Received: 11 September 2021 | Revised: 5 December 2021 | Accepted: 22 December 2021

DOI: 10.1002/hsr2.502

Health Science Reports Open Access WILEY

ORIGINAL RESEARCH

Effect of vaginal washing before Misoprostol insertion on cervical ripening before induction of labor: A randomized single-blind clinical trial

Roya Kabodmehri[1] | Seyedeh Hajar Sharami[1] | Forozan Milani[1] | Fatemeh Hosseinzadeh[1] | Seyedeh Fatemeh Dalil Heirati[1] | Zakie Bakhshipour[1] | Zahra Pourhabibi[2]

[1]Reproductive Health Research Center, Department of Obstetrics and Gynecology, Al-Zahra Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

[2]Vice-Chancellorship of Research and Technology, Guilan University of Medical Science, Rasht, Iran

Correspondence
Forozan Milani, Reproductive Health Research Center, Al-zahra Hospital, Guilan University of Medical Sciences, P.O. Box: 4144654839, Namjoo Street, Rasht, Iran.
Email: forozanmilani@yahoo.com

Funding information
Guilan University of Medical Sciences

Abstract

Background: Vaginal pH is acidic in pregnancy, but there is no information about pH changes in pregnancy, and contradictory results have been reported from the effectiveness of Misoprostol at different vaginal pH. This study aimed to evaluate the effect of vaginal washing before Misoprostol insertion on cervical ripening before induction of labor in comparison with the control group.

Methods: This randomized single-blind clinical trial was performed on 148 pregnant women who were candidates for induction of labor. Subjects were randomly divided into two groups of intervention (vaginal washing with 20 cc of normal saline 0.9% before Misoprostol insertion) and the control group (without vaginal washing). Vaginal pH and Bishop scores were measured before and after the intervention. The two groups were compared in demographic-obstetric variables, the success rate of induction of labor, maternal and neonatal outcomes, and Misoprostol dose.

Results: After the intervention, there was no statistically significant difference between the pH before and after in the group with vaginal washing. There was no significant difference between the two groups in the type and duration of labor, and maternal and neonatal outcomes ($P > .05$). The frequency of normal delivery less than 12 hours in the intervention group was higher than in the control group. Although this difference was not statistically significant due to the small number of subjects, it is clinically significant.

Conclusion: The results of the present study showed that vaginal washing with normal saline before Misoprostol insertion for induction of labor did not affect the success of induction and duration of labor.

KEYWORDS
cervical ripening, induction of labor, misoprostol, vaginal washing

1 | INTRODUCTION

Induction of labor occurs in about 20% of pregnancies for a variety of reasons.[1] Various medical and surgical methods are used to induce labor and cervical ripening. Prostaglandin E1 (Cytotech or Misoprostol) is more recommended for cervical ripening and induction of labor than other prostaglandins because it's cheap and stable at room temperature.[1] Various clinical trials have shown that vaginal Misoprostol can be effective in cervical ripening and promoting uterine contractions by reducing the interval between induction and delivery.[2,3] In general, induction of labor using prostaglandins improves the success rate of normal delivery, reduces the rate of cesarean sections, and is associated with greater maternal satisfaction.[1] Misoprostol cannot be completely dissolved in the vagina, and studies have shown that the effectiveness of the drug is related to the plasma level of the drug and reaching the highest level. Some studies have examined the factors affecting the absorption of this drug and mentioned the role of vaginal pH,[4,5] and others in the solubility and high plasma level of the drug.[6] Both of these items can be effective by a similar mechanism.

It has been reported that vaginal Misoprostol absorption varies in different patients and the effect of soaking vaginal pills in water or saline in increasing its solubility has been observed.[6] Recently, some studies introduced vaginal pH as an effective factor on the prostaglandins function for cervical ripening, which can affect drug ionization and absorption.[7,8] Some studies have reported higher efficacy of Misoprostol in an acidic environment and some in an alkaline environment.[9-11] Studies supporting the acidic pH of the vagina on the higher efficiency of vaginal Misoprostol have reported that prostaglandins are acidophil and Misoprostol dissolves better in an acidic environment.[12,13] When the acidic environment in the vagina is created with acetic acid, the success rate of induction with Misoprostol increases.[12,13] Other studies have found more efficacy for vaginal Misoprostol in moderate acidity and refused the effect of an acidic environment.[14]

In an in vitro study comparing Dinoprostone releasing at vaginal pHs of 7.4, 5.4, and 3.4, it was found that prostaglandin releasing was reduced in acidic pH, and an optimal pH for this purpose is 7.4.[7] The vaginal pH in pregnancy is acidic and vaginal washing reduces the normal flora of the vagina and changes the pH to alkaline, and it seems that according to this hypothesis, Misoprostol can be more effective in a thinner environment and higher pH.[15] However, contradictory results have been reported in other studies. Some studies have found that high vaginal pH is effective in improving the function and bioactivity of prostaglandins, which reduces the active phase of labor.[15,16] Finally, other studies have not reported efficacy and the optimal pH for achieving maximal Misoprostol efficacy. A need for more research has been suggested determining the involved factors in this regard.[17] So, due to the lack of sufficient information about pH changes during pregnancy and contradictory results from the effectiveness of Misoprostol at different pH, the present study has been designed to investigate the effect of vaginal washing before Misoprostol insertion on cervical ripening before induction of labor.

2 | PATIENTS AND METHODS

2.1 | Trial design

This study was a randomized single-blind clinical trial that was registered in the Iranian Clinical Trials Registration Center (IRCT20080826001096N7). This trial design was a parallel randomized clinical trial, and the allocation ratio was usually 1:1. The present study was conducted in 2019-2020 at Al-Zahra Educational and Medical Center, Rasht, Iran.

2.2 | Participants and sampling methods

This study was performed on term pregnant women who were candidates for induction of labor referred to Al-Zahra Hospital, Rasht, Iran during 2019-2020. All the participants signed a written informed consent before the intervention. Inclusion criteria included 18-40 years-old pregnant women with single pregnancy, term last menstrual period (LMP)-approved pregnancy (first day of last menstrual period and first-trimester ultrasound), cephalic presentation, normal fetal heart rate (FHR), no prohibition of normal delivery (such as cephalopelvic disproportion), no spontaneous and effective uterine contractions (less than three contractions in 30 minutes), Bishop score less than 6, fetal weight less than 4000 g. Indications of induction include post-term pregnancy, oligohydramnios, reduced fetal movement, abnormal biophysical profile score, maternal diabetes, fetal growth restriction, and preeclampsia. Exclusion criteria included multiple pregnancies, gestational age less than 37 weeks, rupture of membranes, non-reassuring FHR, fetal anomaly, chorioamnionitis, known prostaglandin allergy, a history of previous cesarean section or scarring of the uterus, and vaginal bleeding.

The two groups of the study were matched in terms of the number of deliveries (primiparous and multiparous) before Misoprostol insertion. The initial Bishop score was recorded by a gynecology resident and then the vaginal pH was determined with Nitrazine paper. In both groups, the gynecological examination was performed with speculum and examined for infection. In the absence of clinical vulvovaginal infection, in the case group, vaginal washing with 0.9% normal saline (20 cc) was performed before Misoprostol insertion (25 μg in posterior vaginal fornix) and then vaginal pH was recorded. In the control group, only Misoprostol suppositories were inserted. When cervical ripening does not occur (Bishop score less than 6), the Misoprostol insertion was repeated every 4 to 6 hours for a maximum of four doses.[1]

Both groups received the same routine treatment at the beginning of the active phase of labor. Uterine contractions and FHR were monitored in all subjects. Labor stages and consequences were recorded in labor by a gynecology resident. Before administration of each dose of Misoprostol, uterine contractions and FHR were monitored for 10 minutes using a fetal monitoring device and vaginal examination was performed. If the number of contractions was more than three times in 10 minutes, the next dose would not be

prescribed. If regular uterine contractions did not occur despite cervical ripening, 4 hours after the last dose of Misoprostol, induction with oxytocin was started according to routine protocol. Patients who entered the active phase and experienced a secondary cessation of labor (no change in dilatation for more than 2 hours) were stimulated by intravenous oxytocin solution. Oxytocin was prescribed at least 4 hours after the last dose of Misoprostol, according to the American College of Obstetricians and Gynecologists guideline. In case of hyperstimulation, suppository remnants were removed from the vagina, the maternal position changed to the left lateral, oxygen therapy was performed with a face mask, oxytocin infusion was stopped. FHR control was performed every half hour during the first phase of labor and every 15 minutes during the second phase of labor. Labor monitoring and other interventions, if necessary, were performed routinely.

2.3 | Randomization, blinding, and concealment of allocation

The study groups were matched in terms of the number of deliveries (primiparous and multiparous) before Misoprostol insertion. Eligible individuals (those with a Bishop score of less than 6) were randomly assigned to the intervention group (vaginal washing) and the control group (without vaginal washing) using four randomized blocks in sealed envelopes. Random sequences were generated using computer software. After generating the list, each person was assigned a unique code and during the study, the person was identified with this code. None of the participants in the study were aware of the randomization list. Registration and random allocation sequence were done by the gynecology resident. Sealed envelopes, numbered in order, were used to conceal the randomization process, and the envelope for each individual was opened only after the eligibility criteria were approved and the individual signed the consent form.

2.4 | Study outcomes

The main outcome of the present study was the success of induction of labor (the time interval from the start of induction to the entry into the active phase of labor). The active phase of labor in this study was defined as having effective and regular contractions simultaneously with cervical effacement and dilatation of 5 cm or more.[1] Secondary outcomes in this study included the time from vaginal Misoprostol insertion to the active phase, type of delivery (cesarean section or normal vaginal delivery (NVD)), hyperstimulation (six or more uterine contractions in 10 minutes), Uterine tachysystole (more than five contractions in 10 minutes, or single contraction lasting longer than 2 minutes or when either condition leads to a non-reassuring FHR pattern), FHR abnormality (tachycardia, late decelerations, bradycardia), failure in the induction of labor, fetal distress, meconium passage, and change in Bishop score after 6 hours, duration of labor, and the dose of used Misoprostol, neonatal weight, 1 and 5 minutes Apgar score and neonatal intensive care unit (NICU) admission rate.

2.5 | Statistical analysis

The sample size was determined based on Yayla Abide et al include 164 participants (two groups of 82 participants).[15] The data were analyzed by SPSS software version 21. After examining the normality distribution of quantitative data with the Kolmogorov-Smirnov test, a *t*-test was used to compare data with normal distribution between groups, and the Mann-Whitney test was used for variables without normal distribution. Chi-square and Fisher tests were used to evaluate the qualitative variables and the Wilcoxon test was used for comparison before and after the test. *P*-values less than .05 were considered significant.

2.5.1 | Ethical consideration

The study was approved by the ethics committee of Guilan University of Medical Sciences (IR.GUMS.REC.1398.107). All stages of this research have been performed according to the Helsinki declaration. All procedures of the study were explained clearly to the participants who had the eligible inclusion criterion. Moreover, all participants voluntarily filled out the written informed consent form before they join the study and they were free to decide whether or not to attend or withdraw at any time and for any reason without changing the medical care.

3 | RESULTS

In the present study, 148 people participated who were divided into two groups of 74 people (Figure 1). The results showed that there was no statistically significant difference between the two groups in terms of maternal age, gestational age, number of pregnancies, initial Bishop Score, and vaginal pH before intervention (Table 1).

Comparing the pH before and after the intervention in the group with vaginal washing using the Wilcoxon sign test, no statistically significant difference was observed (pH before the intervention: 5.25 ± 0.66 and pH after the intervention: 5.39 ± 0.88; $P = .279$). Indications for induction of labor between the two groups are presented in Table 2. No significant difference was observed between the two groups.

There was no statistically significant difference between the two groups in terms of induction of labor success variables (including the interval between Misoprostol insertion and oxytocin prescription, the time interval from induction to rupture of membranes, the time interval from induction to the active phase, and interval from the beginning of induction of labor to complete dilatation) and Bishop scores 6 hours after vaginal washing (Table 3).

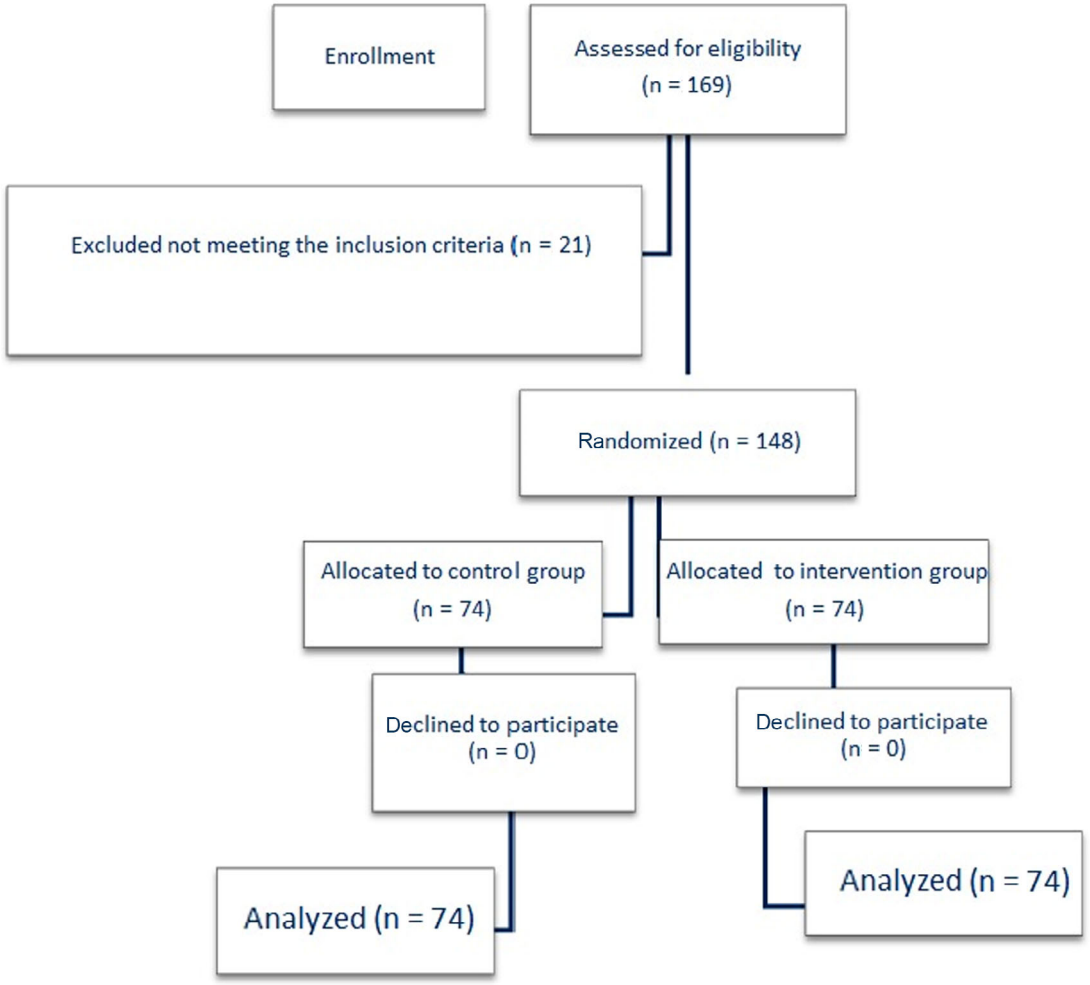

FIGURE 1 Consort flow diagram

TABLE 1 Comparison of demographic characteristics and vaginal pH between the two study groups

	Intervention group (n = 74)	Control group (n = 74)	*P* value
Age (year) (M ± SD)	27.99 ± 6.31	27.38 ± 6.17	.54[a]
Gestational age (wk) (M ± SD)	38.65 ± 1.60	39.01 ± 1.25	.12[a]
Gravidity (M ± SD)	1.57 ± 0.79	1.45 ± 0.81	.35[a]
Initial Bishop	2.65 ± 1.11	2.72 ± 0.91	.52[b]
Vaginal pH before intervention	5.25 ± 0.66	5.32 ± 0.78	.31[b]

[a]Independent-*t* test.
[b]Mann-Whitney.

There was no significant difference between the two groups in terms of the type of delivery and maternal and neonatal outcomes. Also, in none of the study groups, tachysystole, hyperstimulation, and NICU admission were observed. Also, the 5-minute Apgar score was above 7 in the neonates of both study groups (Table 4).

4 | DISCUSSION

The results of this study showed that vaginal washing with normal saline before Misoprostol insertion had no effect on the success of induction of labor and duration of labor (interval between Misoprostol insertion to oxytocin prescription, the time interval from induction to rupture membranes, time interval from induction to the active phase beginning and the time interval from the onset of induction of labor to complete dilatation). Considering that the pH of the vagina changed slightly after the intervention (pH before the intervention: 5.25 ± 0.66 and pH after the intervention: 5.39 ± 0.88), no significant difference between the two groups can be justified. However, the frequency of normal delivery less than 12 hours in the intervention group was higher than in the control group. Although this difference was not statistically significant due to the small number of subjects, it is clinically

TABLE 2 Comparison of frequency of induction of labor indication between study groups

	Intervention group, n (%) (n = 74)	Control group, n (%) (n = 74)	P
Postdate			.62[a]
Yes	17 (22.97%)	26 (35.13%)	
No	57 (77.03%)	48 (86.64%)	
Fm + BPP			.61[b]
Yes	29 (39.2%)	26 (35.1%)	
No	45 (60.8%)	48 (64.9%)	
IUGR			.82[b]
Yes	11 (14.9%)	12 (16.2%)	
No	63 (85.1%)	62 (83.8%)	
DM			.71[a]
Yes	5 (6.8%)	3 (4.1%)	
No	69 (93.2%)	71 (95.9%)	
Oligohydraminuos			.99[a]
Yes	2 (2.7%)	2 (2.7%)	
No	72 (97.3%)	72 (97.3%)	
Preeclampsia			.78[b]
Yes	8 (10.8%)	7 (9.5%)	
No	66 (89.2%)	67 (90.5%)	

[a]Fisher exact test.
[b]Chi-square test.

TABLE 3 Comparison of induction of labor success variables between the two groups

	Intervention group (M ± SD)	Control group (M ± SD)	P[a]
The time interval between Misoprostol insertion to oxytocin prescription (h)	11.46 ± 6.79	13.85 ± 1.27	.40
The time interval from induction to rupture membranes (h)	19.15 ± 2.02	19.17 ± 1.62	.62
The time interval from induction to the active phase beginning (h)	20.37 ± 1.55	22.12 ± 1.09	.21
The time interval from the onset of induction of labor to complete dilatation (h)	22.55 ± 1.48	24.72 ± 1.15	.17
The time interval from induction to delivery (h)	22.32 ± 1.92	23.34 ± 1.71	.49
Misoprostol dose (mg)	45.95 ± 29.84	54.73 ± 46.47	.38
Misoprostol dose (number)			.61
1	39 (52.7)	34 (45.9)	
2	18 (24.3)	21 (28.4)	
3	11 (14.9)	19 (12.2)	
4	6 (8.1)	10 (13.5)	

[a]Mann-Whitney.

significant (29.6% vs 11.4%). Also, there was no statistically significant difference between the two groups in terms of the indications of induction of labor (25 μg in posterior vaginal fornix) type of delivery and maternal and neonatal outcomes.

In recent studies, vaginal pH has been introduced as an effective factor on prostaglandins function in cervical ripening, by an effect on drug ionization, absorption, and ultimately the clinical response of the drug,[7,8] but contradictory results have also been reported in some studies.[9,10] Some studies have reported higher efficacy of Misoprostol in an acidic environment and some in an alkaline environment.[10-13,18] Other studies suggest that when the acidic environment in the vagina is created with acetic acid, the success rate of Misoprostol increases[12,13] and some studies have considered the effectiveness of vaginal Misoprostol in moderate acidity[5] and refused the effect of acidic environment.[14] Other studies have found that high vaginal pH is effective in improving the function and bioactivity

TABLE 4 Comparison of type of delivery and outcomes between the two groups

	Intervention, n (%) (n = 74)	Control, n (%), (n = 74)	*P*
Type of delivery			.18[a]
NVD	27 (36.5%)	35 (47.3%)	
C/S	47 (63.5%)	39 (52.7%)	
Delivery <12 h	8 (29.6%)	4 (11.4%)	.072[a]
Delivery in 12-25 h	19 (70.4%)	31 (88.6%)	
Cause of cesarean section			.06[b]
Fetal distress	21 (44.7%)	20 (51.3%)	
Lack of progress	3 (6.4%)	0	
Meconium excretion	19 (40.4%)	19 (48.7%)	
Cause of cesarean section			.06[b]
No	5 (10.6%)	0	
Yes	42 (89.4%)	39 (100%)	
1 min Apgar score			.99[b]
<7	4 (5.4%)	3 (4/1%)	
>7	70 (94.6%)	71 (95.9%)	
Fetal weight (g)	3204.53 ± 518	3240.1 ± 373	.63

[a]Chi-square test.
[b]Fisher exact test.

of prostaglandins, reducing the active phase of labor.[15,16] Finally, Chandra et al have reported no efficacy and the optimal pH for achieving maximal Misoprostol efficacy has not yet been identified.[17] So, it has been suggested that further studies determine the involving factors.

To compare the results of the present study with other studies, since similar studies in this field are limited, studies with different insertion methods (the type of prostaglandin, type of vaginal washing agent, pH classification into subgroups, and gestational age) is mentioned. Contrary to the findings of this study, Yayla Abide et al reported that vaginal washing with 0.9% normal saline shortened the duration of vaginal Dinoprostol retention, and the time from the onset of vaginal Dinoprostone insertion to the onset of the active phase of labor, and labor.[15] Considering that in both studies, the groups were matched in terms of age, the number of pregnancies, and Bishop score before insertion and also the pH was the same in both groups before the intervention to control the effect of confounders, it seems that the only difference of these studies is the type of prostaglandin used, drug dose and sample size. It should also be noted the slight difference in pH change before and after the intervention in the group with vaginal washing (pH before the intervention: 5.25 ± 0.66 and pH after the intervention: 5.39 ± 0.88).

On the other hand, conflicting results have been obtained in studies that the researcher's hypothesis was prostaglandins are effective in acidic media. Some studies have reported that acidic vaginal pH in the first and second trimesters has no effect on the induction of labor with Misoprostol,[14,19] while Rashwan et al reported positive and effective results.[12] According to the results of indirect studies, it is not yet possible to make an accurate conclusion about the effect of pH on the induction of the labor process.

Zanjani et al performed vaginal washing with 3% acetic acid before vaginal Misoprostol insertion to terminate the second trimester of pregnancy. The two groups were the same in terms of vaginal pH before using vaginal acetic acid. However, in the acetic acid group, vaginal pH was significantly lower after use compared to the control group. Overall, 95% of pregnancies were successful in the acetic acid group compared to 85% in the control group, but this difference was not statistically significant. Success rates between 24 and 48 hours, adverse effects and mean termination time, total Misoprostol consumption, and the number of curettages was comparable between groups, but it was observed that increased vaginal acidity did not improve the effectiveness of vaginal Misoprostol for termination of second-trimester pregnancy.[14] Another study was conducted by Najafian to evaluate the effectiveness of vaginal Misoprostol and vaginal washing with 3% acetic acid for termination of pregnancy in the first trimester. Their results showed that vaginal washing with acetic acid had no effect on induction of first-trimester abortion compared to the control group.[19] However, Rashwan et al reported that vaginal washing with an acetic acid solution before induction of labor with Misoprostol shortened the meantime to reach the active phase of labor compared to the washing with normal saline and alkaline groups.[12] According to the results of these studies, it is not yet possible to draw an accurate conclusion about the effect of acidic pH on the induction of labor, although the difference in gestational age at the time of intervention should be noted.

On the other hand, in some studies without intervention, only the effect of vaginal pH on induction of labor was examined and in these studies, contradictory results were obtained and no agreement was identified on the effectiveness and determination of pH affecting the length of induction of labor. Basirat et al examined the effect of

vaginal pH on the effectiveness of Dinoprostone in cervical ripening and induction of labor, in contrast to the present study, it was reported that the duration of the active phase of labor in patients with high vaginal pH was significantly shorter than the low pH group. However, there was no difference between the two groups with high and low vaginal pH in terms of Bishop score after 12 hours, duration of latent phase and second stage of labor, and the number of cesarean sections, as in the present study.[16] However, unlike the present study, no intervention was performed in Basirat et al study and only two groups were compared based on the difference in pH and the effectiveness of Dinoprostone. Chandra et al reported that vaginal pH less than 5 had no effect on the length of induction of labor with vaginal Misoprostol, and the frequency of cesarean section and pregnancy outcomes did not differ between the two groups.[17] Kurian et al found that women with multiple parities had higher vaginal pH and consequently higher Bishop scores and a higher number of normal deliveries, but no correlation was found between pH and time to enter the active phase. In this study, there was no intervention and only pH was measured before induction with Dinoprostone and compared between groups, also women were included in the study with multiple parties.[20]

In an in vitro study, Dinoprostone releasing at vaginal pHs of 7.4, 5.4, and 3.4 were compared, and the results showed that prostaglandin releasing was reduced in acidic pH and the optimal pH for prostaglandin releasing was 7.4.[7] Although the normal pH of the vagina is acidic and vaginal washing reduces the normal vaginal flora and changes the pH to alkaline, it seems that Misoprostol can be more effective in a thinner environment and higher pH,[15] which contradicts the findings of the present study.

In the present study, there was no significant difference between the two groups in terms of the type of delivery and maternal and neonatal outcomes. The rate of cesarean section in the present study was higher than other studies, which is due to perform in a referral hospital, and the majority of patients were with underlying disease or induction indication due to abnormal biophysical score, reduced fetal movement, and so on. However, in Yayla Abide et al study the frequency of hyperstimulation was significantly higher in the case group compared to the control group, and in the control group, meconium excretion, fetal infection and NICU admission rate were higher than the intervention group. These results can be due to the heterogeneity of the study population in the inclusion criteria.[15] Chandra et al as the present study reported no difference between the two groups of vaginal pH less than and more than 5 in terms of frequency of cesarean section and pregnancy outcomes. However, no intervention was performed in their study and only vaginal pH was compared.[17]

The limitation of this study was that the presence of vaginal infection was only examined clinically, and we did not examine subclinical infections that may affect vaginal pH. Contradictory results have been obtained due to the fact that studies in this field have been different in the method of administration, type of prostaglandin used, type of vaginal washing agent and pH classification into subgroups, and gestational age of the intervention. In addition, other factors appear to be involved in the effectiveness of prostaglandins, so it is suggested that further studies be performed to identify other factors affecting the effectiveness of prostaglandins on induction of labor.

5 | CONCLUSION

According to the results of the present study, although vaginal pH increased slightly after vaginal washing, it had no effect on cervical ripening, and the frequency of normal delivery less than 12 hours was higher in the intervention group compared to the control group. Therefore, this intervention may reduce the duration of labor. Although this difference was not statistically significant due to the small number of samples, it is clinically significant. So, future multicenter studies with larger sample sizes are recommended to further verify the results of this study.

FUNDING

This study was financially supported by the Vice-Chancellorship of Research and Technology, Guilan University of Medical Science.

CONFLICTS OF INTEREST

The authors report no conflict of interest regarding the publication of this paper.

AUTHOR CONTRIBUTIONS

Conceptualization: Roya Kabodmehri, Seyedeh Hajar Sharami, Forozan Milani, Fatemeh Hosseinzadeh
Formal Analysis: Zahra Pourhabibi
Writing – Original Draft Preparation: Seyedeh Fatemeh Dalil Heirati
Writing – Review & Editing: Roya Kabodmehri, Seyedeh Hajar Sharami, Forozan Milani, Fatemeh Hosseinzadeh, Seyedeh Fatemeh Dalil Heirati, Zakie Bakhshipour, Zahra Pourhabibi

TRANSPARENCY STATEMENT

All the authors affirm that this manuscript is an honest, accurate, and transparent account of the study being reported, and no important aspects of the study have been omitted.

DATA AVAILABILITY STATEMENT

Related data of this project are available on request.

ORCID

Roya Kabodmehri https://orcid.org/0000-0003-4162-6846
Seyedeh Hajar Sharami https://orcid.org/0000-0001-7815-3769
Forozan Milani https://orcid.org/0000-0002-0430-6993
Fatemeh Hosseinzadeh https://orcid.org/0000-0002-8871-4483
Seyedeh Fatemeh Dalil Heirati https://orcid.org/0000-0003-2177-0832
Zahra Pourhabibi https://orcid.org/0000-0001-6339-8771

REFERENCES

1. Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. *Williams Obstetrics*. 24th ed. New York, NY: Mcgraw-Hill; 2018.

2. Hofmeyr GJ, Gülmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. *Cochrane Database Syst Rev*. 2010;2010(10):CD000941.
3. Mozurkewich EL, Chilimigras JL, Berman DR, et al. Methods of induction of labour: a systematic review. *BMC Pregnancy Childbirth*. 2011;11(1):1-19.
4. Abd-El-Maeboud KHI, Ghazy A, Ibrahim A, Hassan N, El-Bohoty A, Gamal-El-Din I. Vaginal acidity enhancement with a 3% acetic acid gel prior to misoprostol treatment for pregnancy termination in the midtrimester. *Int J Gynecol Obstet*. 2012;119(3):248-252.
5. Bhattacharjee N, Saha SP, Ganguly RP, et al. A randomized comparative study on vaginal administration of acetic acid-moistened versus dry misoprostol for mid-trimester pregnancy termination. *Arch Gynecol Obstet*. 2012;285(2):311-316.
6. Esteve JLLC, Varela L, Velazco A, Tanda R, Cabezas E, Sanchez C. Early abortion with 800 μg of misoprostol by the vaginal route. *Contraception*. 1999;59(4):219-225.
7. Johnson TA, Greer IA, Kelly RW, Calder AA. The effect of pH on release of PGE2 from vaginal and endocervical preparations for induction of labour: an in-vitro study. *BJOG*. 1992;99(11):877-880.
8. MacDonald IA, Weir RF. The effect of pH on release of PGE2 from vaginal and endocervical preparations for induction of labour. *BJOG*. 1993;100(11):1066-1067.
9. Ramsey PS, Ogburn PL Jr, Harris DY, Heise RH, Ramin KD. Effect of vaginal pH on efficacy of the dinoprostone gel for cervical ripening/labor induction. *Am J Obstet Gynecol*. 2002;187(4):843-846.
10. Özakşit G, Yilmaz B, Güngör T, Bilge Ü, Necdet SUT, Mollamahmutoğlu L. The role of vaginal pH on efficacy of controlled-release dinoprostone vaginal insert for cervical ripening/labor induction: a prospective double-blind study. *J Turkish-German Gynecol Assoc*. 2008;9(4):206-211.
11. Kelekci S, Yilmaz B, Savan K. Misoprostol wetting with acetic acid for pre-abortion cervical priming. *Int J Gynaecol Obstet*. 2004;85(2):188-189.
12. Rashwan ASSA, Alalfy M, Eldesouky A, et al. Comparative study regarding effect of pH on misoprostol in induction of labor in full term primigravida pregnant women, a double blind randomized controlled trial. *J Perinat Med*. 2021;49(1):43-49.
13. Wiebe ER. Misoprostol administration in medical abortion. A comparison of three regimens. *J Reprod Med*. 2001;46(2):125-129.
14. Zanjani M, Kohpayeh J, Karimi Z. The effect of vaginal pH on the efficacy of vaginal misoprostol for the induction of midtrimester pregnancy termination. *J Obstet Gynecol Cancer Res*. 2017;2(1):1-5.
15. Yayla Abide Ç, Kurek Eken M, Ozkaya E, et al. Effect of vaginal washing before intravaginal dinoprostone insertion for labor induction: a randomized clinical trial. *J Obstet Gynaecol Res*. 2018;44(12):2149-2155.
16. Basirat Z, Barat SH, Ghanbarpour A, Golsorkhtabar-Amiri M. Does vaginal pH affect the efficacy of dinoprostone in cervical ripening/labor duration? *Clin Exp Obstet Gynecol*. 2012;39(4):522-525.
17. Chandra S, Allen VM, Lee W, Fanning CA, Young DC. The effect of vaginal pH on labor induction with vaginal misoprostol. *J Matern-Fetal Neonatal Med*. 2005;17(6):387-391.
18. Jain JK, Meckstroth KR, Mishell DR Jr. Early pregnancy termination with intravaginally administered sodium chloride solution–moistened misoprostol tablets: historical comparison with mifepristone and oral misoprostol. *Am J Obstet Gynecol*. 1999;181(6):1386-1391.
19. Najafian A, Rajaei M, Beheshti S. Efficacy of vaginal misoprostol and vaginal washing with 3 acetic acid for first trimester pregnancy termination: a randomized single blind clinical trial. *Hormozgan Med J*. 2016;20(5):301-306.
20. Kurian MJ, Rao B, Rao A, Shameem VPA. Effect of vaginal pH on efficacy of dinoprostone gel for labour induction. *Int J Reprod Contracept Obstet Gynecol*. 2016;5(4):1196-1202.

How to cite this article: Kabodmehri R, Sharami SH, Milani F, et al. Effect of vaginal washing before Misoprostol insertion on cervical ripening before induction of labor: A randomized single-blind clinical trial. *Health Sci Rep*. 2022;5:e502. doi:10.1002/hsr2.502