Obstetrics; Maternal-Fetal Medicine and Perinatology

Does Fetal Fibronectin Predict the Delivery Route in Nulliparous Women at Postterm Induced by Dinoprostone?

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ABSTRACT

OBJECTIVE: Digital cervical evaluation has been used to determine the likelihood of vaginal delivery which is considered by many women to be non-tolerable. Recently, alternative approaches such as transperineal ultrasound, fetal fibronectin test in cervicovaginal secretions have been investigating for the prediction of the delivery route. We aimed to study whether the usefulness of qualitative fetal fibronectin test in cervicovaginal secretions for the prediction of vaginal delivery in pregnant women at postterm induced with dinoprostone.

STUDY DESIGN: A total of 32 nulliparous pregnant women at postterm were enrolled in this prospective observational study. Fetal fibronectin test was applied to all participated women before the induction with dinoprostone and transvaginal ultrasonography was performed to measure cervical length.

RESULTS: The women having positive fetal fibronectin test result gave birth through vaginal route, except one case. Although there is no statistically significant difference, the shorter cervical length was associated with vaginal delivery in our population.

CONCLUSION: Fetal fibronectin test has a predictive value for delivery route in nulliparous women at postterm. Fetal fibronectin test may be used as a "rule out" test because the rate of fetal fibronectin positivity was found to be higher in patients who gave birth via vaginal route. As also shown in our study, although there is no statistically significant difference, the pregnant women with shorter cervical length might have a high possibility to achieve vaginal delivery.

Key words: Cervical length, Fetal fibronectin, Vaginal delivery

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Introduction

The rate of incidence of cesarean section is steadily increasing all over the world in recent years. The most important point is the distinction between necessary and unnecessary cesarean sections. Because postponing the decision of cesarean section could cause undesirable results for the baby and the mother herself. On the other hand, unnecessary cesarean section should be avoided because of its associated risks and complications. Therefore, prediction of delivery route has been assessed in studies to prevent these associated poor outcomes.

The Bishop score including digital assessment of cervical dilatation and effacement, fetal descent, the position and consistency of the cervix has been used to evaluate the labor progress and determine the likelihood of vaginal delivery. But all parameters in this score are subjective, inconsistent and the score itself is associated with infections in recurrent vaginal examinations. Transperineal ultrasound examination allowing direct visualization of the fetal skull has been using widespread to evaluate the progress of labor in recent years (1).

This examination is applicable to all pregnant women with low inter- and intra-observer variability. Fetal fibronectin (fFN) is a glycoprotein which allows the adhesion between decidua and chorion (2). When the interface between fetal membranes and uterine wall disrupt, fFN begins to be detectable in cervicovaginal secretions. So the studies showed that its detection in cervicovaginal secretions is related to the onset of preterm labor (3,4). There are many publications reporting that fFN is a well-tolerated test by pregnant women and it has a higher diagnostic accuracy than digital cervical examinations in the prediction of preterm birth at gestational ages from 22+0 to 35+0 weeks (5,6).

In our study, we aimed to investigate whether qualitative fFN test is a predictive test for delivery route in nulliparous women at postterm induced with dinoprostone independent of the time required or the indication for cesarean section.

Material and Method

A total of 32 nulliparous women at postterm were enrolled in this prospective cohort study from August 2015 to July 2016. Our facility is a large tertiary care center, providing care for practically all of the region's obstetric population, particularly those with complicated pregnancies, administering around 15.000 births per year, with a cesarean delivery rate of 40%. Our hospital's Ethics Committee approved our study which was in accordance with the Declaration of Helsinki (diary number 2015.14.7). All participated women were informed about the study and gave written informed consent.

The pregnant women at gestational age less than 41 weeks and the pregnant women having dilatation greater than 3 cm were excluded from our study. Multiparous pregnant women, the women with multiple pregnancies, fetal anomalies, previous uterine surgery and/or ruptured membranes or labor pain and the fetuses with the occiput posterior position and the presentation other than longitudinal cephalic presentation and the presence of cervical cerclage were also excluded.

Clinical and demographic characteristics of the patients were obtained from the patient. Gestational age was calculated from the last menstrual period and confirmed from the first trimester ultrasonographic measurement of the fetus. Body mass index (BMI) was calculated by measuring the weight and height of the patient on admission.

All participated women were examined before the admission to delivery unit in the supine position with flexed knees and hips and with an empty bladder. Fetal fibronectin determination in cervicovaginal secretions was performed on admission in all patients. Fetal fibronectin test is a qualitative test for the detection of fFN in cervicovaginal secretions which provides a positive or negative result based on a threshold of 50 ng/mL. The secretion was collected using a vaginal swab which is placed in a tube with 1 mL extraction buffer.

Then test strip was placed into the tube for 10 minutes. The double lines were interpreted as positive result. It is important that the test should be performed before digital examination to prevent false positive results.

All ultrasonographic examinations were done by the same obstetrician using a Voluson 730 Expert with a 3.5 MHz convex transabdominal probe. The transabdominal transducer was used to assess fetal biometric measurements, fetal position, habitus and placental location. A transvaginal probe was used to evaluate cervical length.

After the ultrasonographic evaluation, the cervical status was assessed digitally by the obstetrician in the delivery unit. Bishop score is used to determine the stage of labor before and after the induction which is a quantitative means of describing the cervical status to decide the necessity of cervical ripening agents. The parameters in this score are cervical dilatation and effacement, the position and consistency of the cervix and the station of the fetal head. All women in our study having Bishop score lower than 5 were induced with dinoprostone (Propess ovule; Ferring Medical, Istanbul, Turkey). The obstetrician evaluating patients with ultrasonography was not involved during follow-up in delivery unit. The birth attendants were blinded about the ultrasonographic measurements and fFN test results of the patients. All patients were monitored with non-stress test continuously. The obstetrician in the delivery unit decided on the delivery mode based on clinical assessment of the patient.

Statistical Analysis. Data are demonstrated as mean±SD for normally distributed continuous variables and frequencies for categorical variables. Relevant parameters were examined separately by appropriate chi-square test or independent samples t-test depending on the parameter type and their relationship with the delivery method. Statistical Package for Social Sciences (SPSS) for Windows version 22.0 (SPSS Inc., Chicago, IL, USA) was used for the analysis and two-sided p value of <0.05 was considered as significant.

Results

A total of 32 nulliparous women who met the criteria were enrolled in our study. The mean gestational age was 41.0±0.3 weeks. The mean age of patients in the study was 26.6±5.4 years and the mean BMI was 28.5±4.0 kg/m². The clinical and laboratory characteristics of the patients are summarized in table 1. All women in the study were nulliparous. They had a vaginal delivery rate of 43.8%. The mean duration of Propess ovule application was 14.5±8.0 hours. The leading reason for cesarean section was obstructed labor and fetal distress. (61.1% and 38.9%, respectively).

When the women were analyzed according to delivery route, the only statistically significant difference between vaginal birth group and cesarean section group was fFN test

results. Women with positive fFN test results gave birth through vaginal route (85.7%), whereas women with negative fFN test results underwent cesarean section (68%) (*p*=0.011). Although there is no statistically significant difference, women with shorter cervical length have a higher possibility for vaginal birth (Table 2).

Discussion

This study was designed to evaluate the usability of fFN in the prediction of delivery route in nulliparous women at post-term induced by dinoprostone. The decision for cesarean section at the right time to allow appropriate interventions about

Table 1: Clinical and demographic characteristics of the patients

Characteristics	Number (%) or mean ± standard deviation or min-max values
Maternal age	26.6±5.4
BMI (kg/m^2)	28.5±4.0
Maternal health problems	
Absent	28 (87.5)
Present	4 (12.5)
Weight gain (kg)	14.8±5.2
Gestational week (weeks)	41.0±0.3
Fetal fibronectin	
Negative	25 (78.1)
Positive	7 (21.9)
EFW (grams)	3299.8±253.7
Cervical length (mm)	39.9±8.9
Bishop score before induction	1-5 (median=3)
Propess duration (hours)	14.5±8.0
Bishop score after induction	3-9 (median=6)
Duration to birth (hours)	22.1±9.8
Birth way	
Vaginal birth	14 (43.8)
Cesarean section	18 (56.2)
Birth weight (grams)	3318.7±276.3
Indication for cesarean section	
Macrosomia	2 (11.1)
Fetal distress	5 (27.8)
Obstructed labor	11 (61.1)

BMI: Body mass index, EFW: Estimated fetal weight

Table 2: Comparison of women according to delivery route

Characteristics	Vaginal birth (n=14)	Cesarean section (n=18)	*p* value
Age	25.8±5.3	27.3±5.6	NS
BMI (kg/m^2)	28.2±4.6	28.8±3.6	NS
Weight gain (kg)	15.3±5.3	14.4±5.2	NS
Gestational week	41.2±0.3	41.0±0.3	NS
Fetal fibronectin			
Negative	8 (32)	17 (68)	**0.011**
Positive	6 (85.7)	1 (14.3)	
EFW (grams)	3276.3±245.1	3318.1±265.7	NS
Cervical length (mm)	38.4±8.6	41.2±9.3	NS
Bishop score before induction	3 (median value)	3 (median value)	NS
Propess duration (hours)	12.8±4.8	15.9±9.8	NS
Bishop score after induction	7 (median value)	5 (median value)	**0.001**
Duration to birth (hours)	19.6±5.0	24.1±12.1	NS
Birth weight (grams)	3282.9±240.7	3346.7±305.1	NS

BMI: Body mass index, EFW: Estimated fetal weight

the mother and the baby is important. Accurate prediction of vaginal delivery especially in nulliparous women is very difficult. Because the digital cervical examination is unreliable, subjective and inconsistent and prone to high number of errors in the evaluation between the obstetricians. Therefore there is a need for a more objective and comfortable test for pregnant women to predict vaginal delivery.

We studied the utility of qualitative fFN test for the prediction of vaginal delivery on the nulliparous women who had unengaged head with low Bishop score and induced with dinoprostone. The unengaged head is not the only indication for cesarean section, but these women should be observed cautiously for a cesarean possibility. Induction stimulates the uterine contractions before the spontaneous onset of the labor. Some studies found that induction increased the rate of cesarean section compared with the spontaneous labor (7). The response to induction was examined with the Bishop score for many years which does not have a direct relationship with the vaginal delivery (8,9).

Fetal fibronectin test is a very useful and effective test to identify patients who will be at risk for preterm delivery in symptomatic women. It is not useful in asymptomatic women as a predictive routine test (10,11). The application of this test in symptomatic women reduce costs with the avoidance of unnecessary treatments and hospital admissions (12,13). We hypothesized that fFN may be a useful marker to predict delivery route in nulliparous women at postterm based on the knowledge about its usefulness in the prediction of preterm delivery. The detection fFN in cervicovaginal secretions is a marker for disruption of choriodecidual interface which could provide a clue for the delivery route favoring the vaginal birth (14). It has a high negative predictive value and an excellent "rule out" test for preterm delivery (15). We also found that the negative fFN results were associated with cesarean delivery. So we should be careful in women with negative fFN results because of higher risk for cesarean section.

There are publications comparing the predictive strength of qualitative and quantitative fFN measurements (16,17). A recent study showed that quantitative fFN test alone is equal effective to the combination of cervical length and qualitative fFN test (18). Although there is no statistically significance, the shorter cervical length was correlated with the higher likelihood of vaginal birth according to our results. But ultrasound measurement of the cervical length may become to be preferred more widely in future with further studies.

Vaginal bleeding was found as the only external factor reducing the validity of fFN test in the prediction of preterm delivery (19). So we excluded the women with vaginal bleeding or membrane rupture.

The superiority of our study is the first study investigating the utility of fFN for the prediction of vaginal delivery in nul-

liparous women at postterm induced with dinoprostone. There are publications determining the value of pre-induction assessment of cervical FFN in the prediction of successful vaginal birth between 36 to 42 gestational weeks (20). Our limitation is the small number of cases and further studies in a larger population should be conducted for the prediction of labor route with fFN assessment supporting our results. In our results, the high rate of cesarean section may be criticized. But it should not be forgotten that nulliparous women at postterm induced with dinoprostone with Bishop score less than 5 were studied.

As a conclusion, fFN yields useful information identifying the pregnant women at low risk for cesarean section and so unnecessary interventions could be avoided. There is no still objective method to predict the likelihood of vaginal delivery. We believe that alternative methods which are better tolerated for women will be developed for the prediction of delivery route. Fetal fibronectin as one of these alternative methods should be investigated in further studies to help us for clinical decision of delivery route.

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