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MATERNAL-FETAL MEDICINE

Transcervical Foley balloon catheter and vaginal prostaglandin E2 insert combination vs. vaginal prostaglandin E2 insert only for induction of labor at term: a randomized clinical trial

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Abstract

Purpose To analyze the effect of combined application of intravaginal PGE2 insert and intracervical Foley balloon catheter for induction of labor.

Methods Patients with unfavorable cervices who required induction of labor from August 2017 to December 2017 were evaluated for the study. Three hundred and ten participants were randomly assigned to study (n:155) and control group (n:155). Nine patients in study group and seven patients in control group were excluded, because they declined to participate in the study. Totally, 294 women analyzed in this prospective randomized study: Group 1 (control group): labor induction with intravaginal PgE2 vaginal insert alone ($n=148$) and Group 2 (study group): intracervical Foley balloon catheter insertion adjunct to the intravaginal PgE2 insert ($n=146$). The primary outcome of our study was the period from induction to delivery. The secondary outcome was the period from induction to active phase of labor.

Results In the analysis of primiparous pregnants, combination of intracervical Foley balloon catheter and intravaginal PgE2 insertion was shown to be associated with shorter duration from induction to active stage of labor (1000 vs. 585 min, $P<0.001$) and also to delivery (1386 vs. 1001 min, $P<0.001$). Groups were found to be similar in terms of duration from induction to active stage of labor (670.5 vs. 535.2, $P>0.05$) and also to delivery (933.1 vs. 777.9, $P>0.05$, Table 2) in subgroup of women with the previous vaginal delivery.

Conclusions Combined application of intracervical Foley balloon catheter and intravaginal PgE2 insert may result in a shorter time from labor induction to delivery without rising the risk of cesarean section in primiparous women with an unfavorable cervix.

Keywords Dinoprostone · Intracervical Foley catheter · Labor induction · Unfavorable cervix · Prostaglandin insert

Introduction

Induction of labor with appropriate indications provides a safe vaginal delivery for maternal and fetal well-being. An unfavorable cervix during induction decreases the success rate of labor induction and vaginal delivery [1]. Therefore, it is required to apply cervical ripening methods for unfavorable cervices.

There are two recommended cervical ripening methods used globally: (a) mechanical cervical dilators and (b) application of synthetic prostaglandin E1 (PGE1) and prostaglandin E2 insert (PGE_2). Although these methods are effective to ripen the cervix, an optimal management has not been defined in the literature. Application of transcervical Foley balloon catheter (FBC) is an effective mechanical method

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and has advantages of lower cost and lowest rate of fetal heart rate changes secondary to the tachysystole compared with PGE1 and PGE2 inserts. Despite the advantages of mechanical methods, PGE1 and PGE2 inserts were reported to be more effective than mechanical methods to achieve vaginal delivery within 24 h [2, 3].

Although there have been a lot of studies comparing PGE1, PGE2 inserts, and transcervical FBC separately and PGE1 combined with transcervical FBC [4], less is known about combined usage of PGE2 insert and transcervical FBC.

The aim of our study is to analyze the effect of combined application of intravaginal PGE2 insert and intracervical FBC for induction of labor in pregnants with an unfavorable cervix.

Methods

Study protocol

This prospective randomized study was approved by the ethical committee at Zeynep Kamil Education and Research Hospital and was registered with the clinical trials registry (ClinicalTrials.gov #NCT01279343). Patients with unfavorable cervices who required induction of labor from August 2017 to December 2017 were evaluated for the study. Totally, 294 women analyzed in this prospective randomized study.

Inclusion and exclusion criteria

Inclusion criteria were: (1) singleton pregnancy; (2) gestational age ≥ 37 weeks; (3) intact membranes; (4) cephalic presentation; (5) bishop score < 5; (6) had obstetrical indications for induction of labor; and (7) had less than three uterine contractions in every 10 min. On the other hand, patients who had contraindications for vaginal delivery, previous uterine surgery, previous cesarean section, fetal malpresentation, multifetal pregnancy, more than three contractions in 10 min, contraindications to prostaglandins, a category II or III fetal heart rate pattern, anomalous fetus, fetal demise, and women with immediate delivery indications were excluded from the study.

Randomization

The patient flow chart is listed in detail in Fig. 1. Out of 330 eligible patients, 20 patients were excluded, because they did not meet the inclusion criteria. 310 participants were randomly assigned to study (n:155) and control group (n:155). Nine patients in study group and seven patients in control group were excluded, because they declined to participate in the study. Totally, 294 women analyzed in this prospective randomized study: Group 1 (control group): labor induction with intravaginal PgE2 vaginal insert alone ($n = 148$) and Group 2 (study group): intracervical FBC insertion adjunct to the intravaginal PgE2 insert ($n = 146$). Randomization was performed by a computerized random number generator in a 1:1 ratio in blocks of 10. Because of the agents used in each arm of the two groups, blinding was not feasible. After the written informed consent was obtained, patients were enrolled according to randomization for each group.

Interventions

All patients were monitored for fetal heart rate prior to induction of labor for 30 min. After starting induction of labor, patients were managed with continuous fetal heart rate monitoring until labor except when patients were ambulating. In FBC and intravaginal PGE2 group, the cervix was visualized with sterile speculum and vagina was cleansed with povidon–iodine solution. An 18-F Foley catheter was inserted into the endocervical canal and the bulb was filled with 30 mL of saline solution. The previous data which showed labor induction using Foley balloons inflated to 60 mL were associated with no differences in delivery within 24 h, cesarean delivery, labor complications, or neonatal outcomes [5]. The external end of the catheter pulled against the internal os and taped to the medial thigh with minimal tension. Balloon was kept intracervically until it was expelled spontaneously. After insertion of FBC, PGE2 vaginal insert was placed high into the posterior vaginal fornix. When FBC was expelled, PGE2 vaginal insert was left until cervical dilatation was 4 cm. Amniotomy was performed when the cervical dilatation was 4 cm after withdrawal of the vaginal insert outside the vagina. If indicated, induction with oxytocin was started after amniotomy. IV oxytocin was started at 2 mU/min and increased 2 mU/min every 15 min until regular uterine contractions occurred.

In the PGE2 vaginal insert only group, PGE2 vaginal ovule was placed high into the posterior vaginal fornix alone. PGE2 vaginal insert was left until the cervical dilatation was 4 cm. Amniotomy was performed after withdrawal of the PGE2 vaginal insert outside the vagina. If indicated, induction with oxytocin was started as the same protocol for each group. Active phase of labor was defined, as cervical dilatation was 5 cm. Uterine contraction assessment was performed with an external toco-dynamometer and tachysystole was defined uterine contractions which were more than six in 10 min. Hyperstimulation was defined as uterine tachysystole with fetal heart rate changes and patients were needed to perform intravenous ritodrine administration or cessation of oxytocin.

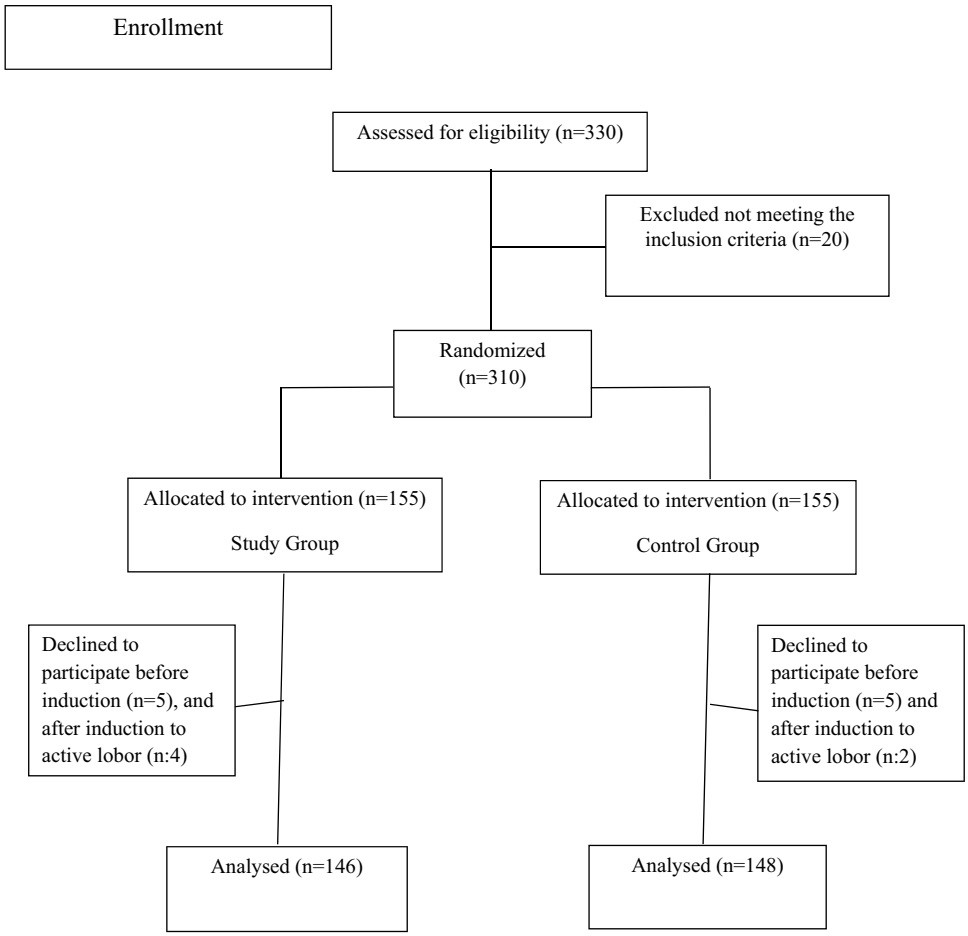

Fig. 1 Flow chart of the study population

The primary and secondary outcomes

The primary outcome of our study was the period from induction to delivery in group with vaginal delivery.

The secondary outcome was the period from induction to active phase of labor.

Sample size calculation

Due to the lack of data regarding the efficacy of combined use of PGE2 vaginal insert and FBC for labor induction and shown similar efficacy and safety between misoprostol and dinoprostone [6], we used data come from a study on combined use of misoprostol and Foley catheter application. This randomized study showed a mean induction to delivery time 3 h shorter using the combination of Foley catheter and misoprostol as compared with misoprostol alone. Sample size was calculated to achieve 80% power to detect a difference of 3 h between the mean induction to delivery times of the two groups, a total of 188 patients (94 in each group) would need to be randomized using a two-sided *t* test and accepting an error of 0.05 and we included 150 cases for each group for possible drop outs [4].

Oligohydramnios was determined in cases with amniotic fluid volume that is less than expected for gestational age. It is typically diagnosed by ultrasound examination and may be described qualitatively (e.g., normal, reduced) or quantitatively (e.g., amniotic fluid index ≤ 5 cm). Our study included cases with amniotic fluid index ≤ 5 cm.

Fetal growth restriction was diagnosed if the fetus who does not achieve the expected in utero growth potential due to genetic or environmental factors. It is defined as an estimated fetal weight < 10th percentile. These cases underwent labor induction when they had non-reassuring fetal heart rate, oligohydramnios, or abnormal Doppler studies.

A prolonged latent phase was defined as painful irregular or regular contractions without rest, for 24 h or more [7]. Dinoprostone effectivity was reported to be lost 24 h after insertion; therefore, due to avoid increasing cesarean rates, balloon and dinoprostone were kept intravaginally for maximum of 24 h.

Statistical methods

Statistical analysis was performed with SPSS 17.0. Normally, distributed data were presented as mean with SD.

Categorical outcomes were summarized using frequency distributions. For quantitative data, Student *t* test was used. For categorical data, we calculated *P* values with Chi-square or Fisher exact tests. For time-to-delivery data, we constructed Kaplan–Meier survival curves and calculated log-rank test and *P* values. To analyze induction to vaginal delivery interval, we used "vaginal delivery" as the end-point. COX multiple regression tests were used to explore variables independently associated with the induction to delivery interval. A *P* value of 0.05 was used as the cut point for significance.

Results

Subgroups

There were 172 pregnants with their first pregnancy, while the number of multiparous women was 122. Analysis was conducted in these subgroups of women separately.

Subgroups analysis

In the analysis of pregnants with their first delivery, combination of intracervical FBC and intravaginal PgE2 insertion was shown to be associated with shorter duration from induction to active stage of labor (1000 vs. 585 min, $P < 0.001$) and also to delivery (1386 vs. 1001 min, $P < 0.001$, Table 1). Groups were found to be similar in terms of duration from induction to active stage of labor (670.5 vs. 535.2, $P > 0.05$) and also to delivery (933.1 vs. 777.9, $P > 0.05$, Table 2) in subgroup of women with the previous vaginal delivery. There were 19 cases with failed labor induction; among these, 19 cases, 12 of them were primigravid, and the remaining seven cases were multigravida. Among these 19 cases, 6 (31.6%) pregnants underwent cesarean section.

Table 1 Comparison of some demographic and labor characteristics of groups in subgroup of women with the first parity

	Control ($n = 148$) Mean ± SD	Study ($n = 146$) Mean ± SD	*P* value
Age (years)	24.8 ± 4.6	26.07 ± 5.4	NS
Gravidity	1.2 ± 0.5	1.2 ± 0.5	NS
BMI (kg/m^2)	29.1 ± 4.9	29.6 ± 4.4	NS
Gestational age (days)	278.3 ± 9.1	278.3 ± 10.6	NS
Bishop score	2.7 ± 0.9	2.5 ± 0.7	NS
Time from induction to delivery (min)	1386.2 ± 474.1	1001.1 ± 608.3	< 0.05
Time from induction to active phase of labor (min)	1000.5 ± 402.9	585.5 ± 494.6	< 0.05
Birth weight (g)	3327.1 ± 443.6	3150.6 ± 483.1	< 0.05
Neonates blood gas pH	7.3 ± 0.03	7.2 ± 0.009	NS

Table 2 Comparison of some demographic and labor characteristics of groups in subgroup of women with the previous vaginal delivery

	Control ($n = 148$) Mean ± SD	Study ($n = 146$) Mean ± SD	*P* value
Age (years)	30.6 ± 6.2	31.6 ± 5.9	NS
Gravidity	3.09 ± 1.2	2.9 ± 0.9	NS
Parity	1.7 ± 1.04	1.7 ± 0.8	NS
Alive	1.7 ± 1.04	1.6 ± 0.8	NS
Miscarriage	0.3 ± 0.6	0.2 ± 0.4	NS
BMI (kg/m^2)	30.3 ± 5.1	31.4 ± 5.9	NS
Gestational age (days)	280.2 ± 10.9	275.7 ± 13.8	NS
Bishop score	3.2 ± 1.09	3.1 ± 0.8	NS
Time from induction to delivery (min)	933.1 ± 532.9	777.9 ± 634.8	NS
Time from induction to active phase of labor (min)	670.5 ± 431.2	535.2 ± 512.7	NS
Birth weight (g)	3432.08 ± 425.3	3173.4 ± 637.4	< 0.05
Neonates blood gas pH	7.3 ± 0.07	7.3 ± 0.04	NS

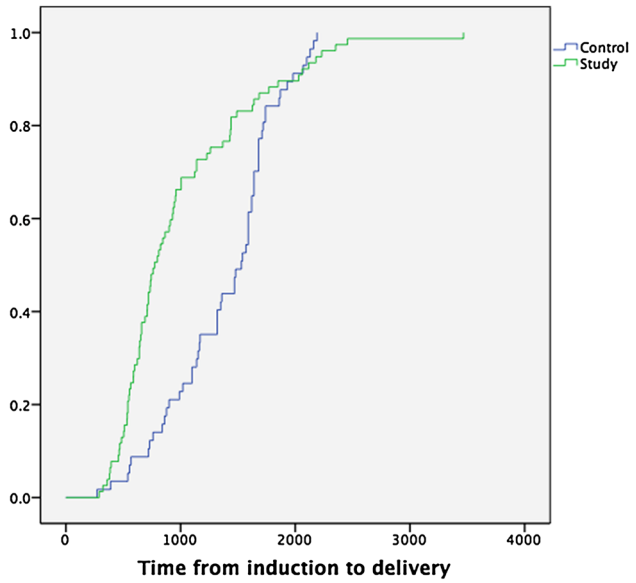

Fig. 2 Survival curve of in intervention groups in subgroup of women with the first parity

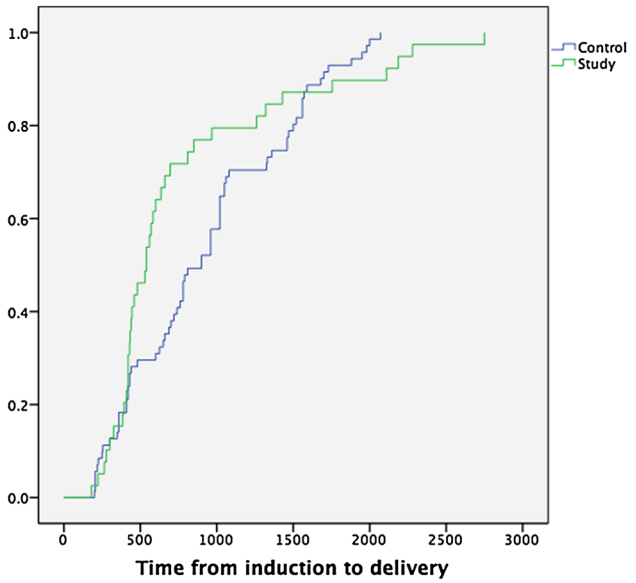

Fig. 3 Survival curve of in intervention groups in subgroup of women with the previous vaginal delivery

Kaplan–Meier survival analysis

Survival analysis also confirmed superiority of combination therapy for the time to induction to delivery ($P < 0.05$, Fig. 2). This superiority of combination therapy for the time from labor induction to delivery remained significant after adjustment for the neonatal birth weight in Cox regression analysis ($P = 0.012$). On the other hand, in subgroup of women with previous vaginal deliveries, comparison of groups showed similar efficacies in terms of time from induction to active phase of labor and to delivery ($P > 0.05$, Fig. 3). Birth weight-adjusted comparison remained insignificant in subgroup of women with the previous vaginal delivery.

Route of delivery rates

Cesarean section rates were similar between the two intervention groups in subgroup of women with their first delivery (19.7% vs. 23.8%, $P > 0.05$). Cesarean section rates were similar between the two intervention groups in subgroup of women with the previous deliveries (7.8% vs. 13.3%, $P > 0.05$).

Induction of labor indications

Distribution of indications between the two intervention groups for labor induction in primiparous group was postdate pregnancy (50.7% vs. 41.6%), oligohydramnios (16.9% vs. 32.7%), IUGR (15.5% vs. 13.9%), hypertension (15.5% vs. 9.9%), and GDM (1.4% vs. 2%) ($P > 0.05$).

Distribution of indications between the two intervention groups for labor induction in multiparous group was postdate pregnancy (61% vs. 53.3%), oligohydramnios is (19.5% vs. 31.1%), IUGR (3.9% vs. 2.2%), and hypertension (15.6% vs. 13.3%) ($P > 0.05$).

There were 47 cases with oligohydramnios in the study group, while the number of pregnants with oligohydramnios was 27 in control group. Tachysystole, neonatal intensive care unit admission rates, oxytocin augmentation requirement, and cesarean section rates were similar between the intervention groups ($P > 0.05$).

Vaginal delivery rates within 24 h

There was a significant difference between groups in terms of delivery rates within 24 h of labor induction (83.6% vs. 59.7%, $P < 0.001$). There was no case who underwent cesarean section within 24 h.

Complication rates

Postpartum endometritis (2% vs. 3.4%, $P > 0.05$) and chorioamnionitis (1.4% vs. 3.4%, $P > 0.05$) rates were similar between the two groups.

Tachysystole rates were 15.1% in study group, while the rate was 15.5% in control group ($P > 0.05$).

Oxytocin augmentation was indicated in 117 (79.1%) women in control group and 112 (76.7%) pregnants in study group ($P > 0.05$).

Newborn outcome

Newborn admission rates were similar between two groups (4.1% vs. 4%, $P > 0.05$).

Discussion

In this study, we aimed to compare combined use of intracervical FBC and intravaginal PgE2 insert with the intravaginal PgE2 insert alone for labor induction. In the analysis of pregnants with their first delivery, combination of intracervical FBC and intravaginal PgE2 insert was shown to be associated with shorter duration from induction to active stage of labor and also to delivery. Survival analysis also confirmed superiority of combination therapy for the time from induction to delivery. On the other hand, in subgroup of women with the previous vaginal deliveries, comparison of groups showed similar efficacies in terms of time from induction to active phase of labor and to delivery. Cesarean section rates were similar between the two intervention groups in both subgroups.

When searching of the literature for cervical ripening and labor induction, there are several trials comparing mechanical methods with medical methods. Less is known about combined use of mechanical and medical methods together especially dinoprostone as the medical method. Several studies in the literature assessed the efficacy of combined use of misoprostol and Foley catheter compared to misoprostol alone, majority of them showed a shorter induction-to-delivery time with combination when compared with vaginal misoprostol alone without increasing complications [4, 8, 9].

Misoprostol and balloon combination was shown to result in shorter time from induction to delivery (12.9 h) compared to misoprostol only (17.8 h, $P < 0.001$). Uterine tachysystole occurred less often in the vaginal misoprostol group (21% vs. 39%, $P = 0.015$). Vaginal delivery within 24 h was found to be significantly more likely with a Foley balloon and oral misoprostol combination [10].

Combination of this two different induction method was assessed in another trial, authors concluded that "A combination of oral misoprostol and a double-balloon catheter improves the efficacy of labor induction in term pregnancies, particularly in women without premature rupture of the membranes" [11].

On the other hand, in a small sample size study, the addition of mechanical ripening with a transcervical Foley balloon to intravaginal misoprostol was not found to improve the efficiency of pre-induction cervical ripening, authors showed that the misoprostol group spent longer periods of time in active labor; however, they stated that these findings did not significantly affect the total ripening-to-delivery time or cesarean section rate which were similar for both groups [12]. In a previous study, 146 singleton gestations ≥ 28 weeks were randomized to three groups and induction by misoprostol alone was compared with Foley alone and with a combination of misoprostol with Foley. Study revealed no differences in the rates of vaginal delivery or in duration from induction to delivery. Misoprostol group was found to have higher rate of tachysystole (47–63%) [13].

Consistent with our result, combination of two different approaches resulted in shorter mean time from induction to delivery in a previous report, in this study, combined approach consist of misoprostol administration and Foley catheter application too [4]. Time from induction to delivery was reduced at a mean time of 4 h by combination approach in a study including 492 pregnants; in their study, authors concluded that "After censoring for cesarean delivery and adjusting for parity, misoprostol–cervical Foley combination resulted in twice the chance of delivering before either single-agent method." [14]. Our data showed 5 h reduction in mean time from induction to delivery in subgroup of women with their first delivery, whereas time reduction was approximately 2.5 h in subgroup of women with the previous vaginal delivery; however, difference in this subgroup did not reach statistical significance. This favorable outcome with combined approach was confirmed in recent study which showed cervical ripening with combined use of misoprostol and transcervical Foley bulb to be an effective method to shorten the course of labor compared with misoprostol alone [8].

Although these study protocols were similar to ours, misoprostol was used as an induction agent in these studies which makes it difficult to compare results with ours.

Sometimes induction of labor becomes inevitable; however, there are also some data, which indicated, altered pattern of labor progression for women with an electively induced labor compared with those with spontaneous onset of labor. In addition, elective induction in nulliparous women with an unfavorable cervix was shown to result in a higher rate of labor arrest and a substantially increased risk of cesarean delivery [15]. Therefore, it is crucial to prefer safest and efficient method for labor induction among specific groups.

Although we performed a power analysis to determine the smallest number of participants to conduct this study, small sample size and the lack of blinding for the interventions may be accepted as drawbacks in this study.

In conclusion, combined application of intracervical FBC and intravaginal PgE2 insert may result in a shorter time from labor induction to delivery without raising the risk of cesarean section in primiparous women with an unfavorable cervix.

Author contributions EA: conception and design of the study and acquisition of data. OE: data analysis and manuscript writing and

editing. YAC: methodology, acquisition of data, and manuscript editing. ET: data analysis and methodology. YEG: design of the study and manuscript writing. AF: data analysis and supervision. TTA: acquisition of data. EM: acquisition of data and supervision.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. ACOG Committee on Practice Bulletins—Obstetrics (2009) ACOG practice bulletin no. 107: induction of labor. Obstet Gynecol 114:386
2. Jozwiak M, Bloemenkamp KW, Kelly AJ, Mol BW, Irion O, Boulvain M (2012) Mechanical methods for induction of labor. Cochrane Database Syst Rev 3:CD001233
3. Chen W, Xue J, Peprah MK et al (2016) A systematic review and network meta-analysis comparing the use of Foley bulbs, misoprostol, and dinoprostone for cervical ripening in the induction of labor. BJOG 123(3):346–354
4. Carbone JF, Tuuli MG, Fogertey PJ, Roehl KA, Macones GA (2013) Combination of Foley bulb and vaginal misoprostol compared with vaginal misoprostol alone for cervical ripening and labor induction: a randomized controlled trial. Obstet Gynecol 121:247–252
5. Delaney S, Shaffer BL, Cheng YW, Vargas J, Sparks TN, Paul K, Caughey AB (2010) Labor induction with a Foley balloon inflated to 30 mL compared with 60 mL: a randomized controlled trial. Obstet Gynecol 115(6):1239–1245
6. Calder AA, Loughney AD, Weir CJ, Barber JW (2008) Induction of labor in nulliparous and multiparous women: a UK, multicentre, open-label study of intravaginal misoprostol in comparison with dinoprostone. BJOG 115(10):1279–1288
7. Spong CY, Berghella V, Wenstrom KD, Mercer BM, Saade GR (2012) Preventing the first cesarean delivery: summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, and American College of Obstetricians and Gynecologists Workshop. Obstet Gynecol 120(5):1181–1193
8. Al-Ibraheemi Z, Brustman L, Bimson BE, Porat N, Rosenn B (2018) Misoprostol with Foley bulb compared with misoprostol alone for cervical ripening: a randomized controlled trial. Obstet Gynecol 131(1):23–29
9. Ugwu EO, Onah HE, Obi SN, Dim CC, Okezie OA, Chigbu CO, Okoro OS (2013) Effect of the Foley catheter and synchronous low dose misoprostol administration on cervical ripening: a randomised controlled trial. J Obstet Gynaecol 33(6):572–577
10. Hill JB, Thigpen BD, Bofill JA, Magann E, Moore LE, Martin JN Jr (2009) A randomized clinical trial comparing vaginal misoprostol versus cervical Foley plus oral misoprostol for cervical ripening and labor induction. Am J Perinatol 26(1):33–38
11. Kehl S, Ehard A, Berlit S, Spaich S, Sütterlin M, Siemer J (2011) Combination of misoprostol and mechanical dilation for induction of labour: a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol 159(2):315–319
12. Rust OA, Greybush M, Atlas RO, Jones KJ, Balducci J (2001) Preinduction cervical ripening. A randomized trial of intravaginal misoprostol alone vs. a combination of transcervical Foley balloon and intravaginal misoprostol. J Reprod Med 46(10):899–904
13. Chung JH, Huang WH, Rumney PJ, Garite TJ, Nageotte MP (2003) A prospective randomized controlled trial that compared misoprostol, Foley catheter, and combination misoprostol–Foley catheter for labor induction. Am J Obstet Gynecol 189:1031–1035
14. Levine LD, Downes KL, Elovitz MA, Parry S, Sammel MD, Srinivas SK (2016) Mechanical and pharmacologic methods of labor induction: a randomized controlled trial. Obstet Gynecol 128:1357–1364
15. Vahratian A, Zhang J, Troendle JF, Sciscione AC, Hoffman MK (2005) Labor progression and risk of cesarean delivery in electively induced nulliparas. Obstet Gynecol 105(4):698–704