti 263 4 731000 ext 2240, kana kuti ve*Medical Research Council of Zimbabwe* pa263 4 791792.

<u>Mvumo</u>

Ndaverenga gwaro iri riri maererano netsvakurudzo iyi kana kuti ndariverengerwa. Ndinonzwisisa njodzi nezvakanaka zvinogona kuwanikwa mutsvakurudzo iyi. Ndinoziva kuti kuva mutsvakurudzo ino hakumanikidzwi. Ndinosarudza kuva mutsvakurudzo iyi. Ndinoziva kuti ndinogona kubuda mutsvakurudzo asi ndisingarasikirwi nezvakanaka zvandinofanirwa kuwana chero zvipi zvazvo. Ndichapiwa rimwe gwaro retenderano rakafanana nerino.

Sainecha yeari mutsvakurudzo

Zuva

Zita reari mutsvakurudzo

Zuva

Zuva

Sainecha yemutsvakurudzi

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