EFFECTIVENESS AND SAFETY OF VAGINAL MISOPROSTOL FOR INDUCTION OF LABOUR IN UNFAVOURABLE CERVIX IN 3RD TRIMESTER

Nasreen Abbasi, Nargis Danish*, Farah Shakoor, Zahida Parveen, Syed Ahmad Bilal**

Department of Obstetrics and Gynaecology, Frontier Medical College, *Women Medical College, **Ayub Medical College, Abbottabad, Pakistan

Background: The use of prostaglandin preparations with or without oxytocin infusion, is widely recognized and accepted as a standard method of induction of labour. It has been shown to reduce induction time and the risk of failed induction. The objective of this quasi-experimental observational study was to determine the effectiveness and safety of Misoprostol administered vaginally for induction of labour to achieve vaginal delivery. **Methods:** This study was conducted from October 2004 to October 2007. The study was conducted at Shaheena Jamil Teaching Hospital, Frontier Medical College, Abbottabad and Women and Children Hospital Abbottabad. A total of 6299 obstetric patients were received for delivery and 946 patients had to undergo induction of labour. Primary outcome measures were to address clinical effectiveness (delivery within 24-hours) and safety (uterine hyper-stimulation, Caesarean Section and serious Maternal Morbidity). Secondary outcome measures included neonatal outcome. **Results:** Out of 946 cases, successful vaginal deliveries were achieved in 843 (89.1%) cases. Time interval between induction and delivery was 4–24 hours. Oxytocin was required in 107 (12%) patients. Caesarean Section had to be done in 103 (10.8%) cases. The indications for Caesarean Section were foetal distress in 42 (40%), occipito-posterior position in 8 (7.7%), abruptioplacentae 2 (1.9%), cord around the neck 9 (7%), uterine hyperstimulation 6 (5.8%) and failure to progress in 20 (19%) cases. Admission to NICU was 28 (3.3%) and Neonatal deaths were 5 (0.5%). Postpartum Haemorrhage (PPH) was observed in 22 (2.3%) patients. There was no case of rupture uterus. **Conclusion:** Vaginal Misoprostol appears to be safe and effective for cervical ripening in 3rd Trimester. It helps vaginal delivery within 24 hours, does not increase incidence of Caesarean Section and has no adverse effect on foetal outcome. It could also be used in circumstances where extensive monitoring techniques are not available though close observation and vigilance is mandatory.

Keywords: Labour induction, Misoprostol, Vaginal, Postpartum Haemorrhage (PPH)

INTRODUCTION

Labour induction is one of the most frequent procedures in pregnant women. It is a major intervention in the normal course of pregnancy, with potential to set in motion a cascade of intervention, particularly Caesarean Section. However, with modern methods of labour induction, this risk appears to have diminished. The use of Prostaglandin preparations with or without oxytocin infusion is widely recognized and accepted as a standard method of labour induction, and has been shown to reduce induction time and the risk of failed induction.[1–2] However, natural prostaglandins are inconvenient to use, expensive and difficult to store as they require refrigeration.

Misoprostol tablet is a white round biconvex 10–11 mm in diameter. It has enteric coated core containing 50 mg diclofenac sodium, surrounded by an outer mantle containing 200 μg Misoprostol. Misoprostol is a synthetic analogue of naturally occurring prostaglandin E_1 originally manufactured for the treatment of peptic ulcer. It is a 15-deoxy,16-hydroxy,16-methyl analogue of prostaglandin E_1.[3] Misoprostol is an effective drug for ripening the cervix and induction of labour.[3–6] It is cheap, easy to handle, and can be stored at room temperature.[3–7]

MATERIAL AND METHODS

This was a quasi-experimental study performed from October 2004 to October 2007 at Shaheena Jamil Teaching Hospital and Women and Children Teaching Hospital Abbottabad, Pakistan.

Women who presented with obstetric or medical indications for labour induction, including those with a pregnancy of >41 weeks were included in the study. Cases with pre-labour rupture of membranes, chronic gestational hypertension or mild to moderate pre-eclampsia and even 3 cases of eclampsia were also included in the study. Additional criteria for inclusion in the study were singleton live pregnancy at term in cephalic presentation, absence of active labour, unfavourable cervix (Bishop Score ≤6) and

gestational diabetes without need for insulin. One case with twin pregnancy having first cephalic presentation was also included in the study.

Previous Caesarean Section, non-vertex presentation, foetal malformation (Macrosomia and growth restriction), unknown uterine scar (Myomectomy and Hysterotomy) were excluded from the study. Informed consent was taken from all patients. One quarter of tablet Misoprostol, (50 µg) was used for one woman. The tablet was cut with scissors, the inner core was discarded, and a drop of water was poured over the outer mantle of the tablet to make it moist for easy absorption. The tablet was inserted in the vagina up to posterior fornix. In very poor bishop score ≤5, the tablet was kept in cervix. Second dose was only given in case of no improvement in bishop score or non-establishment of regular uterine contractions and was not given before 6 hours of the 1st dose. The subsequent dose of Misoprostol was withheld in the presence of at least 3 regular uterine contractions in 10 minutes, active phase of labour (defined as regular uterine contractions with cervical dilatation ≥3 cm), or cervix favourable for amniotomy (Bishop Score ≥8). Oxytocin was required besides Misoprostol in 107 (12%) patients and it was not given earlier than 5 hours after the last Misoprostol dose. Oxytocin was given only when cervix was more than 4 cm dilated and desired uterine contractions were not present. Oxytocin was given at 1 mU/minute and increased by 1 mU/minute every 15 minutes till adequate contractions persisted. Foetal Heart Rate (FHR) was regularly monitored by intermittent auscultation with Foetoscope or Sonicaid. Vigilant monitoring of uterine contractions was done.

Efficacy of Misoprostol was judged by change of Bishop Score, vaginal delivery rate in 24 hours, doses of Misoprostol needed to induce delivery, oxytocin augmentation, rate of Caesarean Section, uterine hyperstimulation rates and maternal adverse effects. Neonatal outcome included APGAR score, incidence of meconeum stained amniotic fluid, and need for Neonatal Intensive Care Unit (NICU) admission.

RESULTS

A total of 946 patients were included in the study out of which 843 (89.1%) were successful vaginal deliveries. Mean age of the subjects was 22±5.2 years. There were 393 (41.5%) primigravida, while 543 (57.3%) were multigravida and 10 (1.05%) were grand multigravida. Mean gestational age was 41±0.9 weeks and mean Bishop Score was 4.3±1.2 (Table-1).

Table-1: Main characteristic of women in trial group (n=946)

Parameter	Value
Total patients	946
Vaginal deliveries	843 (89.1%)
Age (years)	22±5.2
Primigravida	393 (41.5%)
Multigravida	543 (57.3%)
Grand Multigravida	10 (1.05%)
Gestational age (weeks)	41±0.9
Bishop Score	4.3±1.2

Table-2: Indication for induction (n=946)

Indications	Number	%
Post term (>41 weeks)	321	33.9
Post maturity (>42 weeks)	10	1.0
Hypertension (mild to Moderate Pre-eclampsia)	139	14.9
Eclampsia	3	0.3
Gestational Diabetes	41	4.3
Singleton live pregnancy at term with cephalic presentation and non-establishment of labour	354	37.0
Twin Pregnancy	1	0.1
Pre labour rupture of membrane	87	9.1
Maternal mitral valvular disease	1	0.1
Polyhydramnios	2	0.2

Table-3: Maternal outcome in labour (n=946)

Parameter	Number	%
Mode of delivery		
Spontaneous vaginal delivery	736	87.0
Vaginal delivery with episiotomy	102	12.0
Outlet forceps delivery	5	0.5
Caesarean Section	103	10.8
Indication for caesarean section		
Foetal distress	42	40.0
Occipito-posterior Position	8	7.7
Cord around neck	9	8.7
Uterine Hyper stimulation	6	5.8
Abruptio Placenta	2	1.3
Arrest of labour, I stage	11	1.3
Arrest of labour II stage	22	2.6
No response to Misoprostol	1	0.9

Table-4: Neonatal outcome

	Number	%
Total	109	11.52
Birth weight (g) (Mean±SD)	3756±386.3	
APGAR score <7 at 5 minutes	15	1.85
Meconium Passage	38	4.01
Preterm	13	1.37
Neonatal death	5	0.52
Post mature	10	1.05
Admission to NICU	28	2.95

Table-5: Intra partum outcome

	Number	%
Vaginal delivery <24 hours	278	(33%)
Vaginal deliver <12 hours	565	(67%)
Number given only one dose of Misoprostol	615	(73%)
Oxytocin required in	107	(12%)

Table-6: Adverse maternal outcome

	Number	%
Vomiting	21	(2.4%)
Fever	16	(1.8%)
Diarrhea	12	(1.4%)
Post Partum Haemorrhage (PPH)	28	(3.3%)
Rupture of Uterus	0	(0%)

DISCUSSION

'Off' label use of Misoprostol for labour induction has been steadily increasing in the last 10 years, even though this use is approved neither by the US FDA, other national drug regulatory agencies, the Pharmaceutical Industry, the Cochrane Library nor a member of national obstetric organizations, including British Obstetricians and Gynaecologists. Some obstetricians, particularly in the US continue to promote induction with Misoprostol even though the available evidence suggests possible serious risk including uterine rupture, maternal mortality and perinatal mortality.[8–11]

Misoprostol has been in the market since 1985. Many studies have been published showing the usefulness of Misoprostol in obstetrics and gynaecology.

Vaginal Misoprostol appears to be more effective than conventional methods of cervical ripening and labour induction.[5] All induction agents can cause uterine hyper stimulation and foetal distress and Misoprostol is no exception. In our study there was no case of uterine rupture because of our selection criteria minimum dose and repetition of dose only in case of non-establishment of uterine contraction more over we increased the time of second dose, which is the reason that only 27% of our patients required a second dose.

It was our observation that patient tolerated the tablet very well and for initial 2–3 hours after insertion of tablet patients had only dull backache and very mild contraction as this time was from latent to active phase. It mimics more like natural labour. The 2nd dose of Misoprostol was not given before 6 hours of the 1st dose due to cumulative effect of the drug which may lead to uterine hyperstimulation and danger of rupture.

Cervical ripening is a process that is intended to soften, dilate, and efface the cervix. An unripe cervix is generally not yet soft, is dilated less than 2 cm, and is less than 50% effaced. If the artificial rupture of membrane is carried out before 4 cm dilatation of the cervix, it may lead to failed induction, ascending infection and ultimately need for Caesarean Section. Administration of oxytocin in un-effaced cervix leads to uterine hyper-stimulation without affecting the effacement of cervix. In our study ARM was not done before 4 cm cervical dilatation and similarly oxytocin was not given before 4 cm cervical dilatation, and was only given after ARM.

Though our study was conducted in a setting where High-Tech facilities for foetal monitoring like foetal Cord blood sampling and examination of Acid base balance were not available, yet our perinatal mortality and Caesarean Section rate is well within limits.

Misoprostol is believed to be a better option over traditional preparation for labour induction in developing countries.

CONCLUSION

Vaginal Misoprostol appears to be fairly safe and effective for cervical ripening in 3rd trimester. It has an increased rate of vaginal delivery within 24 hours without significant difference in Caesarean Section rate and foetal outcomes. Moreover it can be used in circumstances where extensive monitoring techniques are not available but close observation and vigilance is mandatory.

REFERENCES

1. Hofmeyr GJ. Induction of Labour with an unfavourable cervix. Best Pract Res Clin Obstet Gynaecol 2003;17:777–94.
2. Kelly AJ, Kavanagh J, Thomas J. Vaginal Prostaglandin PGE_2 and PGF_2 for induction of labour at term. Cochrane Database Syst Rev 2003;CD003101.
3. Keirse MJNC. Prostaglandins cervical ripening: meta-analysis of world wide clinical experience. J Repord Med 1993;39:89–100.
4. Varaklis K, Gumina R, Stubblefield PG. Randomized Controlled trial of vaginal misoprostol and intracervical Prostaglandin E_2 gel for induction of labour at term. Obstet Gynaecol 1995;86:541–4.
5. Wing DA, Rahall A, John, MM, Goodwin TM, Paul RH. Misoprostol: an effective agent for cervical ripening and labour induction. Am J Obstet Gynaecol 1995;172:1811–6.
6. ACoG Committee on Practice Bulletins—Obstetrics. Induction of Labour. ACoG Practice Bulletin No. 10, November 1999. Clinical management for obstetrician-gynaecologists. Obstet Gynaecol 1999:94(Part-1):1–10.
7. Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E_2 gel for preinduction cervical ripening and labor induction. Am J Obstet Gynaecol 1995;172:1804–10.
8. Friedman M. Manufacturer's Warning Regarding unapproved uses of Misoprostol. N Eng J Med 2001:344:61.
9. Maternal Mortality and morbidity Review in Massachusetts. A Bulletin for Heath Care Professionals, Number 1. (2000).
10. United Kingdom Department of Health. "Why Mothers Die?" (1993–1996).
11. Majoko F, Magwali T, Zwizwai M. Uterine rupture associated with the use of misoprostol for labour. Int J Gynaecol Obstet 2002;76:77–8.

Address for Correspondence:

Dr. Nasreen Abbasi, Assistant Professor of Obstetrics and Gynaecology, Frontier Medical College, Abbottabad, Pakistan. Cell: +92-300-9117121