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Case Series

Intravaginal misoprostol 100 µg for cervical ripening and induction of labour in nulliparous women with term pregnancy and unfavourable cervix: a case series report

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ABSTRACT

Cervical ripening is a prerequisite for induction of labour in women adjudged to have an unfavourable cervix. Misoprostol administered intravaginally has previously been shown to be effective for cervical ripening and labour induction. It is often used in dosages of 25 µg or 50 µg in single or repeated dose regimen as per guidelines. Higher doses or shorter dosing intervals were reportedly associated with a higher incidence of side effects, especially uterine hyperstimulation syndrome. Studies and clinical experience have shown that 50 µg dose was not as effective in nulliparous women as it was in multiparous women, which implies that this dose might not be optimal for nulliparous women. We report a series of seven carefully selected patients in whom we used 100 µg of misoprostol intravaginally for cervical ripening and induction of labour at term. We achieved a short induction delivery interval, had good improvement in Bishop's score, with less need for oxytocin augmentation and good safety parameters.

Keywords: Cervical ripening, Labour induction, Misoprostol 100 µg, Nulliparous women

INTRODUCTION

Induction of labour, the artificial initiation of uterine contractions after the age of foetal viability but before the onset of labour, is a common intervention during pregnancy in both developed and developing countries.[1] It is employed in a broad range of conditions in which prolongation of the pregnancy would endanger foetal or maternal wellbeing and where there are no contraindications to vaginal delivery.

Successful outcome of labour induction depends largely on the favourability of the cervix at the onset of induction, a successful vaginal delivery is less likely if the cervix is unfavourable (unripe) and may result in prolonged labour and caesarean section.[2,3] This has invariably made cervical ripening a prerequisite for induction of labour, in women adjudged to have an unfavourable cervix.

The last three decades have witnessed the use of prostaglandins as a very potent and reliable alternative to oxytocin in cervical ripening and induction of labour. Studies have shown that vaginal misoprostol (a synthetic prostaglandin) was more effective than placebo and oxytocin in bringing about vaginal delivery within 24 hours, but their use was associated with increased rate of uterine hyperstimulation and foetal heart rate abnormalities.[4,5]

Misoprostol administered orally or intravaginally has previously been shown to be effective for labour induction.[6] Misoprostol is much cheaper and stable under the tropical climate, it is easily stored and transported at room temperature, and therefore, suitable for use in developing countries. It has been used in dosages of 25 µg or 50 µg in single or repeated dose regimen.[7-11] Higher doses or shorter dosing intervals were reportedly

associated with a higher incidence of side effects, especially hyperstimulation syndrome.

Most guidelines for practice (FIGO, ACOG and NICE) recommend 25 µg vaginal misoprostol for induction of labour in term pregnancies. These recommendations are usually arrived at after review of available data, which is scarce for 100 µg. Research have proven 50 µg as a superior alternative to 25 µg, in effectiveness as well as being safe, and is being widely used in developing countries where the 25 µg tablets are hardly available.[8,9,12,13]

A randomized controlled trial showed that the 50 µg dose of intravaginal misoprostol was not as effective in nulliparous women as it was in multiparous women, for achieving the primary outcome of cervical ripening, which implies that this dose might not be optimal for nulliparous women.[12] Clinical experience at our Centre has also shown that the 50 µg dose was not often sufficient in nulliparous women, necessitating the conversion to 100 µg dose or outright commencement of induction of labour using 100 µg. We report a series of seven carefully selected patients in whom we used 100 µg of misoprostol intravaginally for cervical ripening and induction of labour.

CASE SERIES

We report a prospective series of 7 nulliparous women with pregnancies at term, and unfavourable cervix (modified Bishop's score [mBS] <7) who had cervical ripening and induction of labour using 100 µg of misoprostol inserted intravaginally, managed at the obstetric wards of the Rivers State university teaching hospital, a tertiary hospital in Port Harcourt, Nigeria. Consecutive, eligible, and consenting adult nulliparous pregnant women at term (gestational age between 37 and 42 weeks) with single live foetus in cephalic presentation and estimated foetal weight (EFW)<4 kg, who had obstetric or medical indication for induction of labour, with intact foetal membranes and unfavourable cervix (mBS≤6), with no known contraindication to vaginal delivery, were recruited. We excluded elderly (>35 years) nullipara, those with previous uterine scar, severe preeclampsia and eclampsia, antepartum haemorrhage, any contraindication to vaginal delivery, foetal growth restriction or abnormal foetal heart rate pattern on preinduction CTG, EFW ≥4 kg, multiple gestation, malpresentations and unstable lies, contraindication to receiving prostaglandins like asthma and glaucoma, those already having regular uterine contractions, and patients who refused to give consent.

After initial assessment in the antenatal clinic for suitability, eligible patients were educated about the study, they were fully informed about the nature and potential risks, and informed written consent obtained. Thorough general, systemic, and obstetric examination was done by an obstetrician. The bishop's score was recorded. Misoprostol (Cytotec) procured as 200 µg dosage pack was prepared and cut by the pharmacy using pill-cutter into half tablets of 100µg each. The misoprostol was inserted in the posterior vaginal fornix. A repeat vaginal examination was done after 6 hours and Bishop's score was reassessed, and the dose repeated, if necessary, only once. If a favourable cervix (mBS ≥7) is achieved, no further dose was deemed necessary and induction was continued with ARM and synchronous oxytocin titration, in the absence of active labour. Once the patient went into active phase labour, routine intrapartum management was performed.

Labour was defined as regular, painful uterine contractions with cervical changes. Uterine hyperstimulation syndrome was a combination of tachysystole and hypersystole. Tachysystole was defined as six or more contractions in 10 minutes and hypersystole as a single contraction of at least two minutes duration. The patients were monitored with cardiotocogram (CTG) when available and clinically on the partograph, and in the absence of CTG, a Sonicaid was used to monitor foetal heart rate every 15-30 minutes throughout labour. Any hyperstimulation was to be managed by changing the mother's position to left lateral, administering oxygen by face mask, giving terbutaline 0.25mg subcutaneously and irrigating the remnant of the drug immediately from the vagina using normal saline.

Outcome parameters evaluated were the cervical response in terms of the change in modified Bishop's score after first instillation or onset of active labour (defined as cervical dilatation >3 cm), the time interval from insertion to delivery, requirement of oxytocin augmentation, successful vaginal delivery and any side effects or intrapartum complications. Fetal outcome, foetal heart rate abnormalities, passage of meconium and Apgar scores were also noted. The summary of the findings is depicted in the table below:

Table 1: Patient characteristics.

Patient characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Average/ summary
Indication for induction	Postdate	Postdate	Postdate	PIH	GDM	Postdate	PIH	4/7 (57%) postdate
Maternal age (In years)	25	20	29	30	25	29	25	26
Gestational age (In weeks)	41	41	42	39	38	41	38	40
mBS at beginning	4	3	6	3	2	2	3	3.3

Continued.

Patient characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Average/ summary
mBS after 6 hours	6	4	11	10	8	9	12	8.6
Needed 2nd dose	Yes	Yes	No	No	No	No	No	2/7 (29%)
Induction-delivery interval (hours)	16	14	8	8	14	8	8	11
Mode of delivery/ indication for CS	SVD	CS-failed induction	SVD	SVD	SVD	CS-CPD @6 cm dilatation	SVD	2/7 (29%) CS rate
Birth weight (gm)	3200	3900	3400	3100	3300	3900	2600	3343
Apgar score- 1 and 5	8,9	9,10	9,10	8,9	8,9	9,10	3,5	1/7 (14%) asphyxia
Need for ARM/ oxytocin	Yes	Yes	No	No	Yes	No	No	3/7 (43%)
Hyperstimulation	None	None	None	None	None	None	None	Nil
FHR irregularity/ liquor	Nil and clear	Yes, but clear	Nil and clear	Nil and clear	Nil and clear	Nil and clear	Nil and clear	1/7 (14%)
Postpartum haemorrhage	None	None	Yes	None	Yes	None	None	2/7 (29%)

ARM-artificial rupture of membranes; CPD-cephalopelvic disproportion; CS-Caesarean section; FHR-foetal heart rate; GDM-Gestational diabetes mellitus; mBS-Modified Bishop's score; PIH-Pregnancy induced hypertension; SVD-spontaneous vaginal delivery.

DISCUSSION

All the women were delivered within 24 hours, with an average induction delivery interval of 11 hours. In majority of the women (71%) delivery was achieved after a single insertion of 100 µg vaginal misoprostol, with improvement of the initial Bishop's score above 7, and with only 2 of the 7 women (29%) requiring insertion of a second dose after 6 hours. Five of the women achieved vaginal delivery, out of the other two requiring caesarean section, one was for cephalopelvic disproportion after a successful induction and only one was for failed induction. Three of the women (43%) however required a follow up augmentation with oxytocin infusion. A previous study had shown that high dose of vaginal misoprostol (100 µg) resulted in a significantly shorter induction delivery interval, with reduced need for oxytocin augmentation and with no difference in the caesarean section rate, when compared with 50 µg.[14]

In terms of safety, there was no case of uterine hyperstimulation and meconium-stained liquor recorded, which is often the concern when using high dose of misoprostol, and this was an improvement to the 2% and 9.4% of hyperstimulation reported with the 100 µg dose in previous studies by Rockhead et al and Fletcher et al respectively.[15,16] There was however, one case of low (1-minute and 5-minute) Apgar score that required resuscitation and subsequent admission to neonatal intensive care unit, but this might not be attributable to the dose of misoprostol since there was no occurrence of hyperstimulation in the patient.

The previous study by Iqbal et al that compared 100 µg versus 50 µg dose regimens of intravaginal misoprostol reported no differences between the groups in safety parameters of uterine hyperstimulation, meconium staining and neonatal outcome.[14] No differences in Apgar scores and meconium passage between groups of 100 µg versus 50 µg have also been reported in two other studies.[15,17]

CONCLUSION

In summary, with misoprostol 100 µg we achieved a short induction delivery interval, had good improvement in Bishop's score, with less need for oxytocin augmentation and good safety parameters, when used in carefully selected nulliparous pregnant women with unfavourable cervix at term. While this finding cannot be used to advocate immediate change in policy, it warrants further research by way of a randomised controlled trial and a review of existing guidelines.

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