Original Article

Comparison of Misoprostol with Foley Catheter vs Misoprostol alone for Cervical Ripening and Induction of Labor in Patients with Premature Rupture of Membrane: A Randomized Clinical Trial Study

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Abstract

Background: This study evaluates the effect of misoprostol alone in comparison with misoprostol with Foley catheter in preparing the cervix for induction of labor in women with premature rupture of the amniotic sac.

Materials and Methods: This randomized clinical trial study was performed from 2017 to 2019 on 206 pregnant women with singleton pregnancy and gestational age more than 36 weeks, whose rupture of the amniotic sac had occurred less than 12 hours and had a Bishop score less than 4. These women were randomly assigned to two groups of Foley catheters with misoprostol (intervention group, $P = 103$) or misoprostol alone (control group, $P = 103$) to induce labor. In both groups, sublingual misoprostol (25 micrograms) was administered at intervals of 4–6 hours. The collected data were analyzed by SPSS.21 software.

Results: There is no significant difference between age and Bishop score in the two groups ($P = 0.19$, $P = 0.31$, respectively). Lower doses (0 to 3) of misoprostol were used in the intervention group versus 0 to 5 doses in the control group ($P = 0.001$). Delivery time was shorter in the intervention group (10.83 hours vs. 13.10 hours in the control group, $P = 0.001$). Also, the probability of complications such as fever, tachysystole, and hospitalization of an infant in the neonatal intensive care unit (NICU) did not increase.

Conclusion: An intracervical Foley catheter with misoprostol is more effective in inducing labor in pregnancies with premature rupture of the membranes than using misoprostol alone and can be a safe and effective option.

Keywords: Cervical ripening, labor or induced, misoprostol or adverse effect, misoprostol or therapeutic effect, premature rupture of membrane, randomized controlled trial

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Introduction

Premature rupture of the amniotic sac is one of the most common complications of pregnancy, defined as the rupture of membranes before the onset of labor. This complication occurs in 3–19% of all pregnancies and 8–10% of full-term pregnancies. It is also responsible for 30% of all preterm deliveries. Premature rupture of membranes is one of the most important delivery problems due to increased maternal and fetal complications and mortality.[1,2]

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The cause of premature rupture of the amniotic sac is not known. The most likely cause of premature rupture of the amniotic sac is a decrease in the tensile strength of the membranes due to bacterial proteases. Among its causes are urinary tract infections, vaginitis, and sexual intercourse. The rupture of the amniotic sac has various maternal and fetal complications.[3] Maternal complications of premature rupture of amniotic sac include chorioamnionitis and postpartum metritis and sepsis. Fetal complications include umbilical cord prolapse, umbilical cord compression, placental abruption, and neonatal infections.[4] The risk of chorioamnionitis in premature rupture of the amniotic sac depends on gestational age and the time interval between rupture of the amniotic sac and delivery. The longer the time between the amniotic membrane rupture from delivery, the greater the risk of maternal and fetal infection.[5] Several factors increase the success of labor induction, including multiparousity, body mass index (BMI) less than 30, birth weight less than 3500 gr, and favorable cervical condition.[6]

Studies have demonstrated that low Bishop scores (unprepared cervix) are associated with increased rates of cesarean section, maternal fever, and birth asphyxia. To reduce the failure of labor induction, cervical preparation should be performed by any method.[7]

Various methods have been employed to prepare the cervix and induce labor in patients with premature rupture of the amniotic sac, including pharmacological methods (the most common of these drugs: prostaglandin E2, oxytocin, and misoprostol) and non-pharmacological methods (nipple stimulation, sexual intercourse, castor oil, acupuncture, homeopathy, membrane separation, warm water bath, mechanical dilation, laminaria, synthetic osmotic dilator, and trans-cervical Foley catheter with or without extra saline injection), but there is no consensus on the best method.[8]

One of the non-pharmacological methods of cervical preparation is the use of a Foley catheter inside the cervix. Foley catheterization is a cheap and available mechanical procedure that is less likely to cause tachysystole. It has no serious side effects. This catheter has safely and effectively worked in patients with healthy amniotic sacs. However, due to the concern of rising infection in its use in patients with ruptured membranes (amniotic sac), its efficiency and safety have been less evaluated.[9] Methods such as vaginal misoprostol and mechanical procedures have been less commonly used in patients with premature rupture of membranes (PROM) due to infection concerns. Since the combination of the Foley catheter and misoprostol in pregnant women with a healthy amniotic sac has been extensively used, has worked effectively, and is a common method of preparing the cervix in pregnant women with healthy amniotic sac as candidates for termination of pregnancy, this study was conducted with the aim of evaluating the effect of sublingual misoprostol alone in comparison with misoprostol with the Foley catheter in preparing the cervix for induction of labor in women with premature rupture of the amniotic sac.

Materials and Methods

This clinical trial study was performed from 2017 to 2019 on 206 pregnant women with singleton pregnancy and gestational age more than 36 weeks, whose rupture of the amniotic sac had been less than 12 hours and had a Bishop score less than 4 at Mashhad University of Medical Sciences, Umm Al-Banin and Imam Reza (AS) Hospitals, Mashhad, Iran [Figure 1].

This study has been approved by the ethics committee of Mashhad University of Medical Sciences with the code IR.MUMS.fm.REC. 1395/490, and the trial was registered at IRCT20181123041731N1. The study was conducted after explaining the objectives of the study and obtaining written consent from individuals. The sample size was extracted from the article by Garba *et al*., which was published in 2016, and considering $\alpha = 0.05$ and $\beta = 0.2$, the sample size was obtained with the help of Statistical Package for the Social Sciences (SPSS) software in each group of 103 people.

The patients with Singleton live pregnancy, gestational age greater than or equal to 36 weeks (based on ultrasound 8–14 weeks or exact date of last menstruation), cephalic presentation, and Bishop score less than 4 were included in the study.

Patients with symptoms of chorioamnionitis at the time of admission, gestational diabetes, multiple fetuses, fetal distress, previous cesarean section and any contraindications for vaginal delivery, presence of meconium at the time of hospitalization and active genital herpes and seropositive test for acquired immunodeficiency syndrome (AIDS), amniotic sac rupture time greater than 12 hours, active phase of labor, active bleeding (cervical lesion), and withdrawal from participation in the project at any stage were excluded.

All women with singleton and live pregnancies with a ruptured amniotic having clear drainage on examination or Fern test, nitrazine test, or AmniSure test were positive in them. Their gestational age at the time of rupture of the amniotic sac was greater than or equal to 36 weeks (based on ultrasound 8 to 14 weeks or the exact date of the latest mense) and were admitted to Mashhad teaching hospitals for delivery, and after obtaining their informed consent, they entered the study.

At the time of admission, fetal electrocardiograms (ECGs) (electrophysiological activity of the fetal heart) were taken from all patients, and then, patients were randomly assigned by either a computer or the assistant to either misoprostol (control group) or misoprostol group with a Foley catheter (intervention). Random allocation was based on a random list generated by the software.

For patients (control group), induction of labor was performed with misoprostol tablet (Cytotec; Pfizer: SA, Madrid) 25 micrograms sublingually every 4–6 hours, and in the other group (intervention), induction of labor was performed with misoprostol (25 micrograms) sublingually every 4–6 hours with the insertion of catheter Foley No. 18 and filling the

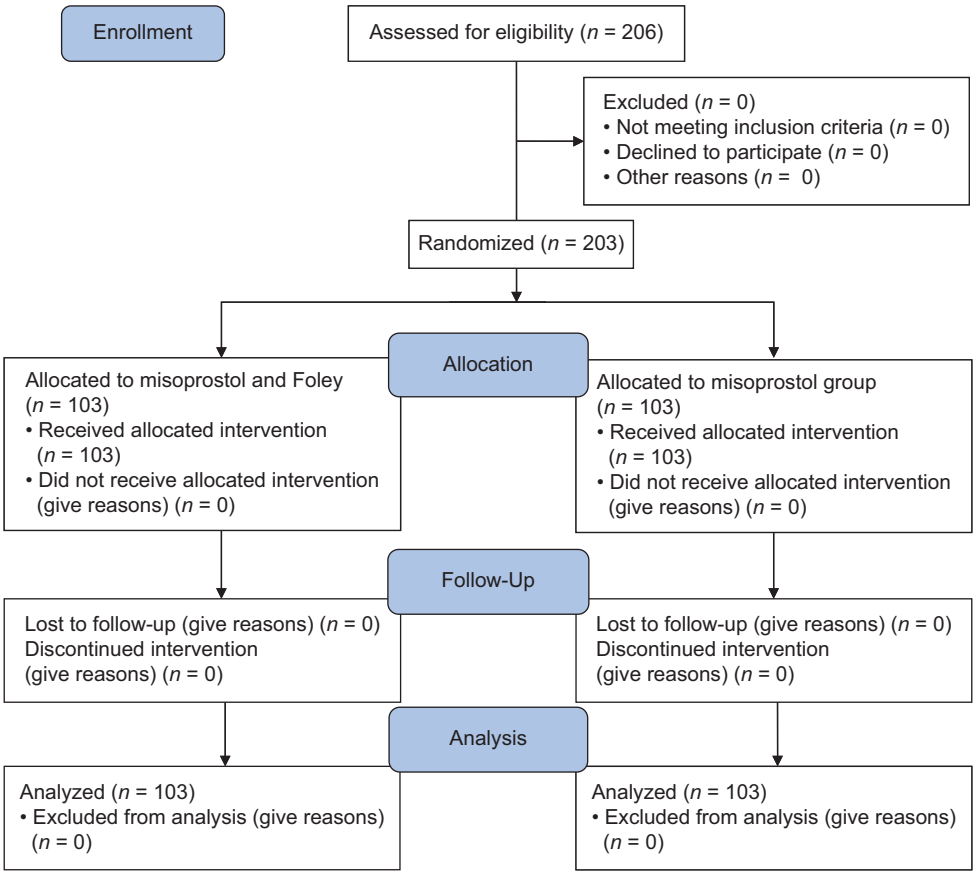

Figure 1: CONSORT diagram

balloon with 50 cc of normal saline by a gynecologist and in dorsal lithotomy and under sterile conditions. In both groups, body temperature was controlled every hour and all patients were monitored continuously for vital signs during labor. A vaginal examination was performed every 4 h; if the uterine contractions did not begin, the patient received another dose. In the presence of spontaneous and frequent contractions (about 40–50 sec every 3 min), the next dose was not administered. Misoprostol was administered up to a maximum of six doses, and oxytocin was started with a low-dose protocol after cervical preparation.

In the group with a Foley catheter, gentle traction was performed every 4 hours to check the catheter exit.

Demographic information and other indicators of the studied women were collected in a self-made checklist. Finally, the time interval between the start of the intervention and the time of delivery, delivery method, delivery, and neonatal complications (incidence of tachysystole, chorioamnionitis, hysterectomy, postpartum hemorrhage, manual placenta removal, fever, and hospitalization in NICU) in both groups was measured and compared by the selected assistant according to the national protocol. The recorded data were analyzed by SPSS version 16 software.

The characteristics of the subjects were presented by descriptive statistical methods including central indicators, dispersion, and frequency distribution in the form of appropriate tables and graphs. The independent-samples *t*-test was used to compare quantitative variables between the two groups if there was a normal distribution, and otherwise, the Mann–Whitney test was used. To compare qualitative variables between the two groups, the Chi-square test, and if necessary, Fisher's exact test was used. In all calculations, the value of 0.05 was considered a significant level.

Results

In this study, in terms of the average age of patients, which was 27.17 ± 6.01 in the intervention group and 28.33 ± 6.90 in the control group, there was no significant difference according to the *t*-test between the two groups ($P = 0.19$). The mean BMI in the intervention group was 28.65 ± 3.98 and in the control group was 28.55 ± 3.50, which was not a significant difference according to the *t*-test ($P = 0.83$). The time of delivery from the beginning of the intervention (catheter insertion into the cervix or misoprostol administration) averaged 10.08 ± 5.78 hours in the intervention group and 13.10 ± 7.37 hours in the control group. According to the *t*-test, this difference was significant ($P = 0.001$) [Table 1].

In the intervention group, 53 people, equivalent to 51.5%, are primigravida and 52.4% of the control group are primigravida, which according to the Chi-square test showed

that there is no significant difference in parity between the two groups ($P = 0.88$). The time elapsed from amniotic sac rupture was 0 to 11 hours in the intervention group and 0 to 12 hours in the control group. The median was 4 hours in both groups, and there was no significant difference according to the Mann–Whitney test ($P = 0.15$) [Table 2].

The Bishop score in the intervention group was 0 to 4 hours with a median of 2 and in the control group was 0 to 5 hours with a median of 2, which according to the Mann–Whitney test were not significantly different ($P = 0.31$). Also, in the intervention group 0 to 3 doses of misoprostol were used and in the control group 0 to 5 doses were used, which according to the Mann–Whitney test showed that this difference was significant and has been less in the intervention group ($P = 0.001$); in the intervention group, 0 to 3 doses of misoprostol were used and in the control group 0 to 5 doses were used, which according to the Mann–Whitney test showed that this difference was significant and has been less in the intervention group ($P = 0.001$) [Table 2].

In terms of delivery type, in the intervention group 73.8% had a normal delivery, 20.4% had a cesarean section, and 5.8% had instrumental delivery (assisted birth), and in the control group, 65% had a normal delivery, 32% had cesarean section, and 3%. had instrumental delivery According to the Chi-square test, there was no significant difference in the type of delivery ($P = 0.12$). In terms of hospitalization in NICU ($P = 0.18$) (according to the Chi-square test), postpartum hemorrhage ($P = 0.36$), manual placental removal ($P = 0.65$), hysterectomy ($P = 1$), fever ($P = 0.44$) (according to Fisher's test), and uterine tachysystole ($P = 0.40$) (according to the Chi-square test), there was no statistically significant difference between the two groups ($P = 0.18$) [Table 3].

Table 1: Characteristics of patients in the two groups of misoprostol (control) and misoprostol with Foley catheter (intervention)

Variable	Group Mean (standard deviation)		Test result
	Intervention ($n=103$)	Control ($n=103$)	
Age (year)	27.17 (6.10)	28.33 (6.099)	0.19
BMI	28.65 (3.98)	28.55 (3.035)	0.83
*Delivery time (hour)	10.83 (5.78)	13.10 (7.37)	0.001
Primigravid (n, %)	53 (51.5)	51 (52.4)	0.88

Chi-square test, t-test. *Mann–Whitney test

Discussion

Due to the increased risk of infection using a Foley catheter in patients with amniotic sac rupture in the previous studies,[3,9] the present study revealed that an intracervical Foley catheter with misoprostol increases the chances of a normal delivery following induction of labor by preparing the cervix without increasing maternal and fetal complications in patients with premature rupture of the amniotic sac and causes a reduction in the time interval between rupture of the amniotic sac and

Table 2: Variable in the two groups of misoprostol (control) and misoprostol with Foley catheter (intervention)

Variable	Group						Test result
	Intervention ($n=103$)			Control ($n=103$)			
	Minimum	Median	Maximum	Minimum	Median	Maximum	
Time elapsed from amniotic sac	0	4	11	0	4	12	0.15
Initial bishop score	0	2	4	0	2	5	0.31
Number of misoprostol doses used	0	1	3	0	2	5	0.001

Mann–Whitney test

Table 3: Complications in two groups of misoprostol (control) and misoprostol with Foley catheter (intervention)

Variable	Number (%)				Test result
	Intervention		Control		
Delivery type	76 (73.8)				0.12
Normal	21 (20.4)		67 (65)		
Cesarean	6 (5.8)		33 (32)		
Instrumental			3 (2.9)		
Variable	**Yes**	**No**	**Yes**	**No**	***P*- value**
Hospitalization in NICU	5 (4.9)	98 (95.1)	10 (9.7)	93 (93.3)	0.18
Postpartum hemorrhage	4 (3.9)	99 (96.1)	1 (1)	102 (99)	0.36
Manual placental removal	7 (6.8)	96 (93.2)	1 (1)	102 (99)	0.65
Hysterectomy	1 (1)	102 (99)	0	103 (100)	1.00
Fever	2 (1.9)	101 (98.1)	5 (4.9)	98 (95.1)	0.44
*Uterine tachysystole	15 (14.6)	88 (85.4)	11 (10.7)	92 (89.3)	0.40

Chi-square test, Fisher's exact test. *Uterine tachysystole is a condition of excessively frequent uterine contractions during pregnancy

delivery, which plays a key role in reducing the complications of rupture of the amniotic sac.

In a study by Garba *et al*. in 2016, 202 pregnant women with premature amniotic sac rupture were randomly divided into two groups of 101. One group received misoprostol, and for the other group, a Foley catheter was inserted into the uterus. It was observed that both groups had the same complications such as neonatal and postpartum infections, as well as similarity in cesarean section rate and delivery time. They concluded that an intracervical Foley catheter or misoprostol can both be used to prepare the cervix in women with premature amniotic sac rupture. In the present study, an intracervical Foley catheter was used concomitantly with cervical preparations (misoprostol), which resulted in reduced delivery time.[10]

In a study by Maier *et al*., in 2018, an intracervical Foley catheter with oxytocin was used to prepare the cervix in nulliparous women with amniotic sac rupture. In the mentioned study, 128 nulliparous women with premature amniotic sac rupture were randomly selected and divided into two groups. One group was given oxytocin, and for the second group, in addition to oxytocin, an intracervical Foley catheter was inserted. In this study, contrary to our study, labor time was not reduced and there was no difference in complications such as postpartum hemorrhage, chorioamnionitis, and tachysystole. Perhaps the reason for this discrepancy is that only nulliparous women were included in this study and misoprostol was not used as well.[11]

In a retrospective study conducted by Kruit in 2014 on deliveries from 2009 to 2012 following premature amniotic sac rupture, of a total of 129 deliveries, 43 were performed using intracervical Foley catheters. In 86 cases, oxytocin or vaginal misoprostol was used. 83.7% of the Foley catheter group were nulliparous women, while in the other group 55.8% were nulliparous. Also, in cases where an intracervical Foley catheter was used, the use of intrauterine pressure catheters (IUPCs), cesarean section rate, mean duration of amniotic sac rupture, and active phase were higher as well. The amount of chorioamnionitis was higher in these people than in the other group, but this difference was not significant ($P = 0.1$). Kruit finally states that the reason for this increase in the incidence of chorioamnionitis in users of intracervical Foley catheter is the increased use of IUPCs and nulliparous individuals and has suggested that further prospective studies be performed in this regard.[12] In the present study, an intracervical Foley catheter with misoprostol is a suitable and safe method for cervical preparation in pregnant women with premature amniotic sac rupture.

Conclusion

Concomitant use of intracervical Foley catheter and misoprostol in women with premature amniotic sac rupture in term pregnancies can reduce labor time and also does not increase complications such as chorioamnionitis.

Ethical considerations

The Mashad University of Medical Sciences Ethics Committee (code: R.MUMS.fm.REC.1395/490) approved this study. Informed consent was obtained from all participants.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sinha R, Gupta S. A comparative study of 25µg versus 50µg vaginal misoprostol for induction of labour at term premature rupture of membrane. Int J Reprod Contracept Obstet Gynecol 2017;6:1511-7.
2. Ehsanipoor R. Practice Bulletin No. 172: Premature rupture of membranes. Obstet Gynecol 2016;128:e165-77.
3. Ahirwar G, Rajput N, Verma YS. Study of patients with premature rupture of membranes. J of Evolution of Med and Dent Sci 2015;4:5388-94.
4. Oza A, Shah JM, Mewada B, Thaker R. A comparative study between PGE1 and PGE 2 for induction of labour in premature rupture of membrane at term. Int J Reprod Contracept Obstet Gynecol 2016;5:202-5.
5. Hannah ME, Ohlsson A, Farine D, Hewson SA, Hodnett ED, Myhr TL, *et al*. Induction of labor compared with expectant management for prelabor rupture of the membranes at term. TERMPROM Study Group. N Engl J Med 1996;334:1005-10.
6. Cunningham FG, Leveno KJ, Bloom SL, Dashe JS, Hoffman BL, Casey BM, *et al*. Williams obstetrics. 25th ed. New York: McGraw Hill education; 2018.
7. Fareed P, Malik S, Mahajan N, Nazir T, Kawoosa S. Comparative study of intra-cervical foley catheter and vaginal misoprostol for pre-induction cervical ripening. IJSS 2015;3:40-3.
8. Kenyon S, Dann S, Hope L, Clarke P, Hogan A, Jenkinson D, *et al*. Evaluation of a bespoke training to increase uptake by midwifery teams of NICE Guidance for membrane sweeping to reduce induction of labour: A stepped wedge cluster randomised design. Trials 2017;18:357.
9. Amorosa JMH, Stone J, Factor SH, Booker W, Newland M, Bianco A. A randomized trial of Foley bulb for labor induction in premature rupture of membranes in nulliparas (FLIP). Am J Obstet Gynecol 2017;217:360.e1-7.
10. Garba I, Muhammed AS, Muhammad Z, Galadanci HS, Ayyuba R, Abubakar IS. Induction to delivery interval using transcervical Foley catheter plus oxytocin and vaginal misoprostol: A comparative study at Aminu Kano Teaching Hospital, Kano, Nigeria. Ann Afr Med 2016;15:114-9.
11. Maier JT, Schalinski E, Gauger U, Hellmeyer L. Cervical ripening with an osmotic dilator (Dilapan-S) in term pregnancies – An observational study. J Gynecol Neonatal Biol 2015;1:1-6.
12. Kruit H, Tihtonen K, Raudaskoski T, Ulander VM, Aitokallio-Tallberg A, Heikinheimo O, *et al*. Foley catheter or oral misoprostol for induction of labor in women with term premature rupture of membranes: A randomized multicenter trial. Am J Perinatol 2016;33:866-72.