Does vaginal pH affect the efficacy of dinoprostone in cervical ripening/labor duration?

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Summary

Background: Prostaglandins are effective in the ripening of the cervix and facilitating labor induction. Vaginal pH is probably an important factor in the effectiveness of vaginal prostaglandins. The aim of this study was to evaluate the effect of vaginal pH on the function of prostaglandin vaginal tablet during labor. *Methods:* This is a double-blinded clinical trial study of 147 pregnant primigravid trated in the Yahyanejad Hospital of Babol (Iran) from January 2006 to December 2007. Initial pH was measured during vaginal examination with nitrazin paper and the Bishop score was determined. All women received vaginal dinoprostone inserted in the posterior fornix of the vagina for cervical ripening and the second dose was administered if the uterine contractions were inadequate. Reassessment of the Bishop score after 12 hours, duration of latent and active phases, and also the duration of the second stage of labor were compared between the two groups with low or high vaginal pH. *Results:* The incidence of Cesarean section was lower in women with high vaginal pH but was not statistically significant. The Bishop score after 12 hours, latent phase, and second stage durations were not different in the two groups of high or low vaginal pH, but active phase duration in patients with high pH was significantly shorter than those with low pH (p = 0.019). *Conclusion:* High vaginal pH influences the function of prostaglandin tablet as a reduction in duration of the active phase of labor.

Key words: Vaginal PH; Prostaglandin; Cervix ripening; Dinoprostone; Labor duration.

Introduction

Labor induction is commonly used in obstetrics [1]. Optional labor induction can increase the Cesarean section incidence rate up to three times [2, 3]. Since Cesarean section is accompanied with the risk of undesired maternal outcomes, most specialists agree with the opinion that optional labor induction is not reasonable in term pregnancies unless there is an indication for termination of the pregnancy [4, 5]. While the maternal or fetal benefits of induction overcome the benefits of continuing pregnancy, labor induction is indicated. Among these indications, emergency conditions, such as rupture of membranes with chorioamnionitis or severe preeclampsia, can be suggested. Rupture of the membranes in the absence of labor, with an uncertain condition of the fetus, and post-date pregnancy are other indications for labor induction [6-8].

With the use of prostaglandins E2 (PGE2), dinoprostone is one of the methods used for cervical ripening. Prostaglandins work in different ways to ripen the cervix and it seems that prostaglandin E especially increases the activity of collagenase in the cervix. Prostaglandins also increase elastase, glycosaminoglycan, dermatan sulphate, and hyaluronic acid and by adding intracellular calcium they cause myometrial muscle contraction [9]. Prostaglandins are organic acids which have diminished dissolution ability in aqueous solution and low pH. Although the vagina has a low pH in normal conditions, several factors such as lower genital tract infections, bacterial vaginosis, and rupture of the membrane can alter vaginal pH. There are a few studies on the vaginal pH effect on the cervical response to prostaglandins. Ramsey *et al*. evaluated the effect of vaginal pH on the efficacy of PGE2 tablet and came to the conclusion that high pH can accelerate the delivery course [10]; there are however controversial results in some studies [11, 12]. To shorten the duration of elective induction of labor and lessen maternal morbidity the authors decided to perform this study, using a cervical ripening method (dinoprostone). This study was conducted to evaluate the association of vaginal pH with the effect of prostaglandin vaginal tablet for cervical ripening/labor induction.

Materials and Methods

This is a single-arm clinical trial study of 147 pregnant primigravid women with an age range of 16 to 35 years treated in the Department of Obstetrics and Gynecology of Yahyanejad Hospital, Babol University of Medical Science in Babol (Iran) from January 2006 to December 2007. The ethics committee of the University approved the study and all patients signed an informed consent.

All cases were prescribed labor induction and termination of pregnancy due to post-term pregnancy. These women had a singleton pregnancy and the fetuses had cephalic presentation. Their Bishop score was 5 or less and no contraindication of vaginal delivery was present and their uterine contractions had not yet begun. All individuals were informed of the process prior to participation in the study and had signed a written consent. Exclusion criteria were: known sensitivity to prostaglandin, ruptured membranes, the probability of chorioamnionitis, prior history of uterine surgery, a previous Cesarean delivery, and previous induction of labor in the current pregnancy.

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Labor processing

All patients were admitted 12 hours before the initiation of labor induction and monitored to be assured that no uterine contractions or fetal distress was present. Then they were examined using a speculum and a sample of cervico-vaginal liquid from external cervical os and superior region of the vagina was obtained by a cotton swab and the vaginal pH was determined by narrow-range pH paper (Hydrion pH paper, Sigma Chemical Co, St Louis, MO). A vaginal examination was then performed to determine cervical conditions with regards to Bishop score [13]. If the situation was suitable, vaginal tablet of PGE2, including 3 mg of dinoprostone was placed into the posterior fornix of the vagina. Placing PG tablet and determining Bishop score at onset and 12 hours later was performed by a physician who was unaware of the vaginal pH condition. Women with fewer than three uterine contractions within ten minutes and an intact amniotic membrane received a second dose of the tablet after six hours. Twelve hours after receiving the initial dose of the drug, the Bishop score was once again measured. If after 12 hours of time, there was still no proper contraction pattern, oxytocine (Aburaihan Co. Tehran, Iran) was administered. Oxytocin infusion was begun at an initial rate of 2 mu/min, with 2 mu/min increased at 20-minute intervals to a maximum dose of 30 mu/min, until an adequate uterine contraction pattern developed. In cases of uterine hyperstimulation, the tablet was removed from the vagina and the patients' position was altered to the left side, oxygen and hydration were provided, and then the maternal and fetal conditions were constantly re-evaluated; if there was no improvement in the fetal condition, or if fetal distress was repeated during the beginning of contractions, they were put to Cesarean section. In individuals who had a proper improvement in their labor course, the results regarding Bishop score after 12 hours, the duration of the latent phase of labor (from the beginning of regular contractions to 3-5 cm dilatation of cervix), active phase (from 3-5 cm cervical dilatation to full dilatation), and the second stage of labor (from full cervical dilatation to fetal expulsion) [14], was recorded in both groups with high or low vaginal pH. With a pH break point of 4.5 ("normal" vaginal pH) and a high vaginal pH group (> 4.5), two populations were created for comparison [10].

Data was statistically analyzed using SPSS statistical software for Windows version 13.0 (SPSS Inc, Chicago, IL, USA). Statistical tests such as Fisher's Exact and Mann-Whitney were used. A *p* value less than 0.05 was considered statistically significant.

Results

The average age of the studied individuals was 23 years. Among 147 pregnant women, 114 individuals (77.3%) had low and 33 cases (22.7%) had high vaginal pH. From these 147 individuals, 70 (50.3%) underwent Cesarean section and 73 (49.7%) had normal vaginal delivery. The delivery method in the two groups with regards to low or high vaginal pH was not significant (p = 0.068) (Table 1). The indication for Cesarean section included no response to induction in 74.3% of the cases, meconium-stained amniotic fluid in 14.9%, and fetal distress in 10.8%. The indication for Cesarean section showed no significant difference between vaginal low and high pH.

The average duration of latent phase between individuals with low and high pH was not significantly different (p = 0.638), but the duration of active phase in patients with high pH was lower than low pH which was significant (p = 0.019). On the other hand, the duration of the second stage of labor showed no significant difference between the two groups (p = 0.678) (Table 2). In both groups with low or high vaginal pH, after 12 hours with a Bishop score of approximately 10 possessed the most frequent percentage and there was no significant difference between the two groups (p = 0.362) (Figure 1). No adverse effects were reported by the patients.

Table 1. — *Distribution of delivery method in all the patients with regards to vaginal pH.*

Vaginal pH	Cesarean	Normal delivery	*p* value
Low pH	(54.4%) 62	(45.6%) 52	
High pH	(36.4%) 12	(63.6%) 21	0.068
Total	(50.3%) 74	(49.7%) 73	

Table 2. — *Distribution of the latent and active phase durations with regards to vaginal pH.*

p value	Total	High pH%	Low pH%	Time	Labor phases
0.638	(23) 17	(23.7) 5	(23.1) 12	3-7	Latent phase duration (hrs)
	(0) 0	(0) 0	(0) 0	8-11	
	(13) 10	(19) 4	(11.5) 6	12-16	
	(61) 46	(57.3) 12	(65.4) 34	17-21	
0.019	(8.2) 6	(14.3) 3	(5.8) 3	2	Active phase duration (hrs)
	(19.2) 14	(23.8) 5	(17.3) 9	3	
	(32.9) 24	(42.9) 9	(28.8) 15	4	
	(28.8) 21	(19) 4	(32.7) 17	5	
	(11) 8	(0) 0	(15.4) 8	6	
0.678	(38.4) 28	(38.1) 8	(38.5) 20	10-20	Second stage duration (minutes)
	(47.9) 35	(57.1) 12	(44.2) 23	21-40	
	(13.7) 10	(4.8) 1	(17.3) 9	41-60	

Discussion

This study aimed to determine the relation of vaginal pH with the efficacy of PGE2 vaginal tablet on cervical ripening and labor induction. The results of the study revealed that after administration of PGE2 tablet in primigravid pregnant women, the duration of the active phase in individuals with high pH was lower than those with low vaginal pH (p = 0.019). Ramsey *et al*. evaluated the effect of vaginal pH on the function of dinoprostone gel and showed that the time of entering into the active phase, full dilatation, and delivery was obviously shorter in women with high vaginal pH compared with women with a low vaginal pH [10], which is similar to this study.

In the Onen *et al*. study, vaginal pH had a significant effect on the duration of latent and active phases of delivery following the administration of dinoprostone vaginal insert [15]. Perry *et al*. showed intracervical dinoprostone decreased time to delivery without increasing the rate of Cesarean section, post-partum infections, or other labor complications [16].

In a research performed by Chandra and *et al*., the effect of vaginal pH on the function of vaginal misoprostol was studied and the time required for vaginal delivery

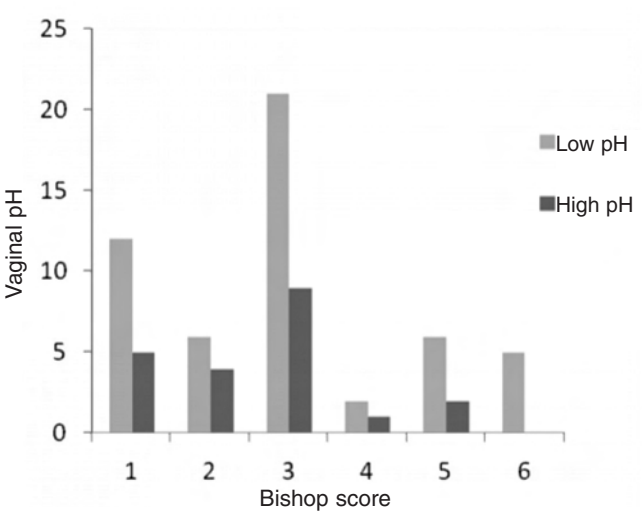

Figure 1. — Distribution and percentage of the Bishop score after 12 hours with regards to vaginal pH.

in both high and low vaginal pH had no difference [12]. However, in another research conducted by Ramsey *et al*., the effect of vaginal pH on the efficacy of on labor induction was studied and the high or low pH of the vagina did not have a noticeable effect on the function of PGE2 tablet and the time of entrance into the active phase of labor and the required time for vaginal delivery had no significant difference in the two studied groups [11]. These results were confirmed in another study of Ramsey *et al*., that the required time until the entrance to the active phase of labor, full dilatation, and delivery after receiving misoprostol had no difference in the two groups with low or low pH [17].

Furthermore in the present study, the Bishop score 12 hours after administration of prostaglandin vaginal tablet did not show a significant difference between the two groups with low and high vaginal pH. Some researchers also showed no difference in the Bishop score 12 hours after administration of dinoprostone gel in the two groups with low or high vaginal pH [10]. On the other hand, in the present study, the Cesarean section rate in women with low or high pH of the vagina showed no difference. Gunalp *et al*. discovered that the Cesarean section rate and unwanted maternal or fetal outcomes following the administration of misoprostol had no difference in both groups with low or high vaginal pH [18]. In the Chandra *et al*. study, after administration of vaginal tablet of misoprostole, the maternal or fetal complications showed no difference in the two groups with high or low vaginal pH [12].

Conclusion

The results of this research revealed that vaginal pH may have an important influential effect on the function of prostaglandin tablet as reduction in the duration of the active phase of labor in high vaginal pH. The vaginal microenvironment may account for the disparate efficacy of the prostaglandins. Some factors can alter the normal acidic vaginal pH. This factor may be considered in women to attempt cervical ripening/labor induction with dinoprostone tablet.

The authors noted one weak point of this study. Another study might be designed as a case-control to compare those who did not take dinoprostone vs those who did take it to evaluate labor duration. A well-designed study that modifies vaginal pH as a primary variable and evaluates the effect of vaginal pH on the overall efficacy of the dinoprostone tablet could be considered.

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