Original Article

Efficacy and Safety of Vaginal Misoprostol for Cervical Ripening and Labour Induction in Late Pregnancy
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Abstract

Background: Induction of labor is its intentional initiation before spontaneous onset, with the aim of vaginal birth which is safe for mother and newborn. The well documented effectiveness of misoprostol in several gynecological and obstetric applications has resulted in enthusiasm for its use. Objective: To see the efficacy and safety vaginal Misoprostal for cervical ripening and labour induction in late pregnancy. Materials and Methods: This single center clinical trial was carried out in the Department of Obstetrics and Gynaecology at Khwaja Yunus Ali Medical College and Hospital in Sirajgonj, Bangladesh from June 2019 to May 2020 for a period of one year. A total of 90 women requiring indicated induction of labour with an unfavourable cervix (Bishop score ≤ 4) were included in the study. They were randomly divided into two groups: 53 women induced with intravaginal misoprostol (Group I) and 37 women induced with transcervical Foley catheter (Group II). Results: Spontaneous vaginal delivery was 35(66.0%) in misoprostol group and 15(40.5%) in Foley catheter group. Caesarean section was higher in Foley catheter group than misoprostol group (37.8% vs 18.9%). The mean birth weight, APGAR score 1 minute, 5 minute, admission in neonatal intensive care unit and meconium aspiration syndrome were not statistically significant between two groups (p>0.05). Only one baby was died in Foley catheter group, but the difference was not statistically significant between two groups (p>0.05). Conclusion: The present study suggests intravaginal Misoprostol results in a shorter induction to delivery time, a reduction in the rate of caesarean delivery.

Key words: Late pregnancy, Labour induction, Cervical ripening, Vaginal Misoprostal.

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Introduction

Induction of labor is its intentional initiation before spontaneous onset, with the aim of vaginal birth which is safe for mother and newborn. Established indications for induction include post-term pregnancy, pre-labor membrane rupture (PROM), and maternal hypertension.1 The use of misoprostol results in a shorter induction to delivery time, a reduction in rate of caesarean section and without any adverse effect on the mother and the neonatal outcomes. It is rapidly absorbed and is more effective than oxytocin or dinoproston for induction of labour. Misoprostol is a cheap and stable PGE1 analogue that is active both by the vaginal and oral route of administration for cervical ripening and induction.2 Serum levels after vaginal absorption are more prolonged; irrespective of serum levels, vaginally absorbed misoprostol has locally mediated effects; thus there has been increasing interest in misoprostol for use as a pharmacological agent for labour induction.1 Induction of labor usually involves not a single intervention but a complex set of interventions with a tendency of posing challenges for both the obstetrician and mother.2,3 The search for an ideal agent, timing and dosage interval to convert an unfavorable cervix to one receptive to delivery is an ongoing process.4 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

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monitored. The well documented effectiveness of misoprostol in several gynecological and obstetric applications has resulted in enthusiasm for its use. The purpose of induction of labor is to achieve vaginal delivery by stimulating uterine contractions before the spontaneous onset of labor. However, it does appears challenging to a obstetricians when the cervix is not favorable.

Materials and Methods
This single center clinical trial was carried out in the Department of Obstetrics and Gynaecology at Khwaja Yunus Ali Medical College and Hospital in Sirajgonj, Bangladesh from June 2019 to May 2020 for a period of one year. The included criteria were singleton pregnancy cephalic presentation, gestation age >40 weeks on the basis of LMP or first trimester ultrasonography, intact membranes, unfavorable cervix (Bishop score ≤ 4), and imminent delivery for fetal or maternal indication. Women were excluded from the study if any of the following criteria were encountered: rupture of membranes, chorioamnionitis, antepartum haemorrhage, cervical dilation >2.5 cm, temperature >38°C, contracted pelvis, fetal distress, polyhydramnios, indication for immediate delivery, and previous caesarean section or other uterine surgeries (for Group I). A total of 90 women requiring indicated induction of labour with an unfavourable cervix (Bishop score ≤ 4) were included in the study. They were randomly divided into two groups: 53 women induced with intravaginal misoprostol (Group I) and 37 women induced with transcervical Foley catheter (Group II). At first, the method of the study was completely explained to them; if the written consent was obtained, they were enrolled in the study. Cases were selected from antenatal clinic (ANC), outpatient department (OPD), and patients admitted in the hospital. The two groups were comparable with respect to maternal age, parity, and gestational and preinduction Bishop score. Demographic and clinical data were collected at routine antenatal visits. In Group I, 50 mcg of misoprostol tablet was placed intravaginally, 4 hourly for maximum 6 doses. In the presence of spontaneous and frequent contractions (>40–45 seconds every 3 minutes), the next dose was not administered. If there were no effective uterine contractions after the sixth dose, then it was considered as failure of induction by the concerned method. In Group II, 18 F Foley catheter was inserted into the endocervical canal under direct vision by doing a perspeculum examination. The catheter was advanced into the endocervical canal. Once past the internal os, the balloon was filled with 50mL of sterile saline solution and the catheter was taped to the inner thigh to maintain traction. The catheter was checked for extrusion of the balloon from the cervix every 6 hours by cervical examination and the catheter remained in place until the balloon was expelled spontaneously and labour augmentation was done by artificial membrane rupture or oxytocin drip (2.5 or 5 IU in 500mL of Ringer’s lactate solution was started then and it was titrated according to frequency and intensity of uterine contractions) which ever is indicated. The primary outcome measures were induction to delivery interval and secondary outcome measures include uterine contractile abnormalities like uterine tachysystole (6 contractions in a 10-minute period), uterine hypertonus (a single contraction lasting longer than 2 minutes) and uterine hyperstimulation is when either condition leads to a nonreassuring fetal heart rate pattern, meconium stained liquor, mode of delivery, maternal and neonatal outcome, neonatal birth weight, and Apgar score. Any maternal or fetal complications were also recorded.

Results
Table 1 shows that age, gravidity, gestational age, indication for induction and initial Bishop score were not statistically significant compared between two groups (p=0.05). Table 2 shows that mean induction to delivery intervals was significant higher in Foley catheter group than misoprostol group (17.5±7.6 hrs vs 13.9±8.2 hrs), p=0.037. However, induction to active phase interval was almost similar between two groups (p=0.847). Table 3 shows that oxytocin drip was found 25(47.2%) in misoprostol group and 27(73.0%) in Foley catheter group. Artificial rupture of membrane was 37(69.8%) and 35(94.6%) in misoprostol and Foley catheter group respectively. Oxytocin+ARM was 22(41.5%) in misoprostol group and 26(70.3%) in Foley catheter group. Oxytocin drips, artificial rupture of membrane and oxytocin + ARM were significantly higher in Foley catheter group than misoprostol group. Complications rate was also similar between two groups, that was not significant (p=0.05). Table 4 shows that spontaneous vaginal delivery was 35(66.0%) in misoprostol group and 15(40.5%) in Foley catheter group. Caesarean section was higher in Foley catheter group than misoprostol group (37.8% vs 18.9%). The difference was statistically significant (p<0.05) between two groups. Table 5 shows that mean birth weight, APGAR score 1 minute, 5 minute, admission in neonatal intensive care unit and meconium aspiration syndrome were not statistically significant between two groups (p=0.05). Only one baby was died in Foley catheter group, but the difference was not statistically significant between two groups (p=0.05).

Table 1: Demographic characteristic of the study patients (n=90)

| Parameters                      | Misoprostol (n=53) | Foley catheter (n=37) | p value |
|---------------------------------|-------------------|-----------------------|--------|
| Age years (mean±SD)             | 26.6±3.5          | 27.1±3.9              | 0.52ns |
| Gravidity                       |                   |                       |        |
| Primigravida n (%)              | 23                | 13                    | 0.43ns |
| Multigravida n (%)              | 30                | 24                    |        |
| Gestational age (weeks) (mean±SD)| 40.6±1.2         | 40.8±1.3              | 0.45ns |
| Indication for induction        |                   |                       |        |
| Oligohydramnios n (%)           | 11                | 8                     | 0.92ns |
| Preeclampsia n (%)              | 9                 | 4                     | 0.41ns |
| IUGR n (%)                      | 6                 | 3                     | 0.61ns |
| GD n (%)                        | 2                 | 1                     | 0.78ns |
| Initial Bishop score (mean±SD)  | 3.81±0.9          | 3.86±1.01             | 0.80ns |
Table 2: Induction to delivery interval of the patients (n=90)

| Parameters                  | Misoprostol (n=53) | Foley catheter (n=37) | p value |
|-----------------------------|--------------------|-----------------------|---------|
| Induction to active phase interval (hrs) | 12.1±4.6          | 11.9±5.2              | 0.84ns  |
| Induction to delivery intervals (hrs)    | 13.9±8.2          | 17.5±7.6              | 0.03ns  |

s=significant; ns=not significant
P value reached from unpaired t-test

Table 3: Outcome of labour of the study patients (n=90)

| Augmentation required                   | Misoprostol (n=53) | Foley catheter (n=37) | p value |
|-----------------------------------------|--------------------|-----------------------|---------|
| Oxytocin drip                           | 25 47.2            | 27 73.0               | 0.01s   |
| Artificial rupture of membrane          | 37 69.8            | 35 94.6               | 0.00s   |
| Oxytocin + ARM                          | 22 41.5            | 26 70.3               | 0.00s   |
| Complications                           |                     |                       |         |
| Hyperstimulation                        | 5 9.4              | 0 0.0                 | 0.05ns  |
| Uterine contraction abnormalities       | 1 1.9              | 1 2.7                 | 0.79ns  |
| Uterine tachysystole                    | 1 1.9              | 0 0.0                 | 0.40ns  |
| Uterine rupture                         | 0 0.0              | 1 2.7                 | 0.22ns  |
| Postpartum hemorrhage                   | 1 1.9              | 1 2.7                 | 0.79ns  |

s=significant; ns=not significant
P value reached from Chi square and Fisher’s exact test

Table 4: Distribution of the study patients by mode of delivery (n=90)

| Mode of delivery               | Misoprostol (n=53) | Foley catheter (n=37) | p value |
|-------------------------------|--------------------|-----------------------|---------|
| Spontaneous vaginal delivery  | 35 66.0            | 15 40.5               |         |
| Instrumental vaginal delivery | 8 15.1             | 8 21.6                | 0.04s   |
| Caesarean section             | 10 18.9            | 14 37.8               |         |

s=significant; P value reached from Chi square test

Table 5: Distribution of neonatal outcome (n=90)

| Neonatal outcome          | Misoprostol (n=53) | Foley catheter (n=37) | P value |
|---------------------------|--------------------|-----------------------|---------|
| Birth weight (kg)         | 2.81±0.45          | 2.89±0.51             | 0.43ns  |
| Apgar score (at 1 minute) | 7.85±0.73          | 7.93±0.35             | 0.53ns  |
| Apgar score (at 5 minute) | 8.95±0.32          | 8.97±0.19             | 0.73ns  |
| Admission in NICU         | n %                | n %                   |         |
| 4 7.5                    | 6 16.2             | 0.68ns                |
| Meconium aspiration       | 5 4                  | 3 8.1                 | 0.30ns  |
| syndrome                 |                     |                       |         |
| Alive                    | 53 100.0            | 36 97.3               |         |
| Dead                     | 0 0.0               | 1 2.7                 | 0.41ns  |

s=significant; ns=not significant
P value reached from unpaired t-test
P value reached from Chi square and Fisher’s exact test

Discussion

In this study observed that age, gravidity, gestational age, indication for induction and initial Bishop score were not statistically significant compared between two groups(p>0.05). Nyango et al.\(^\text{10}\) reported that the mean age of the participants was 31.28 ± 5.09 years for the misoprostol and 30.16 ± 7.14 years for the Foley’s catheter respondents. The indication for induction of labor, mean gestational age, and Bishop Score before cervical ripening was comparable in both groups. The major indications for induction of labor were prolonged pregnancies and hypertensive disorders. Noor et al.\(^\text{3}\) reported maternal baseline characteristics were similar between the two groups in terms of age, parity, gestational age, preinduction Bishop score, and indications for induction. Saeed et al.\(^\text{11}\) observed that the two groups were matched for confounding factors such as age, gravidity, and Bishop score. The mean age of the women in the study group was 26.22 years. There was no statistical difference (p=1.00) between the gestational age of women in both groups and the most common reason for induction of labor was post-date pregnancy in both groups. The mean Bishop score was poor 3.1± 95% confidence interval though not statistically significant (p = 0.6).

In present study observed that mean induction to delivery intervals was significant higher in Foley catheter group than misoprostol group (17.5±7.6 hrs vs 13.9±8.2 hrs) , p=0.037. However, induction to active phase interval was almost similar between two groups (p=0.847). Nyango et al.\(^\text{10}\) reported In the misoprostol group, 58 (77.3%) women achieved cervical ripening (cervical dilation of ≥4) within 12 h, compared to 43 (57.3%) in the Foley catheter balloon group. In the catheter group, eight women had the catheter removed on gentle
traction, while five women their catheter balloon delayed for about 24 h. Sixteen (21.3%) of the women in the catheter balloon group had an induction to delivery interval of ≥12 h. This agrees with the previous findings, which showed that induction of labor following the use of transcervical extra-amniotic Foley catheter as the cervical ripening agent is associated with longer labor ward stay and higher costs due to longer induction to delivery interval.\(^\text{12,13}\) In addition to the fact that some patients had the duration of their catheter extended from 12 to 24 h, shows that Foley catheter balloon, which dilates the cervix mechanically, is associated with a delayed transition to active labor. Therefore, our study also suggest that longer period of stay of the Foley catheter balloon may reduce the problem of longer induction to delivery interval since studies have shown that the Foley catheter balloon is safe for up to 24 h provided that the membranes are intact and the fetomaternal conditions remain satisfactory.\(^\text{14}\) Our findings were similar to Promila et al.\(^\text{15}\), Sheikher et al.\(^\text{16}\), Filho et al.\(^\text{17}\) and Roudsari et al.\(^\text{18}\) who also found significantly shorter induction to delivery interval in misoprostol group. Tuulii et al.\(^\text{19}\) reported that the total duration of labour was not significantly different in women induced with misoprostol compared with the Foley catheter (median duration from 1 to 10 cm: 12 versus 14.2 hours, \(p = 0.19\)). Promila et al.\(^\text{15}\) also reported shorter interval for misoprostol compared to Foley’s catheter (11.58 hours versus 19.45 hours). The shorter induction delivery interval in misoprostol group could be explained on the basis of greater oxytocic effect on uterus via vaginal route due to direct access to myometrium by cervical canal. In the study performed by Chung et al.\(^\text{20}\) and Adeniji et al.\(^\text{21}\) the induction to delivery interval did not differ significantly between the two groups.

In this study observed that oxytocin drip was found 25(47.2%) in misoprostol group and 27(73.0%) in Foley catheter group. Artificial rupture of membrane was 37(69.8%) and 35(94.6%) in misoprostol and Foley catheter group respectively. Oxytocin+ARM was 22(41.5%) in misoprostol group and 26(70.3%) in Foley catheter group. Oxytocin drip, artificial rupture of membrane and oxytocin + ARM were significantly higher in Foley catheter group than misoprostol group. Complications rate was also similar between two groups, that was not significant (\(p > 0.05\)). Noor et al.\(^\text{7}\) reported the use of oxytocin and ARM for labour augmentation was significantly higher in women induced with Foley catheter as compared to women induced with intravaginal misoprostol 77.2% versus 48.3% and 95.5% versus 66.7%, respectively. Combined use of oxytocin and ARM was 41.7% and 77.2% in misoprostol and Foley catheter group, respectively, and statistically it was very highly significant (\(\chi^2 < 0.001\)). Uterine contractile abnormalities like hyperstimulation were reported in 11.7% of women while there was no case of hyperstimulation. Nyango et al.\(^\text{10}\) reported significant finding in their study that is a high percentage (34.7%) of the women had precipitate labor and uterine hyper-stimulation 8 (10.7%) in the misoprostol group as compared with 9.3% and none in the Foley catheter balloon group, respectively, even though the same oxytocin regimen was used. This agrees with the previous reports showing that misoprostol is associated with risk of uterine hyperstimulation which increase with higher dosage.\(^\text{22}\) Saeed et al.\(^\text{11}\) found a greater need for later on use of oxytocin in dinoprostog set group as compared to misoprostol. They used the Cochrane Database\(^\text{23}\) definitions while evaluating uterine hyperstimulation, tachysystole, and CTG abnormalities. Abnormal CTGs were read by pelvic obstetrician on call in labor ward, and abnormalities in terms of fetal heart rate changes such as late decelerations, persistent variable decelerations, persistent brady or tachycardia, and decreased baseline variability were indicators used to label the CTG as abnormal.

In this study that spontaneous vaginal delivery was 35(66.0%) in misoprostol group and 15(40.5%) in Foley catheter group. Caesarean section was higher in Foley catheter group than misoprostol group (37.8% vs 18.9%). The difference was statistically significant (\(p<0.05\)) between two groups. Nyango et al.\(^\text{10}\) reported spontaneous vaginal delivery within 12 h was 88.0% and 66.3% in the misoprostol and Foley catheter group, respectively. This is similar to the previous studies.\(^\text{24,25}\) The overall spontaneous vaginal delivery rate of 66.6% and 88.0% in Nyango et al\(^\text{10}\) study is higher than the range of 48–66% previously reported.\(^\text{26}\) Saeed et al.\(^\text{11}\) reported the two groups were compared regarding mode of delivery, there were 84 (54.2%) normal deliveries in the misoprostol group and 71 (45.8%) in the dinoprostog set group. Instrumental deliveries were required in 39.4% women in the misoprostol group and 60.6% women in the dinoprostog set group. It was noted that 25% women induced with misoprostol and 75% women induced with dinoprostog set required cesarean section. But these differences did not reach statistical significance (\(p = 0.06\)). On the contrary, Van Gemund and Scherjon found a longer median induction-delivery interval in misoprostol group compared with dinoprostog set; however, the caesarean section rate was lower in the misoprostol group: 16.1% versus 21%.\(^\text{27}\)

In this study observed that mean birth weight, APGAR score 1 minute, 5 minute, admission in neonatal intensive care unit and meconium aspiration syndrome were not statistically significant between two groups (\(p > 0.05\)). Only one baby was died in Foley catheter group, but the difference was not statistically significant between two groups (\(p > 0.05\)). Nyango et al.\(^\text{10}\) reported there were no significant differences in the incidence of meconium staining and 1st min Appgar scores of the babies in the two groups: Foley’s catheter balloon and misoprostol groups. However, six babies had Appgar scores of <7 in the misoprostol group in the 5th min, though they did not require any intervention. Noor et al.\(^\text{3}\) observed that the birth weight (mean±SD) was 2.79±0.43 kg and 2.91±0.53 kg in misoprostol and Foley catheter group. The difference in the birth weight between the two study groups was statistically not significant (\(p > 0.05\)). The Appgar score at 1 minute and 5 minutes (mean±SD) was 7.80±0.77 versus 7.91±0.33 and 8.92±0.38 versus 8.98±0.15 in misoprostol and Foley catheter group, respectively. Statistically there was no significant difference in the Appgar score between the two groups at 1 minute and 5 minutes (\(p > 0.05\)). Statistically there was no significant difference in the Appgar score between the two groups at 1 minute and 5 minutes. Similar results were obtained by Filho et al.\(^\text{17}\) and Roudsari et al.\(^\text{18}\) and our present study supports these results.
Conclusion
The present study suggests intravaginal Misoprostol results in a shorter induction to delivery time, a reduction in the rate of caesarean delivery and also did not appear to produce miserable adverse effects on the method of delivery or the foetus in comparison Foley’s catheter.

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