International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Gajraj S et al. Int J Reprod Contracept Obstet Gynecol. 2021 Oct;10(10):3817-3822
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20213843

Original Research Article

Maternal and neonatal outcome after the use of low dose sublingual 25 µg misoprostol for labour induction in women with term pregnancy

Sumitra Gajraj[1]*, Anupam Kapur[2]

[1]Department of Obstetrics and Gynecology, Military Hospital Jodhpur, Rajasthan, India
[2]INHS Sanjivani, Naval Base Kochi, Kerala, India

Received: 20 August 2021
Revised: 08 September 2021
Accepted: 09 September 2021

***Correspondence:**
Dr. Sumitra Gajraj,
E-mail: sumitra.gajraj@gmail.com

ABSTRACT

Background: Aim of this study was to assess the maternal and fetal/neonatal outcome after the use of low dose (25 µg) misoprostol for labour induction in women with term pregnancy (gestational age >37 weeks POG) with a live foetus.
Methods: The prospective interventional study was designed at the department of obstetrics and gynaecology of a tertiary health care hospital, with a sample size of 150 pregnant ladies who had to undergo induction of labour, were selected depending on the defined inclusion and exclusion criteria. Data was analysed using SPSS 18. Descriptive statistics were used to describe the data. Qualitative variables were presented as frequencies and percentage.
Results: About 41% (61 patients) of the total study population was in the age group of 26 to 30 years with only two patients aged >35 years of age. The study group comprised of 88 primigravida (59%) and 62 multigravida (41%). The most common indication for induction of labour in my study was post-dated pregnancy (47%) followed by PROM (22%).
Conclusions: The use of low dose (25 µg) misoprostol sublingually is definitely very effective in cervical ripening and induction of labour in term pregnancies particularly in those with poor Bishops score. There was no significant neonatal or maternal morbidity associated with induction of labour with low dose sublingual misoprotol.

Keywords: Bishop's score, Caesarean section, Labour, Neonatal outcome, Sublingual misoprostol

INTRODUCTION

Induction of labour refers to the process wherein uterine contractions are initiated by medical or surgical means before the onset of spontaneous labour. In 1968, Karim and colleagues were the first to report the use of prostaglandins for labour induction.[1] The use of prostaglandins have since, in different varieties and forms of administration, become a common method of labour induction.[2] Recently, the synthetic prostaglandin analogue misoprostol has gained favour as an effective and safe method of labour induction.[3,4]

The use of misoprostol has many advantages. It has a long shelf life, cheaper, easy to administer and does not require special storage facility. Misoprostol can be administered orally, vaginally, and sublingually.[5] The onset of action is rapid via the oral or the sublingual route.[5,6] The higher doses of misoprostol can cause uterine tachysystole and hyperstimulation syndrome.[7,8] So, the optimal dosage, dosage regimen, and route of administration and their safety for pregnant women and neonate are still a matter of debate. There are only very few studies which simultaneously study the both maternal and foetal/neonatal outcome following induction of labour with low dose misoprostol and Indian data in this context is lacking.

This study was conducted to address this lack in maternal and foetal/neonatal outcome data in the Indian context.

Aims and objectives

Aim of the study was to assess the maternal and foetal/neonatal outcome after the use of low dose (25 µg) misoprostol for labour induction in women with term pregnancy (gestational age ≥37 weeks POG) with a live foetus.

METHODS

The prospective interventional study was designed at the department of Obstetrics and Gynaecology of INHS Asvini, Mumbai (India), a tertiary health care hospital, with a sample size of 150 pregnant ladies who had to undergo induction of labour, were selected depending on the inclusion and exclusion criteria. Permissions from Institutional Ethical Committee were obtained vide letter number 500/CA/28- proposal number 10 dated 22 December 2014. Informed consent was obtained from all the participants enrolled in the study.

Inclusion criteria

Term pregnancy with singleton live foetus with cephalic presentation (gestational age >37 completed weeks) with one or more of the following conditions - i) hypertensive disorders in pregnancy, ii) premature rupture of membranes (> 6 hours duration, iii) post-dated pregnancy (gestation >40 weeks 3 days) and iv) maternal medical conditions (diabetes mellitus, renal disease, chronic pulmonary disease, chronic hypertension, heart disease).

Exclusion criteria

Patients with cephalopelvic disproportion, oligohydramnios (AFI <5 cm), IUGR, multiparity (>3), APH, fetal distress and previous caesarean section/ scarred uterus were excluded from the study.

Dosage

Tab Misoprostol 25 µg were given sublingually 4 hourly till the onset of active labour or till a maximum of six doses. Onset of active labour interval was measured from first dose of misoprostol sublingual to time of onset of active labour. The following parameters were measured:

Maternal outcome- Following parameters were assessed:- Induction- onset of active labour interval, total number of doses required, number of patients who delivered vaginally, caesarean section rate, induction to delivery interval and number of adverse events like tachysystole, hypertonus and hyperstimulation

Fetal/neonatal outcome- Following parameters were assessed:- abnormal fetal heart rate tracings on CTG monitor, absence of beat to beat variability, late decelerations, variable decelerations, bradycardia/ tachycardia, meconium passage in utero was detected as meconium stained liquor which could be thin or thick in consistency, 5 minute APGAR score, neonatal resuscitation required- if any positive pressure ventilation or CPR done was recorded and adverse neonatal outcome- transient tachypnea, sepsis, asphyxia and respiratory distress syndrome.

Methodology

All patients were counselled on admission in detail, regarding the purpose of study, the drug being used for induction of labour, its mode of action and its side effects. Written informed consent and detailed history was taken from every patient. A thorough systemic as well as obstetric examination was performed. All protocol for induction of labour was followed. Bishop's scoring was done and pre induction non stress test performed. The patients were administered 25 µg of misoprostol sublingually and the dose repeated after 4 hours. A maximum of six doses were given.

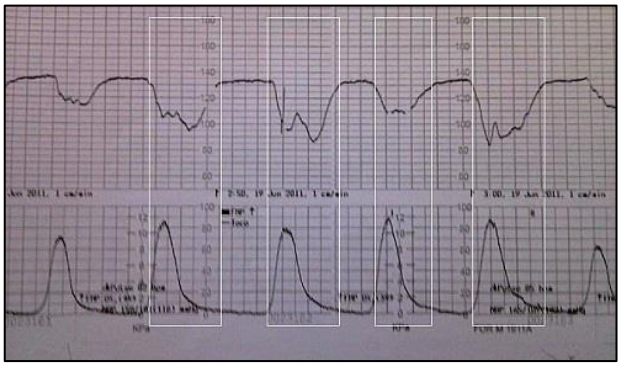

Figure 1: Fetal CTG tracing suggestive of late decelerations (fetal distress).

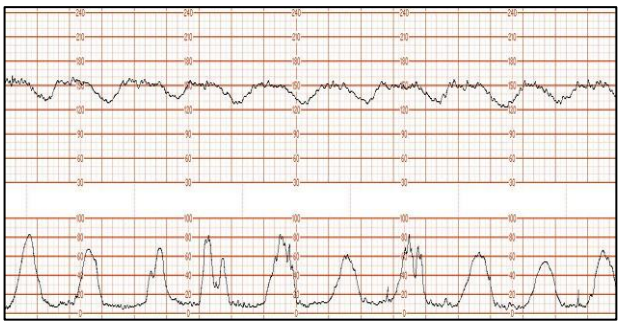

Figure 2: Tracing suggestive of tachysystole with late deceleration.

During labour, the patients vital signs were judiciously monitored, partogram was maintained and continuous cardiotocography (CTG) performed to monitor the foetus. The patients were monitored for uterine hyperstimulation and fetal distress (Figures 1 and 2). Where the patients did not go into active labour with three or more contractions (each persisting for at least 40-45 seconds), in ten minutes, despite six doses of misoprostol or in case patient were in labour but progress was unsatisfactory, the cases were reviewed and managed accordingly. Augmentation of

labour was started with oxytocin infusion with 5 units in 50 ml of Ringers lactate solution at the rate of 1-2 mU/ml using infusion pump and titrated according to contractions. Induction of labour was considered as failed if patient did not go into active labour or the rate of cervical dilatation was less than 1 cm/hour, in primigravida and <1.5 cm/hour, in a multigravida after the onset of active labour.

A pediatrician was called to receive the newborn at the time of delivery. Neonatal outcome was observed by noting the APGAR score, resuscitation requirement and admission to NICU. Immediate neonatal problems like transient tachypnea of the newborn, respiratory distress syndrome, sepsis, asphyxia neonatorum and seizures were also noted. Data was analysed using SPSS 18. Descriptive statistics were used to describe the data. Qualitative variables were presented as frequencies and percentage.

RESULTS

The study was carried out in a tertiary care Armed Forces hospital over a period of 2 years. About 41% (61 patients) of the total study population was in the age group of 26 to 30 years with only two patients aged >35 years of age. The youngest was 21 years old and the oldest was 38 years of age. The study group comprised of 88 primigravida (59%) and 62 multigravida (41%).

Indication for induction of labour

The most common indication for induction of labour in our study was post-dated pregnancy (47%) followed by PROM (22%) (Table 1).

Table 1: Indication for induction of labour.

Indication	Frequency (N=150)	Percentage
Postdate	71	47
Hypertensive disorders of pregnancy	27	18
GDM	09	06
PROM	33	22
IUGR	10	07

Bishop score of patients at the beginning of induction

The maximum number of inductions were with a Bishop score of 4 to 5 (48%) though in 44% cases the Bishop score was ≤3 to begin with (Table 2).

Table 2: Bishop score of patients at the beginning of induction.

Score	Frequency (N=150)	Percentage
0-3	66	44
4-5	72	48
6-7	12	08
8-10	Nil	00

Induction- labour onset interval

The onset of labour occurred in 46% within 12 hours and in 94% cases within 24 hours. 05 patients did not go into active labour even with 06 doses of misoprostol (Table 3).

Table 3: Induction- labour onset interval.

Time (in hours)	Frequency (N=150)	Percentage
<6	06	04
6-12	63	42
12-24	72	48
>24	04	03
Did not respond	05	03

Number of doses required for onset of active labour

Of the total 150 cases, 31% went into labour with two doses and 45% went into labour with three doses of low dose sublingual misoprostol. 21% required four or more doses to go into active labour. A total of 5 (3%) cases did not respond to even 06 doses of misoprostol and were treated as failed induction (Table 4).

Table 4: Number of doses required for onset of active labour.

Doses required	Number of patients (%)
Two	47 (31%)
Three	68 (45%)
Four	17 (12%)
>four	13 (09%)
Did not respond	05 (03%)

Mode of delivery

Spontaneous vaginal delivery occurred in 97 (65%) cases while 18 (12%) underwent vacuum or forceps delivery. LSCS was performed in 35 (23%) cases (Table 5). Among those undergoing LSCS, 5 (14.3%) were due to meconium staining of liquor (thick), 8 (22.8%) had a non-reassuring CTG, 9 (25.7%) due to failure of labour to progress, 5 (14.3%) were due to failed induction. The remaining 8 (22.8%) cases underwent caesarean section due to fetal distress which was detected in the form of late or variable FHR decelerations.

Table 5: Mode of delivery.

Mode of delivery	Number of patients (%)
Normal delivery	97 (65%)
Instrumental vaginal delivery	18 (12%)
Caesarean section	35 (23%)

Meconium stained liquor was observed in 18 (12%) cases (Figure 3), however thick meconium with FHR abnormality was seen in only 5 cases. Apgar score at 5 minutes was <7 in 8 (5%) cases (Figure 4).

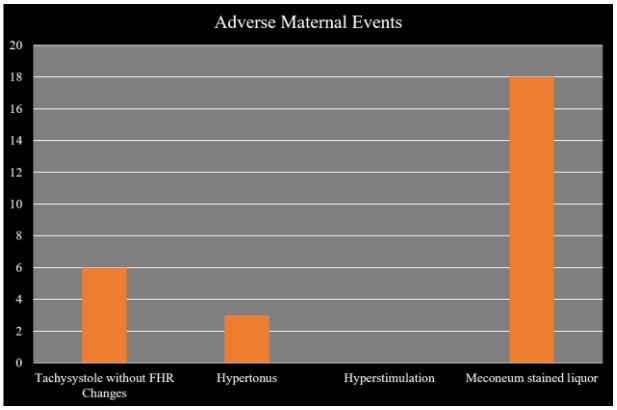

Figure 3: Graph depicting adverse maternal outcomes.

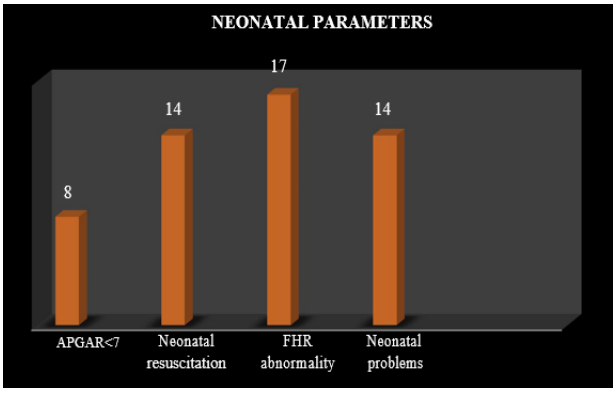

Figure 4: Graph depicting neonatal parameters assessed in our study.

These neonates were observed in the NICU. They only required to be kept under oxygen hood for 2 hours. Requirement of neonatal resuscitation was observed in 14 (9%) cases in the form intermittent positive pressure ventilation with Ambu bag and mask at 5 minutes and beyond.

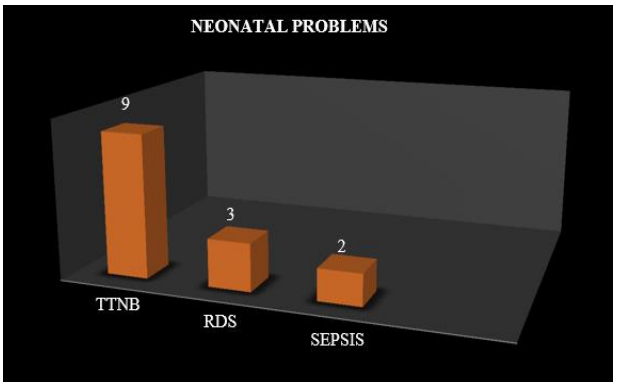

Figure 5: Graph depicting neonatal problems encountered in our study.

Fetal heart rate abnormality in the form of tachycardia, late decelerations and variable decelerations were observed in 17 (11%) cases (Figure 4). Neonatal problems were detected in 14 (9%) cases. These were transient tachypnea of the newborn in 9 cases, respiratory distress syndrome in 3 cases and sepsis in 2 cases (Figure 5).

DISCUSSION

The effectiveness and efficiency of misoprostol in termination of pregnancy has led to its use for induction of labour in term pregnancies. Method of induction should be both safe in terms of maternal health and labour outcome with the least neonatal morbidity and mortality. Several studies have been conducted to establish the route of administration, safest dosage regime and their outcome. Various doses (25, 50 and 100 µg), routes of administration and comparison to dinoprostone and oxytocin have been studied.[9] All studies have shown low doses to be free of side effects, safe and more efficient as compared to dinoprostone and oxytocin.[9,10]

In our study, the sublingual route as used by Kundodyiwa et al was used and it was found to be convenient as well as effective.[11] This route was acceptable to the patients as well. In my sample group, 31% went into active labour with two doses and 45% in three doses (Table 4) as compared to 66% in the study by Majid et al.[12] However the requirement for the fourth dose was almost similar, 8% in Majid et al study and 12% in our study. Augmentation with oxytocin was required in only 15% of our patients as compared to 58% in Majid et al study. The latent phase too was not long with 46% going into labour within 12 hours.

In our study, labour outcome in terms of rate of normal deliveries was good with 65% normal deliveries and 12% instrumental deliveries with a total of 77% through the vaginal route (Table 5). Utman et al showed similar results with 68% normal deliveries and 30% instrumental deliveries.[13] In her study 98% deliveries were through the vaginal route and only 2% were by CS. The rate of CS was also low in the study of Bugalho at 12%.[15] In our study the caesarean section rate was higher at 23%. This increase in caesarean section rates may be attributed to the fact that this institution being a tertiary care centre receives many high risk cases like recurrent pregnancy loss or bad obstetric history. Only 6 patients experienced tachysystole without FHR changes and none had hyperstimulation, mainly because the dose was low. This was similar to Utman et al.[13] There was no case of uterine rupture. Cecatti et al had a vaginal delivery rate of 70% and caesarean rate of 21% as compared to 65% and 23% respectively in my study.[16] The rate of tachysystole was 6% which is similar to my study. The need for oxytocin augmentation was 21% whereas in my study it was 15%.

Neonatal morbidity was low as well but meconium staining was seen in 12% cases and low APGAR in 5% which is comparable to the 6% in Utman et al study.[13] Although she documents a 10% rate of NICU admission, meconium staining has not been mentioned in that study, which would have been useful to see the effect of higher doses of misoprostol. The rate of non-reassuring CTG and

meconium staining is likely to rise with higher doses of misoprostol.

In our study, 94% patients went into active labour within 24 hours. This is similar to Has et al and Khoury et al (88% and 96% respectively).[17,18] The 76% patients went into active labour after the third dosing of misoprostol in my study which is similar to Shetty et al, Lo et al and Bartusevicius et al (71%, 69% and 65% respectively).[6,7,19] The vaginal delivery rate in our study was 65% which was similar to Cecatti et al and Hofmeyer et al (70% and 66% respectively).[16,20] The CS rates in our study were 23% which is similar to Ceccatti et al and Hofmeyer et al (21% and 24% respectively).[16,20] Only 15% cases required oxytocin augmentation in my study which is similar to Has et al, Bartusevicius et al and Srisomboom et al (21%, 25% and 17% respectively).[17,19,21]

In our study, an APGAR score <7 at 5 minutes was found in 5% cases. Comparable results were found by Eroglu et al.[14] Requirement for neonatal resuscitation in our study was observed in 9% of cases. This is similar to results of Srisomboon et al (10%).[21]

In this study, fetal heart rate abnormality was detected in 11% cases. Bartusevicius et al detected it in 12% cases.[19] Has et al also found similar results. Neonatal problems were detected in 9% cases in my study. This is similar to those detected by Eroglu et al and Caliskan et al (09% and 12% respectively).[14,22] In our study meconium stained liquor was observed in 12% cases. Similar results were seen by Eroglu et al, Bartusevicius et al and Srisomboon et al.[14,19,21]

Apart from the clinical advantages of oral misoprostol over vaginal misoprostol, oral misoprostol would also seem to offer other advantages in terms of patient satisfaction. Majority of women should find the oral route more acceptable because of the ease of administration and avoidance of vaginal examination. Furthermore, oral doses can continue to be used despite vaginal bleeding or ruptured membranes. Oral misoprostol can be used in the peripheral set ups. All these factors make the oral route an attractive option with similar efficiency.

Limitation of the study were smaller sample size. Study conducted at a tertiary care hospital comprising of a subset of population. Data validation is required through more such studies.

CONCLUSION

The use of low dose (25 µg) misoprostol sublingually is definitely very effective in cervical ripening and induction of labour in term pregnancies particularly in those with poor Bishops score. There is no significant neonatal or maternal morbidity associated with induction of labour with low dose sublingual misoprotol.

Low-dose oral/sublingual misoprostol seems to be as effective as both vaginal dinoprostone and vaginal misoprostol. Many trials have consistently shown it to be of equal efficacy but with additional benefits. Low dose oral/sublingual misoprostol would therefore seem to be the cost effective and optimal choice for induction of labour.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee vide letter number 500/CA/28- proposal number 10 dated 22 December 2014

REFERENCES

1. Karim SMM, Trussele RR, Patel RC, Hillier K. Response of pregnant human uterus to prostaglandin F2 alpha induction of labour. BMJ. 1968;IV:621-3.
2. Sanchez-Ramos LU, Kaunitz AM, Del Valle GO, Delke IS, Schroeder PA, Briones DK. Labour induction with the prostaglandin E1 methyl analogue misoprostol versus oxytocin: A randomized trial. Obstet Gynecol. 1993;81:332-6.
3. Agarwal N, Gupta A, Kriplani A. Six hourly vaginal misoprostol versus intracervical dinoprostone for cervical ripening and labour induction. J Obstet Gynaecol Res. 2003;29:147-51.
4. Crane JM, Butler B, Young DC, Hannah ME. Misoprostol compared with prostaglandin E2 for labour induction in women at term with intact membranes and unfavourable cervix: a systematic review. BGOG. 2006;113:1366-76.
5. Bartusevicius A, Barcaite E, Nadisauskiene R. Oral, vaginal and sublingual misoprostol for induction of labour. Int J Gynecol Obstet. 2005;91:2-9.
6. Shetty A, Danielian P, Templeton A. Sublingual misoprostol for the induction of labour at term. Am J Obstet Gynecol. 2002;186:72-6.
7. Lo TK, Lau WL, Wong KS. Sublingual misoprostol compared to artificial rupture of membranes plus oxytocin infusion for labour induction in nulliparous women with favourable cervix at term. Hong Kong Med J. 2006;12:345-50.
8. ACOG Committee Opinion. American College of Obstetrician and Gynecologist. New U.S. Food and Drug Administration labeling on Cytotec (misoprostol) use and pregnancy. Obstet Gynecol. 2003;101:1049-50.
9. Hissane EM, El Karroumim M, Mikou F, Ghazli M, Matar N. Misoprostol sublingually versus vaginally for labour induction at term: a randomized study. Department of Obstetrics and Gynecology "B", Averoes Hospital, Casablanca, Morocco. Res Obstet Gynecol. 2012;1(3):27-9.
10. Dodd JM, Crowther CA, Robinson JS. Oral misoprostol for induction of labour at term: randomized controlled trial. BMJ. 2006;332(7540):509-13.

11. Kundodyiwa TW, Alfirevic Z, Weeks AD. Low-dose oral misoprostol for induction of labour: a systematic review. Obstet Gynaecol. 2009;113:374-83.
12. Majid N, Nasir F, Akhtar T, Fatima H. Misoprostol: an effective agent for labour induction in full term parous women. Med Channel. 2009;15(2):51-4.
13. Utman N, Akhtar S, Jamshid A. Usefulness of 100 microgram misoprostol in term gravid patients regarding labour,fetal and maternal outcome. JPMI. 2007;21(02):136-40.
14. Eroglu D, Oktem M, Yanik F. Labour induction at term: a comparison of the effects of 50 µg and 25 µg vaginal misoprostol. Clin Exp Obstet Gynecol. 2007;34:102-5.
15. Bugalho A, Bique C, Machungo F, Faundes A. Low-dose vaginal misoprostol for induction of labor with a live fetus. Int J Gynecol Obstet. 1995;49(2):149-55.
16. Cecatti JG, Tedesco RP, Pires HM. Effectiveness and safety of a new vaginal misoprostol product specifically labelled for cervical ripening and labour induction. Acta Obstet Gynecol Scand. 2006;85:706-11.
17. Has R, Batukan C, Ermis H. Comparison of 25 and 50 µg vaginally administered misoprostol for preinduction of cervical ripening and labour induction. Gynecol Obstet Invest. 2005;59:155-61.
18. Khoury AN, Zhou QP, Gorenberg DM. A comparison of intermittent vaginal administration of two different doses of misoprostol suppositories with continuous dinoprostone for cervical ripening and labour induction. J Matern Fetal Med. 2001;10:186-9.
19. Bartusevicius A, Barcaite E, Krikstolaitis R, Gintautas V, Nadisauskiene R. Sublingual compared with vaginal misoprostol for labour induction at term: a randomised controlled trial. BJOG. 2006;113:1431-7.
20. Hofmeyr GJ, Gülmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database Syst Rev. 2010;10:CD000941.
21. Srisomboon J, Singchai S. A comparison between 25 micrograms and 50 micrograms of intravaginal misoprostol for labour induction. J Med Assoc Thai. 1998;81:779-83.
22. Caliskan E, Bodur H, Ozeren S. Misoprostol 50 microg sublingually versus vaginally for labour induction at term: a randomized study. Gynecol Obstet Invest. 2005;59:155-61.

Cite this article as: Gajraj S, Kapur A. Maternal and neonatal outcome after the use of low dose sublingual 25 µg misoprostol for labour induction in women with term pregnancy. Int J Reprod Contracept Obstet Gynecol 2021;10:3817-22.