Vaginal Misoprostol For Induction of Labour in Women With Intrauterine Fetal Death at Aba, South-Eastern Nigeria

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Abstract

Context: Intrauterine fetal death is a common obstetric problem in the developing countries of the world. Its management by induction of labour in poor resource settings requires an oxytocic agent that is not only effective but also cheap and requiring less supervision.
Objective: To evaluate the efficacy and safety of intra-vaginal misoprostol for induction of labour in women with intrauterine fetal death.
Design, Setting and Subjects: A prospective descriptive study carried out at Nigerian Christian Hospital, Aba, Nigeria from July 2001 to June 2004. The study group consisted of 67 cases of intrauterine fetal death seen at the maternity unit during the study period.
Intervention: Intra-vaginal administration of misoprostol.
Main Outcome Measures: Successful induction rate; induction Delivery interval; Adverse reaction to misoprostol.
Results: The Successful induction rate was 85.1 percent. The mean induction delivery interval was 18.43 hours; with 77.2 percent of the parturients delivering within 24 hours of induction. The mean dose of misoprostol used was 244.74μg; with 70.2 percent of the cases requiring 200μg of misoprostol or less. Favourable Bishop's score was significantly associated with lower dose of misoprostol ($P< 0.001$) and shorter induction-delivery interval ($P< 0.001$). There were 7 cases of retained placenta, 4 cases of primary post-partum haemorrhage but no cases of gastrointestinal side effects or ruptured uterus.
Conclusion: Misoprostol was effective and safe for induction of labour in parturients with intrauterine fetal death. This study supports other studies that have demonstrated the efficacy and safety of misoprostol in women with intrauterine fetal death.

Key Words: Intrauterine Fetal Death, Induction of Labour, Misoprostol [Trop J Obstet Gynaecol, 2006, 23:141-145]

Introduction

Intrauterine fetal death is a common problem in the obstetric practice of developing countries such as Nigeria.[1,2,4,5] It may be complicated by consumptive coagulopathy, amniotic fluid embolism, emotional distress and intrauterine infection if the membranes are ruptured.[2,3,6] Although a significant number of women with intrauterine fetal death will go into spontaneous labour within several weeks, many do not.[3] In addition, after the diagnosis, the social pressures and emotional aspects of delivery are enormous. Consequently, medical induction to expel the dead fetus is recommended.[1,2,3] Oxytocin infusion is widely accepted as a safe and effective labour induction method.[1,5,7] Unfortunately, its success is highly dependent on the gestational age and favourability of the cervix and most intrauterine fetal deaths occur during the second or early third trimester (when response to oxytocin is less).[1,7,8] Moreover, it is associated with cost, storage administration and supervision problems. [1,5,8]

Intra-vaginal prostaglandin E2 (Prostin, UpJohn) is an alternative to oxytocin for induction of labour in intrauterine fetal death as it is effective and safe in both cervical ripening and pre-term induction of labour.[7,8,9,10] Its use, however, has attendant problems. It is expensive, largely unavailable and is associated with special storage and transportation requirements that make it difficult for use in poor resource settings like Nigeria.[7,9,10,11]

The Department of Obstetrics and Gynaecology, Nigerian Christian Hospital, Aba, receives most of the cases of intrauterine fetal death within Aba and its environs. These represent about 6.07% of the 840 deliveries conducted annually in this hospital. In our environment, typical of most of the third world countries, the questions of cost, conditions for storage of drugs, and supervision during attempted induction of labour are crucial. Therefore the ideal drug would be one that is cheap, easy to administer, stable at room temperature, with long shelf life and that does not require direct supervision during induction.

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Misoprostol, (Cytotec, Searle, England) a prostaglandin E1 analogue may be closer to meeting the above criteria.[11,12,13,14,15,16,17,18,20] It has been shown to be effective both orally and vaginally for inducing labour women with live fetuses.[11,12] There are however few reports for its use in intrauterine fetal death in Nigeria. The objectives of this study, therefore, were to evaluate the effectiveness and safety of intra-vaginal misoprostol for induction of labour in intrauterine fetal death in a Nigerian mission hospital.

Materials and Methods

This is a report of a 36-month prospective descriptive study, evaluating the effectiveness and safety of misoprostol used for induction of labour in women with intrauterine fetal death at Nigerian Christian Hospital Aba, Abia State. The study period was from July 2001 to June 2004. Sixty-seven women with ultrasonically proven intrauterine fetal death above 18 weeks of gestation and who gave informed consent were recruited for the study. Patients excluded from the study included those with previous uterine scars, strong/regular uterine contractions, abnormal lie/presentation, pelvic tumor and major degree placenta praevia.

Obstetric history, physical and obstetric examination, including Bishop's scores, were carried out and recorded at admission. Gestational age was calculated from the last menstrual period or from earlier sonogram of the viable pregnancy.

The misoprostol used was Cytotec® (Searle England) sold in 200 microgram tablets for oral consumption. The tablets were cut into quadrants with a blade, so that each part would contain 50 micrograms of misoprostol.

After admission and selection for the study 50 microgram of misoprostol was inserted into posterior vaginal fornix of the parturient every four hours until the parturient went into active labour. If uterine contractions did not start after the second dose, the dose of misoprostol was increased to 100μg every four hours. Insertions of misoprostol were continued for up to 48 hours after which the parturient was re-evaluated. Each patient was observed for vital signs, uterine contractions, progression of labour, fever, nausea/vomiting, diarrhoea, primary postpartum haemorrhage and occurrence of precipitate labour.

Induction delivery interval was defined as the time from the initial administration of misoprostol to the complete delivery of the fetus.

Data entry and analysis were carried out with the SPSS 11.1 for Windows Statistical Package (SPSS Inc., Chicago, Illinois, USA). Data was summarized using mean, standard deviations, ranges and frequency tables. Comparison of the means of continuous variables was performed with the students't-test. P-values of <0.05 were considered to be statistically significant.

Results

The general characteristics of the parturients and of the process of induction are shown in Table 1. The mean maternal age was 28.6 years (range 18-45). Thirty-four (50.5%) of the parturients were less than 30 years. The modal parity was 0 (range 0-8). Grand multiparity comprised 15% of the cases. The gestational age ranged from 18-49 weeks. Twelve (17.9%) of the cases were less than 28 weeks while the remainder (82%) were 28 weeks or above. The majority of the cases (61.2%) had unfavourable Bishop Score.

The overall mean induction delivery interval was 18.43 hours. Forty-four (77.2%) of the parturients delivered within 24 hours of induction with misoprostol. The overall mean dose of misoprostol used was 244.74μg. Forty (70.2%) required 200μg or less. Ten parturients could not initiate uterine contractions after the second dose of their 50μg misoprostol and therefore the dose was increased to 100ug. Six of these ten had successful induction.

Of the 67 parturients with intrauterine fetal death 57 (85.1%) had vaginal deliveries (successful induction). 10 (14.9%) had failed induction. Failed induction cases were defined as those who had no initiation of contractions after 48 hours of being on induction with misoprostol and those whose inductions were terminated by caesarean section. Five (50%) of the 10 patients who had failed induction had premature rupture of membranes (PROM) before induction was commenced. The successful induction rate for cases less than 28weeks was 91.67% while that of those 28 weeks and above was 83.64%. This difference was not statistically significant P=0.479. The successful induction rate of nulliparous cases was 77.78% compared to 90% for multipara (P=0.294). Those with unfavourable Bishop's score (0-5) had successful induction of 85.37% which was comparable to the 84.62% for those with favourable Bishop's score ($\geq$6); P= 1.000.

A favourable Bishop's score was significantly associated with shorter induction-delivery interval and lower dose of misoprostol ($P<0.001$): (Table II and III). Gestational age of less than 28 weeks was associated with neither a significantly higher induction-delivery interval nor higher dose of misoprostol ($P> 0.1$). (Table II and III). The mean birth weight of babies born was 2.43kg (standard deviation 1.30).

There were seven cases of retained placenta, 4 cases of primary post-partum haemorrhage and 1 case of precipitate labour. Hypercontractility, uterine rupture and gastrointestinal effects such as vomiting and diarrhoea were not observed. The 3 maternal deaths were secondary to hepatic encephalopathy, giving a maternal mortality rate of 4.5%.

Discussion

Misoprostol was effective in induction of labour in parturients with intrauterine fetal death with a successful induction rate of 85%. The mean induction delivery interval was 18.43 hours, with 77.2 percent of the parturients delivering within 24 hours of induction. The mean dose of misoprostol used was 244.74μg, with 70.2 percent of cases requiring 200μg of misoprostol or less. Favourable Bishop's score was significantly associated with lower dose of misoprostol ($P<0.001$) and shorter induction-delivery interval. Gastrointestinal side effects and ruptured uterus were not observed.

Table 1:

Selected Characteristics of 67 patients, Dose of Misoprostol and Induction Delivery Interval in Intrauterine Fetal Death.

Parameter	No	Percentage (%)	Mean	SD	Range
Age					
< 20	1	1.50	28.6	5.28	18 - 45
20 - 29	33	49.00			
30 - 39	32	48.00			
≥ 40	1	1.50			
Parity					
0	27	40.3			
1 - 4	30	44.8	1.79	2.08	0 - 8
≥ 5	10	14.9			
Gestational Age					
< 28	12	17.9			
28 - 36	24	35.8	34.27	6.99	18 - 49
≥ 37	31	46.3			
Bishop Score					
0 - 5	41	61.2	5.25	2.85	0 -11
6 - 13	26	38.8			
Induction Delivery Interval					
≤ 12 hours	22	38.6			
13 - 24 hours	22	38.6	18.43	16.39	2.37 - 96.00
> 24 hours	13	22.8			
Dose of Misoprostol					
50 - 200 ug	40	70.2			
250 - 400 ug	9	15.8	244.74	235.22	50 - 1400
> 400 ug	8	14.0			

Table 2: Association of Parity, Gestational age and Bishop's score with Induction Delivery interval.

	Mean	SD	Significance	No
Parity				
0	13.67	7.60	P < 0.05	21
≥ 1	21.21	19.37		36
Gestational Age				
< 28 weeks	16.13	8.97	P > 0.10	11
≥ 28 weeks	18.98	17.74		46
Bishop Score				
0 5	23.60	18.81	P < 0.001	35
≥ 6	10.20	5.26		22

Table 3: Association of Parity, Gestational age and Bishop Score with Dose of Misoprostol.

	Mean	SD	Significance	No
Parity				
0	195.24	143.97	P = 0.10	21
≥ 1	273.6	272.68		36
Gestational Age				
< 28 weeks	322.73	183.53	P >0.10	11
≥ 28 weeks	226.09	243.98		46
Bishop Score				
0 - 5	318.57	271.73	P < 0.001	35
≥ 6	127.27	66.77		22

This study was a prospective description of an open trial with misoprostol and is obviously better than its retrospective equivalent. A randomized comparison of misoprostol with standard agents such as oxytocin and prostaglandin E2 would have made a better study. The observation in this study that nulliparity was significantly associated lower induction-delivery interval is suprising and might be associated with the relatively small sample size and a few skewed observations in the multiparity group that affected the mean.

The 85% successful induction rate observed in this study is less than the 100% reported by others.[1,2,4,5] The latter studies however used higher dosage regimens. The mean induction delivery interval of 18.43 hours observed in this study is comparable to that of some studies.[3,4] It is however longer than that observed in some studies.[1,2,5] It is also longer than the 8.5 hours observed in a previous report using a combination of mifepristone and misoprostol in the management of intra-uterine fetal death.[6] The shorter induction-delivery interval associated with favourable Bishop's score (≥6) in this study has been reported by others.[1,2,5] The difference in the induction delivery interval observed between those with unfavourable and favourable Bishop's score might be a reflection of the time required to ripen the cervix before the commencement of the active phase of labour. The majority of the parturients in this study required 200ug of misoprostol or less. This is in accordance with other reports.[1,2,5,12]

The absence of gastrointestinal side effects as observed in this study has been reported by others who utilized the vaginal route of administration [2,4,5,14,15,16]. The commonest complications recorded in this study were retained placenta and primary post-partum haemorrhage. Although ruptured uterus has been reported in some studies,[21] none occurred in this series despite the fact that about 15 percent of the study group were grand-multipara. Some studies comparing the efficacy and safety of misoprostol with other agents have reported the superiority of misoprostol over oxytocin and prostaglandin E2.[1,5,9,10] Most studies comparing the routes of administration of misoprostol have reported a shorter induction delivery interval with the vaginal route.[14,15,18,19] However a study from Thailand showed that misoprostol (400μg given orally every 4 hours) was more effective than misoprostol 200μg given vaginally every 12 hours) for termination of second and third trimester pregnancy with intrauterine fetal death.[3]

The maternal mortality rate of 4.5% associated with series was due to hepatic encephalopathy, a condition well known for its high case fatality rate.

In view of the growing body of evidence that has shown that misoprostol is cheap, easy to administer, stable at room temperature with no requirement for direct supervision during induction, [1,2,13,16,17,20] its efficacy and safety as observed in this study and other studies mean a dramatic change and improvement in the management of cases of intra-uterine fetal death in poor resource settings like Nigeria. For the pharmaceutical companies, this creates the opportunity to develop misoprostol for reproductive health indications as the currently available misoprostol was meant for oral treatment of gastric ulcer.[17,20]

Most studies that have investigated the use of misoprostol had used varying dosage regimens. There is therefore need for further research to clarify optimal dosage regimens.

Conclusion

Misoprostol was effective and safe for induction of labour in parturients with intrauterine fetal death. This study supports other studies that have demonstrated the efficacy and safety of misoprostol in women with intrauterine fetal death.

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