



TO STUDY THE EFFECT OF MISOPROSTOL GIVEN BY ORAL AND VAGINAL FOR INDUCTION OF LABOUR IN 3rd TRIMESTER

Obstetrics & Gynaecology

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ABSTRACT

Background: Induction of labour defined as artificial initiation of uterine contractions before the onset of spontaneous labour, after the period of viability, by any methods. The successful outcome depends on the Bishop Score, maternal age and parity. Authors compared the most preferred two routes; vaginal and oral for induction and outcome, adverse events and side effects were noted.

Methods: This was a prospective comparative study carried out at Department of Obstetrics and Gynaecology, SKMCH, Muzaffarpur, Bihar from June 2021 to December 2021, 100 patients who required induction were randomly divided in two groups- Group A received 25µg oral misoprostol, Group B - received 25µg vaginal misoprostol repeated 4 hourly up to maximum five doses in both groups. The induction to delivery interval, mode of delivery, maternal and neonatal outcome and complications were observed.

Results: The mean induction to delivery interval was less in vaginal group than oral (18.7 hours in vaginal versus 22.4 hours in oral). Vaginal delivery and caesarean section rates were comparable in both groups. 60% patients in Group A required more than two doses as compared to 36% in Group B. No major complications or adverse events were observed.

Conclusions: Both oral misoprostol in a dose of 25µg and vaginal misoprostol 25µg every four hours, to a maximum of five doses, have safety and efficacy for induction. With The vaginal route, delivery occurs in less time and few doses required as compared to oral.

KEYWORDS

Induction of labour, Misoprostol, Oral route, Uterine contractions, Vaginal route

INTRODUCTION

Induction of labour defined as artificial initiation of regular uterine contractions before their spontaneous onset by medical or surgical methods.¹ It is most debatable when done prior to achievement of maturity or at term in normal patient for the convenience of patient and the doctor. Normally, all pregnancies should continue to term, and labour should begin spontaneously resulting in vaginal delivery. Induction of labour is indicated when the risks to maternal or foetal health outweigh the benefits of continuing the pregnancy.² The status of the cervix, its form, consistency and dilatation and station, has a significant impact on the prognosis of labour induction.³ Induction of labour, performed when the cervix is not favourable, and is associated with higher incidence of prolonged labour and caesarean section. Different methods are used to prepare the cervix, which include two main mechanical and pharmacological methods. Mechanical and surgical methods include, hygroscopic dilators, balloon catheter, membrane stripping and amniotomy. Pharmacological methods include the use of prostaglandin E2 (dinoprostone), prostaglandin E1 (misoprostol), oxytocin, oestrogen, mifepristone and anapristone.^{4,5}

Amongst the available pharmacological methods, prostaglandins play an important role in labour induction and are available in two forms; dinoprostone and misoprostol.⁴ Dinoprostone is most commonly used in vaginal form; it is expensive and needs to be kept in the refrigerator.⁶ In comparison, misoprostol is a methyl ester of PGE1. Misoprostol acts by selectively binding to EP-2/EP-3 prostanoid receptors. It can be prescribed in oral, vaginal and sublingual forms are widely used to induce labour for its high efficacy, considerable safety, reasonable price, easy to use, and easy to store at room temperature.⁷ Also, misoprostol causes fewer side effects such as nausea, vomiting, diarrhoea, fever and abdominal pain.⁸ Also, unlike other prostaglandins, misoprostol has a selective effect on the uterus and cervix and has no systemic effect on the bronchi, blood vessels and gastrointestinal.⁹ Most clinical trials have used doses ranging from 25µg to 100µg, inserted intra-vaginally into the posterior fornix.¹⁰⁻¹⁴ The commonest vaginal dose used is 50µg inserted once or administered every four to six hours but more side effects are noted, inserting 25µg every six hours intra-vaginally has been associated with the minimal side effects.¹⁴⁻¹⁶ Maximum plasma concentration of orally administered misoprostol is achieved faster than in vaginal method, so that in oral method, it occurs within 30 minutes and in the vaginal method, it takes about an hour but the plasma concentration of the drug in vaginal method lasts for longer time, so that oral misoprostol is

eliminated within 2-3 hours, but vaginal misoprostol elimination takes more than 4 hours.^{17,18} Therefore, vaginal route seems to be more efficacious than oral and results in shorter induction to delivery interval and reduced need for other pharmacological augmentation.

This study was conducted to compare the effect of oral misoprostol 25µg and vaginal misoprostol 25µg for induction of labour in 3rd trimester.

MATERIAL AND METHODS

This was a prospective comparative study conducted in department of obstetrics and gynecology at Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar from June 2021 to December 2021. Total 100 pregnant women admitted through the emergency or OPD (outpatient department) with an indication for induction of labour at term. After confirming eligibility criteria, informed written consent was taken. The patients were randomly assigned to two groups -Group A, received tab misoprostol 25µg orally repeated every 4 hours for maximum five doses, Group B received misoprostol 25µg vaginally every 4 hours for maximum of five doses.

Inclusion Criteria

- Single intrauterine pregnancy beyond 37 weeks gestation
- Vertex presentation
- Clinically adequate pelvis
- Unfavorable cervix (Bishop score <6)
- Reactive non stress test
- Absence of uterine contractions.

Exclusion Criteria

- Malpresentation
- Presence of uterine contractions \geq 3/10 min
- Cephalo-pelvic disproportion
- Favourable cervix (Bishop score > 6)
- Preterm pregnancy (<37 weeks of gestation)
- Previous scarred uterus
- Multiple gestation
- Placenta previa
- Non-reactive non stress test
- Contraindication to vaginal delivery
- Hypersensitivity to prostaglandins
- Grand multipara
- IUFD
- Congenital malformation of foetus.

A detailed history and general physical examinations were done. Per abdomen obstetrical examination included fundal height, lie, presentation, foetal heart sound, per vaginal examination for assessing bishop's score and pelvis. Routine blood investigations were done. Antenatal Ultrasound was done to confirm gestational age and foetal well-being. Maternal vitals were monitored. Duration, frequency and intensity of uterine contractions were noted. Non-stress test (NST) was done for 20 minutes at the time of admission and before administration of each and every dose of Misoprostol in all patients.

Partograph was maintained from the onset of labour till the delivery of foetus to assess progress of labour. Induction was discontinued soon the patient entered in active labour which was considered if, either she had adequate uterine contractions rated as at least 3 contractions/10 minutes each lasting for 40 seconds duration or dilatation of cervix ≥ 4 cm. Amniotomy was done once internal os was >4 cm dilated to assess the colour of liquor and also it aids the progress of labour. Oxytocin was started for augmentation, in absence of adequate uterine contraction after Amniotomy and four hours after the last dose of misoprostol. Once the patient was in active labour, routine intrapartum management was carried out.

The efficacy of misoprostol was measured by successful induction which is considered as number of women who achieved active labour within 24 hours of induction and also by their induction to delivery interval. Other parameters were number of vaginal deliveries within 24 hours, total doses of misoprostol required for delivery and route of delivery. The measures of safety included the uterine tachysystole, uterine hyper tonus, abnormal non stress test, incidence of meconium stained liquor post amniotomy and the neonatal outcome. Baseline data included maternal age, parity, indication for induction and pre-induction Bishop's score.

RESULTS

Table 1 describe various demographic characteristics which were comparable in both groups. Values are expressed as median (range or percentage). The mean Pre induction Bishop score was 3.5 in oral group and 4.0 in vaginal group which was again comparable. Most women in each group were primigravida.

Table 1 : Demographic Characteristics

| Characteristics | Group A (n=50) | Group B (n=50) |
|-------------------------------------|----------------|----------------|
| Maternal age (in years) | 26(20-40) | 25(20-40) |
| Gestational age (in weeks) | 39(37-42) | 39(37-42) |
| Pre-induction Bishop's Score (mean) | 3.5(3-4) | 4.0(3.5-4.5) |
| Primigravida | 33 | 34 |
| Multigravida | 17 | 16 |

Table 2 depicts indication of induction of labour. Most common indication for induction was PROM (preterm spontaneous rupture of membranes) followed by postdate pregnancy (>40 weeks of gestation) and oligohydramnios.

Table 2 : Indications Of Induction

| Indication | Group A (n=50) | Group B (n=50) |
|-----------------|----------------|----------------|
| PROM | 30 | 21 |
| Post-date | 12 | 10 |
| Oligohydramnios | 10 | 11 |
| Preeclampsia | 6 | 5 |
| IUGR | 2 | 3 |

Table 3 depicts various outcome of induction. The successful induction rate number of women who achieved active labour within 24 hours of induction was 90% in Group A and 86% in Group B which was almost similar. Spontaneous vaginal delivery and caesarean section rates were almost same in the groups, 74% in Group A and 76% in Group B, 26% in Group A and 24% in Group B, respectively. There was no difference in the route of delivery in two groups; however, the induction to delivery interval was less in Group B. Amongst the patients delivered vaginally more than 50% patients delivered in less than 24 hours in both the groups.

Table 3 : Outcome Of Labour Induction

| Characteristics | Group A (n=50) | Group B (n=50) |
|----------------------|----------------|----------------|
| Successful induction | 45(90%) | 43(86%) |
| Vaginal delivery | 37(74%) | 38(76%) |
| Caesarean delivery | 13(26%) | 12(24%) |

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|-------------------------------------|-----------|-----------------|
| Induction-delivery Interval (hours) | 22(21-23) | 18.5(17.5-19.5) |
| Vaginal delivery within 24 hours | 25(50%) | 28(56%) |
| Oxytocin administration (n%) | 68% | 50% |

Table 4 shows 60% patients in Group A (oral group) required more than two doses of misoprostol to effect delivery which was comparable to 36% in Group B (vaginal group).

Table 4 : Number Of Dose Of Misoprostol Required

| Number of doses | Group A (n=50) | Group B (n=50) |
|-----------------|----------------|----------------|
| 1 | 5(10%) | 9(18%) |
| 2 | 15(30%) | 23(46%) |
| 3 | 20(40%) | 15(30%) |
| 4 | 5(10%) | 2(4%) |
| 5 | 5(10%) | 1(2%) |

Table 5 : Adverse Events And Maternal Side Effects

| Characteristics | Group A (n=50) | Group B (n=50) |
|-------------------------|----------------|----------------|
| Tachysystole | 1(2%) | 2(4%) |
| Hyperstimulation | 0 | 2(4%) |
| Nonreactive NST | 7(14%) | 4(8%) |
| Meconium stained liquor | 9(18%) | 6(12%) |
| Fever | 6(12%) | 5(10%) |
| Nausea/vomiting | 8(16%) | 1(2%) |

Table 6 : Neonatal Outcome

| Characteristics | Group A (n=50) | Group B (n=50) |
|---------------------|----------------|----------------|
| Apgar at 1 min <7 | 1(2%) | 1(2%) |
| Apgar at 5 min <7 | 3(6%) | 2(4%) |
| Still birth | 0 | 0 |

Very few adverse events were noted. Tachysystole developed in one woman in Group A and two women in Group B. Uterine hyper stimulation occurred in two women (4%) in the vaginal misoprostol group only. Both primigravida women delivered by caesarean section. None of the patients developed hyper tonus. Non-reactive NST patterns were defined as late deceleration, variable deceleration, prolonged deceleration, foetal tachycardia, or reduced foetal heart rate variability which was 14% in Group A and 8% in group respectively. Meconium stained liquor was seen in 18% in oral group and 12% in vaginal group, respectively. Maternal side effects were minimal and manageable. No uterine rupture was observed in any patients.

Table 6 suggests that in neonatal outcome, no differences between the two groups were found in the proportion of neonates with Apgar score <7 at 5 minutes. No still birth recorded.

DISCUSSION

The use of misoprostol for induction of labour has been increasing nowadays. There is increasing evidence that misoprostol, administered either through vaginal or oral route, is as effective as other pharmacological methods for induction of labour at term which authors used to use since decades.¹⁹ Doses from 25 μ g to 200 μ g have been used but more than 50 μ g is associated with hyper stimulation, hyper tonus, meconium stained liquor and uterine rupture.¹⁹ This study shows that women who receive misoprostol by vaginal route had faster induction-to-delivery interval when compared with a similar group of women receiving misoprostol by oral route. These findings coincide with those of other studies.²⁰

Main problem with this drug is that there is chance of excessive uterine contractions and uterine rupture. The chances of uterine rupture in primi gravida is lesser in comparison with multigravida so, it is used very cautiously in multigravida patients. These complications are dose related, higher the dose; more is uterine stimulation but shorter is the induction delivery interval.²¹ Higher incidence of foetal distress and meconium staining of liquor are result of hyper stimulation of uterus.

Vaginal misoprostol significantly reduces induction to delivery interval and increases chances of vaginal delivery, although caesarean section rates are similar in orally used misoprostol, making both routes comparable in outcomes in both study groups, though higher dose is required when used orally due to reduced bioavailability and high first pass metabolism. This study compared 25 μ g misoprostol orally versus 25 μ g vaginally and findings were comparable with other studies.

FIGO (2017) recommended 25 μ g misoprostol vaginally every 6 hours or orally every 2 hours regimens for induction of labour. 25 μ g of misoprostol should be considered as the initial dose for cervical

ripening and labour induction.

CONCLUSION

This study suggests that vaginal route for misoprostol is associated with shorter induction-to-delivery interval than oral route. Route of delivery is not affected. Higher dose is required in oral route due to less bioavailability, high first pass metabolism and rapid excretion, vaginal administration on other hand may be noncompliant and uncomfortable to the patient. There is a need for a greater number of appropriately designed double-blinded randomized controlled trials with a larger sample size to validate the efficacy and safety of 25µg oral misoprostol in comparison with 25µg vaginal misoprostol.

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