A Comparison of Two Methods of Pre-Labour Cervical Ripening Following Intrauterine Fetal Death

Joseph Eigbefoh[1], Chukwuwendu. A. Okonkwo[2], Felix Okogbo[1], Sylvanus Okogbenin[1]
Departments of Obstetrics &Gynaecology, [1]Irrua Specialist Teaching Hospital, Irrua, Edo State and
[2]University of Benin Teaching Hospital, Benin City, Edo State, Nigeria

Correspondence: Dr. Joseph .O. Eigbefoh, Departments of Obstetrics &Gynaecology, Irrua Specialist Teaching Hospital, Irrua, Edo State, Nigeria. **E-mail:** eigbefoh2003@yahoo.com

Abstract

Objective: To compare the efficacy of intra-vaginal misoprostol tablets with trans-cervical Foley catheter for pre-induction cervical ripening in patients with intrauterine foetal deaths.
Methods: A study of 121 pregnant women with intrauterine fetal death where pelvic scores were less than 5. Sixty five (65) patients had intra-vaginal misoprostol (100-200 micrograms every 4 hours for a maximum of 6 doses) and 56 women had Foley catheter inserted and the bulb filled to 30 ml.
Results: There were no differences between groups in delivery indications, maternal demographics, ultrasound findings, labour interventions, intra-partum times, mode of delivery. There was no statistically significant difference between the groups in terms of change in Bishop Score, pre-induction cervical ripening times, total induction time, mode of delivery and postpartum complications
Conclusion: Misoprostol and the Foley catheter are equally effective in pre-labour cervical ripening. They offer a cheap efficient, low risk way to achieve expeditious uterine evacuation with minimal complications

Key Words: Intrauterine Fetal Death, Cervical Ripening, Misoprostol, Catheter

Introduction

Intrauterine death is a term used when the foetus dies *in-utero* after the age of viability but the fetus is retained for a prolonged period of time. Death before the age of viability under similar circumstances is classified as a missed abortion. This sub-classification, and thus the frequency of occurence is determined by the age of fetal viability, which varies widely from centre to centre. Twenty-four weeks is the age of viability accepted by the World Health Organization. An incidence of 9 per 1000 live births is quoted for intrauterine fetal death in developed parts of the world [1,2,3].

There has been a paradigm shift in the management of fetal death from the erstwhile expectant approach of the past to the modern approach of expeditious uterine evacuation. Hysterotomy and the use of hypertonic solutions are now considered obsolete. The standard method of induction of labour is by oxytocin infusion [1, 3]. Oxytocin a traditional means of labour induction familiar to most obstetricians is safe and effective. Important predictors of labour outcome with oxytocin administration include the gestational age, parity and the pre-labour cervical state [4, 5, 6]. The outcome of labour induction correlates well with the state of the cervix at the beginning of the induction process [5, 6]. Induction of labour in the presence of an unripe cervix is frequently associated with failure and recourse to caesarean section. However, in the face of an intrauterine death, an abdominal delivery is not a favoured option in the presence of failed induction of labour.

Various methods of pre -labour cervical manipulation have been reported**.** Prostaglandins or their analogues are currently favoured, followed by osmotic dilators and the Foley catheter. Initial pharmacological efforts to effect cervical ripening focussed on cervical or vaginal prostaglandin E_2 preparations (Dinoprostone). Subsequently, other pharmacological methods developed include either oral or vaginal prostaglandin E_1 analogues (misoprostol). Prostaglandin is used either as a gel or pessary. It is however expensive and unavailable to majority of women in the third world environment. Complications with the therapy are frequently reported. Misoprostol (Cytotec® PGE1) is an analogue of PGE_1. It is effective and less expensive than PGE_2 and offers better results at less cost.[7, 8.]

Cervical dilators are also important in pre-labour cervical manipulations. They include Foley catheter with inflated balloon, laminaria tents and Dilapin or osmotic dilators [7]. The osmotic dilators are placed in the endocervix. Other methods of cervical ripening

include membrane sweeping. The digital separation of the chorioamniotic membranes from the wall of the lower uterine segment causes release of prostaglandins locally and thus causes ripening of the cervix. Stripping of the membranes also excites autonomic neural reflex and/or cause the release of maternal oxytocin from the posterior pituitary [9, 10]

There have been a number of studies comparing pharmacological techniques of cervical ripening such as oral and vaginal misoprostol with mechanical techniques such as extra amniotic infusion through a trans-cervical 30 mls Foley catheter (albeit with a live fetus) [11, 12, 13]. This study presents comparative data on the effectiveness of misoprostol and the Foley catheter on pre-labour cervical manipulation following intrauterine fetal death in Irrua, Nigeria. Also assessed were labour outcome and post delivery sequelae. The cost-benefit analysis of the two methods was done and the specific advantages/disadvantages of the different methods are highlighted

Materials and Methods

This was a study of patients with a diagnosis of intrauterine fetal death after the 24th week of gestation that had induction of labour from January 2000 to December 2004 at the Irrua Specialist Teaching Hospital. The department has a protocol for management of patients with intrauterine fetal death. All patients with a Bishop score less than 5 requiring pre-induction cervical ripening were included, except those with a contraindication for vaginal delivery. Also excluded were those with a previous caesarean section or abruptio placenta. Intrauterine death was confirmed in all cases by ultrasound scan.

The protocol for management involved a detailed history, clinical examination and other specific investigations such as complete blood count, Rhesus factor and blood type, urinalysis, Venereal Disease Research Laboratory (VDRL) test, prothrombin time and partial thromboplastin time kaolin (PTTK). A preliminary endocervical swab and urine culture was obtained. All patients were admitted into the hospital prior to the initiation of therapy and the pre-induction Bishop score was assessed and recorded. In the five years of the study, patients had cervical ripening with either misoprostol or Foley catheter. Consecutive recruitment of patients was done with random allocation of patient to the two treatment arms. Patients who had cervical ripening with the combination (misoprostol and Foley catheter) were excluded from the analysis

The Foley catheter bulb was usually inflated with 30 mls of sterile water after being passed into the cervical canal. The Foley catheter is inserted at about 2000 hours and kept in situ for 10-12 hours. The Bishop score was then reassessed and if the score was still 4 or less, the procedure was repeated. The maximum number of Foley catheter insertions permitted was 4. This is because of the fear of spontaneous rupture of membranes with repeated insertion. If the cervix remained unfavourable, oxytocin induction was commenced, irrespective of the cervical state.

Cytotec (misoprostol). 100-200 micrograms (depending on gestational age) was inserted as a pessary every 4 hours up to a maximum of 6 insertions. Further medication was withheld with the occurrence of spontaneous rupture of membranes, entry into active phase of labour, or a "prolonged contraction response. For gestations of 24-34 weeks, 200 microgram of intra-vaginal misoprostol was administered at four hourly intervals. Gestations over 34 weeks were given a similar regimen but a reduced dose of 100-microgram misoprostol. The woman remained recumbent for at least 30 minutes following application. Patients were closely monitored for periods ranging from 30 minutes to 2 hours. If there was no change in uterine activity, she was transferred to the ward. When contractions occurred, they were usually apparent in the first hour and showed peak activity in the first 4 hours

Oxytocin induction was commenced if the Bishop score reached 5 and above. The minimum safe interval between misoprostol and the initiation of oxytocin was 6 to 12 hours. Induction of labour commenced at 0800 hours. Intravenous oxytocin infusion (with an oxytocin concentration of 5 i.u per ml of 5% dextrose) was set up. The initial flow rate of 2 milliunits per minute was increased stepwise every 30 minutes and titrated against the contractions. The fetal membranes were normally kept intact until the second stage of labour. Labour progress is closely monitored using the partograph with vaginal examination every 8 to 12 hours. Maternal pulse, blood pressure, body temperature and respiratory rate were monitored. The third stage of labour was actively managed. The oxytocin infusion was continued for 2 hours post partum. The products of conception were sent for histopathological study.

The study compared the personal and pregnancy characteristics for patients having pre-induction cervical manipulation with Foley catheter or with Misoprostol .

For the purpose of analysis, the patients were categorised by personal characteristics such as age and parity, as well as by pregnancy factors such as gestational age, diagnosis-intervention interval, probable cause of death, duration of cervical ripening, pre-induction Bishop scores, mean oxytocin dose, mode of delivery, post delivery complications and duration of

hospital stay. Statistical analysis was done using the t- test and the chi square test. The level of significance was set at $p < 0.05$

Results

During the 5 years of the study (January 2000 to December 2004), there were a total of 2943 deliveries out of which 157 patients were confirmed to have a diagnosis of fetal death *in utero* after the twenty fourth week of gestation. A total of one hundred and twenty one patients (121) were recruited. Thirty-six patients were excluded because they did not meet inclusion criteria.. Also excluded from analysis were patients with incomplete data. Sixty five (65) had cervical manipulation with intra-cervical Foley catheter (Group A) while fifty-six had intravaginal misoprostol for cervical ripening (Group B).

The clinical characteristics of the 121 patients involved in the study are as shown in Table 1. There was no statistically significant difference between the two treatment groups with respect to age, parity, gestational age and Bishop scores on admission. The mean Bishop scores on admission for the two groups was 3. Majority of the patients (94.8%) had a successful cervical ripening with either misoprostol or intra-cervical Foley catheter. Failure of cervical ripening occurred in 7(5.8%) of the patients. The duration for cervical ripening was similar in the two treatment groups. Seventy four percent (74%) of patients in the two groups had improvement in Bishop score within 24 hours

Table 3 presents a summary of the labour outcome. The difference in labour outcome was not statistically significant. The mean induction delivery intervals for the two treatment groups were 13.88 hours for patients treated with Foley catheter and 14.1 hours for patients treated with misoprostol respectively. Prolonged labour (duration in excess of 16 hours) occurred in 14 (21%) of the patients treated with Foley catheter and 11(19.6%) of the patients treated with misoprostol. There was no significant difference between the two groups with respect to mean oxytocin dose, mode of delivery and complication rates. The mean oxytocin dose was 12.78 I.U for the misoprostol group and 14.63 I.U for the Foley catheter group. The vaginal delivery rate for the two groups was 85.1%. The instrumental delivery rate was 8.3% while the destructive operation rate was 4.1%. The caesarean section rate was 2.4%. The differences in the mode of delivery did not reach statistical significance. The overall post partum complication rate was 4.1%. The mean duration of hospital stay varied between 5 to 6 days the differences in the complication rate and duration of hospital stay did not reach statistical significance.

Table 1: Clinical Chracteristics

	Group A	Group B	*p*
Mean Bishop Score on Admission	3.41	2.67	N/S
Pre-induction Bishop Score			
4	3(4.6%)	4(7.1%)	N/S
5-8	53(81.5%)	50(89.3%)	N/S
9-13	9(13.8%)	2(3.6%)	N/S
Duration of Cervical Ripening			
24hrs	48(73.8%)	42(75%)	N/S
24-48hrs	14(21.5%)	10(17.9%)	N/S
48hrs	3(4.6%)	4(7.1%)	N/S

Table 2:

Bishop Score and Duration of Cervical Ripening.

	Group A	Group B	*p*
Mean Induction Delivery Interval(Hrs)	13.88 4	14.1 5.9	N/S
Precipitate Labour	0	1	N/S
Mean Oxytocin Dose (I.U)	12.75	14.63	N/S
Mode Of Delivery			
Spontaneous Vaginal Delivery	55(84.6%)	48(85.7%)	N/S
Forceps/ Vacuum	6(9.2%)	4(7.1%)	N/S
Destructive Operation	2(3.1%)	3(5.4%)	N/S
Caesarean Section	2(3.1%)	1(1.8%)	N/S

Table 3: **Clinical Summary**

Complications	Group A	Group B	*p*
Genital Tract Infection	1	0	N/S
Postpartum Haemorrhage	2	0	N/S
Retained Products of Conception	0	2	N/S
Uterine Rupture	0	0	N/S
Mean Duration of Hospital Stay	6(2.54)	5(3.24)	N/S

Table 4:

Postpartum Complications and Duration of Hospital Stay

	Group A	Group B	*p*
Mean Age	29.5 6.1	28.6 5.1	N/S
Parity Distribution			
0	10	14	N/S
1	14	13	N/S
2	13	11	N/S
3	14	10	N/S
4	6	5	N/S
5	8	3	N/S
Gestational Age	34.7 3.9	35 4.41	N/S

Discussion

The incidence of intrauterine fetal death in this study was 53.34 per 1000 total births. This is comparable to the figure from other parts of West Africa but much higher than those from the more developed parts of the world [1, 2, 3] The management of patients with intrauterine fetal death has always been a difficult problem for the obstetrician. The most common approach was expectant waiting with the rationale that spontaneous labour and delivery occurs in 80% of women within two weeks and only 10% remained undelivered for more than three weeks. However the gestational age at the time of death influences the probability of expulsion within a given time frame. The more remote from term, the longer the time required [1,3, 14, 15]. Expectant waiting is psychologically distressing to the mother and there is the added risk of hypofibrinogenemia if the products of conception are retained for 4 weeks or more [16].

Watchful expectancy is no longer favoured because of the plethora of methods for cervical manipulation. In this study the two methods used for cervical ripening were the intracervical Foley catheter and misoprostol. The patient's characteristics for the two treatment groups were similar. There was no statistical difference between the two groups with respect to age, parity gestational age and admission bishop score. The low admission bishop score was a prerequisite for admission into the study. The Foley catheter and misoprostol were equally effective in cervical ripening as reflected in the pre-induction (post cervical ripening) Bishop scores for the two groups, as observed differences did not reach statistical significance. This agrees with finding of various other authors [11, 12, 13, 17, 18, 19].

The ideal method for cervical ripening should be effective within 24 hours, simple, non-invasive and must not stimulate labour excessively and must not compromise the mother or the fetus[7]. The importance of a short diagnosis-intervention interval is underscored by the findings of excessive anxiety and emotional strain in the patients if diagnosis–intervention interval is in excess of 24 hours [20].

A Foley catheter passed into the cervical canal lies between the membranes and the internal os. The procedure enhances prostaglandin release from the membranes and the adjacent decidua to initiate cervical softening and dilatation. Misoprostol acts like prostaglandins by causing dissolution of collagen bundles, with increase in sub-mucosal oedema (increased water content). These changes are similar to those observed in early labour [7] The pre-induction cervical ripening time for the two methods was comparable to the ideal. Majority of the patients had successful cervical ripening with either misoprostol or intra-cervical Foley catheter treatment. This is similar to observation by others [11, 12, 13, 17, 18, 19].

Patients with persistently unfavourable cervix following treatment with either of the two methods who had oxytocin induction despite the cervical state

were included in the study. However patients who had a combination of the two methods in an attempt to improve the cervical state were excluded from the study. The combination of mechanical ripening like a transcervical Foley balloon to intravaginal misoprostol does not improve the efficiency of pre induction cervical ripening. Mechanical and pharmacologic cervical ripening agents appear to act independently rather than synergistically [12,13]

The study also confirmed the relationship between the pre-induction cervical state and a successful induction [3, 4, 21]. The mode of delivery in the two treatment groups was similar. Complications in the puerperium were few. The low incidence of post partum haemorrhage is attributable to the policy of active management of the third stage practised in this unit. There were no significant differences in the routes of delivery. These observations are similar to findings by various other authors [11,12,13,17,18,19]

The other advantages of the two methods of treatment including cost are worth highlighting. Misoprostol cost US$0.36/100 micrograms and is cheaper than dinoprostone (US$75/0.5 mg). It is stable at room temperature and easily administered orally or placed into the vagina but not the cervix. Initial studies suggested that misoprostol tablets placed into the vagina were either superior to or equivalent in efficacy compared with intra-cervical prostaglandins $E_{2\ GEL}$. Oral misoprostol is equally effective[16]. Foley catheter balloon treatment is also cheap, with a cost lower than 1 dollar. Studies done conclude that it results in a greater increase in bishop score in less time than vaginal prostaglandins E_2 [12, 13]. However the Foley catheter requires moderate skills to be inserted correctly and insertion techniques should be sterile unlike misoprostol and prostaglandin pessary. Facilities for asepsis may be lacking in many poor resource environments. The principal advantage is the fact that contractile abnormalities are fewer with the Foley catheter [14, 15]. The minimum safe intervals between misoprostol and the initiation of oxytocin have not been established. According to manufacturer guidelines, oxytocin induction should be delayed for 6 to 12 hours. This is unlike with the Foley catheter when oxytocin titration can be started immediately. Thus undue delay may occur with misoprostol if this guideline is adhered to [16].

The very favourable outcome with active intervention in situations of intrauterine death, even in patients with unfavourable cervix, is a cause for optimism in relieving the distress of these patients. Pre-induction cervical ripening with misoprostol or Foley catheter balloon are equally effective, safe and cheap. They have been found in many studies to be as, if not more, effective than prostaglandins. The complications with them are minimal. They offer the obstetrician greater latitude in management of intrauterine foetal death in the presence of an unfavourable cervix. Delays in commencing treatment with attendant adverse maternal medical and psychological is cut to a minimum.

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