The Use of Misoprostol for Induction of Labour in a Low-Resource Setting

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Abstract

Context: Several studies have been done on the effect of misoprostol on the pregnant uterus. These have generally been in well-endowed hospitals that can afford cardiotocographs, intrauterine monitors, scalp electrodes and related items of equipment. Similar studies are needed in settings that would benefit best from the cheapness and stability of the drug

Objective: To assess the efficacy and safety of misoprostol for induction of labour in a health care facility with limited resources.

Study Setting and Subjects: An observational descriptive study at Korle Bu Teaching Hospital, Accra, Ghana on one hundred and sixty patients requiring induction of labour.

Methods: One hundred and sixty women had labour induced using 50μg of misoprostol inserted vaginally at four hourly intervals. The patients were monitored with the standard clinical tools, including intermittent auscultation with the Pinard stethoscope.

Results: Eighty-three percent of the women had vaginal deliveries while the remainder had caesarean sections for various obstetric indications. Patients who had uterine stimulation for premature rupture of membranes (PROM) responded very well to misoprostol, with majority requiring only a single 50μg dose to go into active labour. Women with sickle cell disease showed no adverse effect to misoprostol responded in a manner similar to the normal population.

Conclusion: We have confirmed that misoprostol can be used safely for induction of labour in settings where there are no items of sophisticated monitoring equipment. Patients with sickle cell disease and premature rupture of membranes can have successful labour induction with misoprostol with no adverse effect.


Introduction

Induction of labour is one of the most important interventions in obstetric practice. Although the biochemical events associated with labour have been studied, the actual trigger mechanism that initiates labour in humans is not known. Alterations in the levels of estrogen and progesterone have been proposed without firm evidence. Prostaglandins are now the focus of attention as important mediators and possible initiators of uterine contractions. Hence, the various methods used for ripening the cervix before induction of labour are either prostaglandin or agents leading to the release of prostaglandin.

Induction of labour is indicated when continuation of a pregnancy would put the mother and/or the fetus at risk. The success of an induction depends on the nature of the cervix at the beginning of the induction. Complications are encountered if an induction is started on an unfavourable cervix. Various formulations have been used to ripen the cervix, the most popular being intravaginal prostaglandin E2 (Prostin, Upjohn). However the use of intravaginal PGE2 has its attendant problems. It is not cheap and has special storage and transportation requirements that make it difficult for use in deprived areas where refrigeration and electricity are erratic.

The ideal induction agent would be one that is efficient, cost effective, easy to store, non-invasive, without side effects, and whose effects on mother and fetus can be readily monitored. Misoprostol (Cytoyce®; Searle, Chicago IL, USA) is a PGE1 analogue (15-deoxy-16-hydroxymethyl PGE1) approved for the treatment of peptic ulcer. It has no significant vasoactivity in humans1 and is cheap. It is active both by the oral and vaginal route for the induction of labour2,3 and can be stored at room temperature with a shelf life of several years3. Its safety has been established by several pharmacological studies and extensive experience in its use as an anti-ulcer drug4. Absorption is very rapid and it can be detected in the circulation within two minutes of oral ingestion5. Bioavailability after vaginal insertion is three times that of the oral dose6. It ripens the cervix and also enhances uterine contractions, thereby reducing the need for oxytocin7. These factors make misoprostol very attractive as an agent for induction of labour.

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Studies on the effect of pH on the efficacy of misoprostol have yielded conflicting results. Thus, its use for induction of labour in patients with premature rupture of membranes requires further investigation since the liquor amnii alters the pH of the vagina.

Most of the studies that have been published on the effect of Misoprostol on the pregnant uterus had been conducted in well-endowed hospitals that can afford cardiographs, intrauterine monitors, scalp electrodes and the like, and not in areas which would benefit best from the cheapness and the stability of the drug. The aims of this study, therefore, were to assess the efficacy and safety of misoprostol for labour induction in patients with live fetuses, in a setting with limited resources; and to assess its effects in patients with premature rupture of membranes.

Materials and Methods

This study was conducted in the University Teaching Hospital of a city with a population of about 3 million people. About 12,000 babies are delivered in the hospital annually. The hospital was primarily set-up as a tertiary referral hospital but now serves as the main provider of obstetric services for complicated and uncomplicated cases from the city and the surrounding rural areas. Nurse-midwives, residents, and obstetricians provide care for pregnant women. The study period was from May 1999 to November 2000 and at the time of the study, there were no facilities for electronic fetal monitoring, intrauterine pressure monitoring, scalp electrodes or fetal blood pH for assessment of the fetus.

Misoprostol had been introduced to our department a year before the commencement of the study. A departmental meeting was held to decide on a protocol for its use after reviewing the literature. Outcomes were discussed at subsequent meetings. One hundred and sixty consecutive women admitted for induction of labour for medical or obstetric reasons were included in the study after informed consent had been obtained from them.

Patients were excluded from the study if they had:
(a) Previous uterine surgery e.g. myomectomy and cesarean section,
(b) Multiple pregnancies,
(c) A baby whose presenting part is other than vertex,
(d) Bishop’s score of 6 or higher, or
(e) Fetopelvic disproportion.

The patients had cervical scoring done on the morning of the induction and a quarter of the 200 µg tablet of misoprostol (Cytotec) was inserted into the posterior fornix of each patient every four hours until the patient went into active labour; that is, having two to three contractions in ten minutes, each lasting greater than thirty seconds or the cervix was three centimetres dilated with 80% effacement. In the event that the maximum of 200µg was reached, the patient was to be reassessed and oxytocin drip set up not earlier than 6 hours after the last dose of misoprostol was prescribed, if the cervix was considered favourable. Each baby was monitored closely with auscultation of the fetal heart using the Pinard stethoscope every 15 minutes in the first hour after insertion of the drug and every 30 minutes afterwards. It had been noticed prior to this study that there were a few instances of fetal tachycardia in the first hour after inserting misoprostol, even when the mother was not having any contractions.

The liquor was observed for meconium staining and surgical interventions were made if fetal tachycardia, bradycardia or late decelerations were noted that did not respond to resuscitative measures, whether meconium staining of liquor was present or not. Each patient was monitored for hyperstimulation, fever, tachysystole, and hypertonus. Tachysystole was defined as at least six contractions in ten minutes for two consecutive ten-minute periods. Hypertonus was defined as a single contraction lasting greater than two minutes. Hyperstimulation was defined as four or more contractions in a ten-minute period.

A maximum dose of 200µg was administered and if any patient had not gone into labour by then, the patient was to be re-evaluated. Artificial rupture of membranes was done at the next examination after the cervix exceeds three centimetres’ dilatation. Patients presenting with premature rupture of membranes had misoprostol inserted after a sterile speculum examination had confirmed the diagnosis together with an undilated cervix.

Results

One hundred and sixty (160) patients had induction of labour performed with misoprostol during the study period. Of these, 70% were induced on account of post-term gestations, 11.2% for sickle cell disease at term, and 9.4% each for hypertensive disorders in pregnancy and premature rupture of membranes.

The mean maternal age was 28 years (range: 16 to 40 years). The modal parity was 0 (range: 0 to 7). The gestational ages ranged from 32 to 42 weeks, with the majority of the patients having induction at 41 weeks. One hundred and thirty two patients (82.5%) had vaginal deliveries whilst (17.5%) had caesarean section for indications such as fetal distress (6%)
failed induction (4%), cephalopelvic disproportion (5%), chorioamnionitis (1%), and face presentation (1%). One patient did not go into labour after a total of 200µg was inserted. Artificial rupture of membranes was done and oxytocin infusion was set up 6 hours after insertion of the last tablet as the cervix was then favourable and the patient went into labour and delivered vaginally.

The number of 50µg tablets used per induction ranged from 1 to 4 (mean 2) for parous patients. Mean number of inserts for nulliparae was 3. The mean cervical score before treatment was 4.5 (SD: 1.44), improving to 9.8 (SD: 1.6) after a mean priming period of 8.0 (SD: 2.5) hours. The mean induction time from Cytotec treatment to delivery was 10.2 hours (SD: 3.8).

There were 21 sickle-cell disease patients who had induction of labour. Of these, 81% had vaginal deliveries and 19% were delivered by caesarean section for failed induction or fetal distress. Each of these patients made satisfactory recoveries post delivery and neither they nor their babies suffered any adverse effect.

Fourteen percent of the patients who had induction of labour on account of premature rupture of membranes (PROM) had caesarean sections. Active labour was achieved with insertion of only one 50µg dose in all but 4 of these cases. Of the exceptions, one was a patient who had a maturity of 32 weeks, two had sickle cell disease, and the fourth had PROM at term. Complications included fetal distress in labour, hyperstimulation, and precipitate labour and one patient had a ruptured uterus. No patient complained of nausea and vomiting, or fever. Fetal distress requiring surgical intervention occurred in 6% of the patients. In each of these patients, management was initially conservative using nasal oxygen, adequate hydration and nursing on the left side. Caesarean sections were done when these measures failed to correct the adverse fetal cardiac activity. Doses of misoprostol associated with these cases of fetal distress range from 50 to 150µg. All except 2 of the babies had five-minute Apgar scores of 9 or more.

Hyperstimulation occurred in four patients and these were managed successfully by an infusion of normal saline. Precipitate labour (delivery less than two hours after onset of labour) occurred in three patients, two of who had PROM at term. There were no cases of tachysystole or hyper tonus.

Eighty percent of the patients studied were between para 0 and 2. Grandmultiparous women (para 5 and above) formed seven percent and they had successful induction of labour without any evidence of uterine rupture. One patient, para 2, was noticed to have a ruptured uterus after vaginal delivery of a live infant and a hysterectomy was done. It was later discovered that she had had a previous termination of pregnancy that was associated with complications.

Discussion

Several authors have reported on the efficacy of misoprostol as a cervical ripening and induction agent. In comparison to other induction agents, it has proved to be cheaper, easier to handle and to transport. It is also less invasive, and more effective. These are advantages that make the drug have great appeal, especially in the third world where the cost of drugs, refrigeration and electricity cannot be taken for granted. However most of the studies of the use of this drug have been done under conditions that vary significantly from the conditions that exist in the third world, especially in the rural areas. In such areas, monitoring of labour is done with only intermittent auscultation of the fetal heart and clinical assessment.

Our study showed the mean length of induced labour to be 10.2 (SD: 3.8) hours. This is comparable to findings in another study which showed an induction-delivery interval of 11.1 (SD: 4.8) hours using extra-amniotic prostaglandin E2 administration compared to 14.9 (SD: 5.5) hours using amniotomy and oxytocin titration. This shows a reduction of approximately 25 per cent in the length of induced labour when a prostaglandin is used compared to syntocinon use. Other workers compared Foley’s catheter and prostaglandin gel and found no statistically significant difference between the two.

Sickle cell disease is commonly seen at the Korle Bu Teaching Hospital where 50 to 60 patients with the condition deliver every year. Owing to their susceptibility to infections, anaemia, and eclampsia, delivery by induction of labour is a very important option in their management. They usually have severe financial constraints and cannot afford the more expensive types of prostaglandin. That there was no adverse effect on any of the sickle cell patients and vaginal delivery was achieved in similar proportions to the normal population suggests that misoprostol can be used safely for labour induction in this category of pregnant women. However larger studies well-planned trials would have to be done to confirm this observation. The caesarean section rate of 17% was slightly higher than the 13-15% found in other studies. This may be due to the fact that the limited monitoring facilities available lowered the threshold for surgical interventions.

The management of premature rupture of membranes (PROM) at term in our hospital had been expectant...
management for 12 to 24 hours followed by induction of labour with synthetic oxytocin (syntocinon).

The disadvantage of this approach was that in patients with an unfavourable cervix, there was an increased risk of a failed induction. Conventional wisdom suggested that the use of intravaginal misoprostol would be unsuccessful, as the liquor would wash it away. Some studies had been done on the use of prostaglandin E2 in PROM but information on the use of prostaglandin E1 in PROM is sparse. Fourteen patients in this study had induction of labour for PROM and ten of these needed only a single 50μg dose to achieve active labour. Only one patient needed four doses to induce labour but this was for a 32 week old pregnancy. This reduced sensitivity may be due to the small number of oxytocin receptors associated with pregnancies of small maturity.

Induction with misoprostol in patients with one previous section for a non-repetitive cause was not attempted in this study. This was because as at the time of the study, the authors were not fully convinced as to the safety of misoprostol in a patient with a uterine scar. However, some investigators have successfully induced labour in patients attempting vaginal delivery after caesarean section (VBAC). One would however suggest that such inductions be carried out in well-equipped obstetric units.

References