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Prediction of the induction to delivery time interval in vaginal dinoprostone-induced labor: a retrospective study in a Chinese tertiary maternity hospital

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Abstract

Objective: This study aimed to investigate the potential factors that affect the induction to delivery time interval in women undergoing induction of labor with a controlled-release dinoprostone vaginal insert.

Methods: Pregnant women who presented for delivery at Hubei Maternal and Child Health Hospital from January 2016 to August 2016 were recruited. Finally, 1265 women who underwent labor induction with a vaginal dinoprostone (PGE2) insert were analyzed. Univariate and multivariate linear regression analyses were used to estimate the relevant risks for delivery time.

Results: Among the1265 subjects, the mean delivery time was 18.92 ± 12.50 hours. Univariate and multivariate analyses showed that fetal weight, an obstetric complication (premature rupture of the membranes), and the delivery history were significantly associated with the induction to delivery time. Biparietal diameter was related to the vaginal delivery time in univariate analysis, but there was no significant difference after adjustment in multivariate analysis.

Conclusions: Vaginal dinoprostone is an effective method for successful induction of labor. Gestational age, parity, and fetal weight are major factors that predict the induction to delivery time interval.

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Introduction

Since the discovery of uterine sensitivity to oxytocin in 1906 and to prostaglandin $F2_a$ in 1964, pharmacological induction of labor has steadily become more widespread.[1] Induction of labor reduces some risks of ongoing pregnancy, such as development of preeclampsia, oligohydramnios, macrosomia, and intrauterine fetal demise at a later gestational age.[2] The aim of successful induction is to reduce the risk of expectant pregnancy, shorten the induction to delivery interval, reduce the rate of cesarean section, and achieve spontaneous vaginal delivery. The newborn should be delivered in a good condition within an acceptable time frame and maternal side effects or discomfort should be minimized.[3]

The process of labor induction is usually associated with cervical ripening, using mechanical or pharmacological methods. Prostaglandins increase the rate of vaginal delivery and reduce the need of oxytocin within 24 hours, and significantly decrease the rate of cesarean delivery.[4] With regard to prostaglandin administration, a prostaglandin E2 (dinoprostone, PGE2) vaginal suppository is the preferred method for cervical ripening and induction of labor, and it is widely used in clinical practice.[5] PGE2 is the only prostaglandin that is approved by the Food and Drug Administration of the United States for cervical ripening in pregnant women near or at term with a medical or obstetric indication.[6] The controlled-release vaginal PGE2 not only relaxes cervical smooth muscle and promotes cervical dilatation, but also stimulates the synthesis and release of endogenous PGE2. After administration, PGE2 increases cervical ripening and uterine contractions, and thus improves the success of vaginal delivery and shortens the time to labor. The time interval from induction to labor is an important aspect to evaluate. Prolonged delivery is associated with a higher infection rate, increased maternal distress, increased need for oxytocin supplements, and increased demand for staff and hospital resources.[7] Prolonged delivery may also cause uterine atony and further extension. In recent years, more attention has been paid to the delivery time, which can be used to evaluate the comfort of women in the process of labor.

The clinical outcomes of labor induction are variable and may be affected by many factors. Induction of labor is more likely to succeed in multiparous,[8] taller,[9] and younger women and in women with a lower body mass index (BMI).[10,11] However, induction of labor is less likely to be successful where the neonate has a higher birth weight[10] or is in a persistent occipitoposterior position.[8] The time from induction to vaginal delivery has not been well established. Therefore, our study aimed to investigate the relevant factors that may affect the induction to vaginal delivery time when a dinoprostone vaginal insert is used for induction of labor and cervical ripening.

Materials and methods

A total of 14,954 pregnant women who presented for labor at Hubei Maternity and

Child Health Hospital from January 2016 to August 2016 were reviewed in this study. Among them, 1892 women who underwent induction of labor with a controlled-release dinoprostone vaginal insert were identified. Inclusion criteria were as follows: (1) gestational age $\geq$38 weeks; (2) normal fetal heart rate; and (3) a Bishop score <6. Patients were excluded for the following reasons: (1) with planned or medically indicated cesarean deliveries; (2) multiple pregnancies, fetal anomaly, malpresentation, placenta previa, and any antenatal complication; (3) previous cesarean section or uterine surgery; (4) hypersensitivity to dinoprostone; and (5) any other contraindications to vaginal delivery. A total of 235 women were excluded because of the above-mentioned criteria. Additionally, 392 women chose cesarean delivery. This study was approved by the Ethics Committee of Hubei Maternity and Child Health Hospital. Informed consent was obtained from all subjects.

A dinoprostone vaginal insert (Propess 10 mg; Controlled Therapeutics, East Kilbride, Scotland) was placed into the posterior vaginal fornix for induction of labor. The insert is a preparation of PGE2, which is packaged in a hydrogel polymer matrix. The dose was repeated if the cervix was still unfavorable (Bishop score $\leq$6). This insert is designed for slow intravaginal release of 10 mg dinoprostone at a rate of 0.3 mg/hour over 24 hours. The suppository was removed when there was tachysystole or abnormal fetal heart rate tracing. Intravenous oxytocin augmentation was initiated in women with inadequate uterine contractions or failure to progress 30 minutes after removal of the insert. Failure to progress was defined as failure of progressive cervical dilatation and fetal descent, and/or inefficient uterine activity. Continuous electronic fetal monitoring was performed during active labor. Obstetric complications included oligohydramnios, premature rupture of the membranes (PROM), and hypertensive diabetes or gestational diabetes at the time of inducing labor.

The demographic and clinical data of all subjects were abstracted from the medical records. The primary outcome was time from administration of PGE2 to onset of labor and to delivery. The secondary outcomes were maternal side effects and the requirement for neonatal resuscitation, with evaluation of the Apgar score at 1 and 5 minutes requiring neonatal intensive care unit admission within 24 hours of delivery.

Statistical analysis was performed using Statistica 7.1 Software (StatSoft Inc., Tulsa, OK, USA). Values are presented as mean $\pm$ standard deviation, median (interquartile range), or number (percentage). Descriptive statistics were tabulated for demographic and neonatal outcomes. Univariate and multivariate linear regression analyses were performed to determine the potential factors that affect the induction to delivery time. $P<0.05$ was considered statistically significant.

Results

From January 2016 to August 2016, a total of 1265 women were included in the study. Detailed characteristics of the individuals are shown in Table 1. The mean maternal age was 28 ± 3.05 years and the mean BMI was 26.73 ± 2.91 kg/m^2. Most of the subjects were primiparas (88.77%). The mean biparietal diameter (BPD), which was prenatally measured by ultrasound, was 9.36 $\pm$ 0.37 cm. The mean time from PGE2 administration to delivery was 18.92 $\pm$ 12.50 hours in our study population (Table 2). The mean birth weight was 3.35 $\pm$ 0.40 kg. The 5-minute Apgar score was $\geq$7 in 99.6% of newborns.

Univariate analysis showed that women with a short gestational age, obstetric

Table 1. Clinical characteristic of women with dinoprostone-induced vaginal delivery.

Clinical characteristics	Vaginal delivery (n = 1265)
Maternal age (years)	28 ± 3.05
Menarche age (years)	13 ± 1.21
Gestational age (n, %)	
<39 weeks	251 (19.84)
39–41 weeks	547 (43.24)
≥41 weeks	467 (36.92)
BMI (kg/m^2)	26.73 ± 2.91
Education (n, %)	
Senior high school and below	170 (13.44)
College degree and above	1095 (86.56)
Regular menstruation (n, %)	1124 (88.85)
Abortion (n, %)	390 (30.83)
Obstetric complications (n, %)	554 (43.79)
Parity (n, %)	
Primigravida	1123 (88.77)
Multipara	142 (11.23)
Baseline Bishop score	4 (4–5)
Fetal heart rate (bpm)	144 ± 6.48
BPD (cm)	9.36 ± 0.37

Values are shown as mean ± standard deviation or n (%).
BMI, body mass index; BPD, biparietal diameter.

Table 2. Perinatal outcome of women with dinoprostone-induced vaginal delivery.

Perinatal outcome	Vaginal delivery (n = 1265)
Time to onset of labor (hours)	11.33 ± 11.09
Time to delivery (hours)	18.92 ± 12.50
Oxytocin augmentation (n, %)	334 (26.40)
Amniotomy (n, %)	208 (16.44)
Instrumental delivery (n, %)	15 (1.19)
Cervical lacerations (n, %)	13 (1.29)
Birth weight (kg)	3.35 ± 0.40
Apgar score <7 at 1 minute (n, %)	7 (0.55)
Apgar score <7 at 5 minutes (n, %)	5 (0.40)
Fetal distress (n, %)	7 (0.55)
Meconium-stained amniotic fluid (n, %)	316 (24.98)
Neonatal intensive care unit admission (n, %)	13 (1.03)

Values are shown as mean ± standard deviation or n (%).

Table 3. Univariate analysis of categorical variables and delivery time in women with dinoprostone-induced vaginal delivery.

Categorical variable	Delivery time (hours)	*P*
Gestational age		0.001
<39 weeks	15.61 ± 11.03	
39–41 weeks	19.18 ± 12.67	
≥41 weeks	20.40 ± 12.73	
Education		0.238
Senior high school and below	19.97 ± 13.17	
College degree and above	18.76 ± 12.39	
Menstruation		0.179
Regular	19.07 ± 12.66	
Irregular	17.72 ± 11.05	
Abortion		0.648
Yes	18.68 ± 11.93	
No	19.03 ± 12.75	
Obstetric complications		0.002
Yes	17.70 ± 12.04	
No	19.87 ± 12.77	
Parity		<0.001
Primigravida	19.48 ± 12.57	
Multipara	14.46 ± 10.95	

Values are shown as mean ± standard deviation.

complications, parity of multipara, and small neonates (BPD and fetal weight) had a shorter induction to delivery time interval (all $P < 0.01$). However, there were no significant associations between other variables, such as the initial Bishop score and BMI, and the induction to delivery interval (Tables 3 and 4). Further multivariate linear regression analysis indicated that gestational age, parity, and fetal weight were independent factors that were significantly associated with the duration of the induction to delivery interval (all $P < 0.05$). Furthermore, among the obstetric complications, PROM was a significant independent factor that was associated with the induction to delivery interval ($P < 0.001$). However, BPD was not significant after

Table 4. Univariate linear regression analysis of continuous variables and delivery time in women with dinoprostone-induced vaginal delivery.

Continuous variables	β (95% CI)	*P*
Maternal age (year)	−0.029 (−0.255, 0.197)	0.799
BMI (kg/m^2)	0.186 (−0.050, 0.423)	0.123
Menarche age (years)	−0.014 (−0.584, 0.555)	0.961
Fetal heart rate (bpm)	0.021 (−0.085, 0.128)	0.690
BPD (cm)	3.758 (1.887, 5.629)	<0.001
Bishop score	−0.436 (−1.449, 0.578)	0.399
Fetal weight (kg)	4.965 (3.246, 6.683)	<0.001

CI, confidence interval; BMI, body mass index; BPD, biparietal diameter.

Table 5. Multivariate linear regression analysis of delivery time in women with dinoprostone-induced vaginal delivery.

Variables	β	*P*
Gestational age		
<39 weeks	Reference	
39–41 weeks	2.190 (0.247, 4.133)	0.027
≥41 weeks	2.906 (0.833, 4.978)	0.006
PROM	−6.512 (0.694, 88.08)	<0.001
Parity		
Primigravida	Reference	
Multipara	−5.392 (−7.529, −3.255)	<0.001
Fetal weight (kg)	4.099 (2.214, 5.985)	<0.001

PROM, premature rupture of the membranes.

adjustment in multivariate analysis (Table 5).

Discussion

The time interval from induction to vaginal delivery is an important issue in induction of labor. Vaginal prostaglandins are highly effective in achieving cervical ripening and vaginal delivery, as well as decreasing the time from administration to onset of labor. Therefore, in this study, the induction to delivery interval and its potential predictive factors were assessed in dinoprostone-induced vaginal delivery. We found that 76.3% (1265) of women delivered vaginally following induction of labor with dinoprostone. This finding is consistent with a previous successful vaginal delivery rate of 75% to 86%.[12] In our study, the mean induction to delivery time interval was 18.92 ± 12.50 hours, which is shorter than that in a previous study by Danielian et al.[13] who found that the average interval from induction to vaginal delivery was 22.9 hours in the dinoprostone group. Tan et al.[12] found that the mean time interval from insertion of dinoprostone to delivery was 19.1 ± 1.1 hours. Most of our newborns were in good health and five neonates had an Apgar score of <7 at 5 minutes. No serious neonatal complications or hyperstimulation was found in our study. Our results suggested that controlled-release dinoprostone vaginal inserts were effective for achieving induction of labor.

The induction to delivery time interval can be affected by several factors. Our study showed that gestational age, parity, and birth weight were major predictive factors that affected the induction to delivery time. These results are partially consistent with the results of a previous study by Braems et al.[14] These authors found that the cervix score, parity, gestational age, and the number of prostaglandin tablets administrated were significant explanatory variables for the induction to delivery time interval. The duration of induction to delivery has been reported to be shorter with increasing gestation.[15] Gestational age and

parity significantly predict the delivery time in women undergoing induction of labor.[16] Therefore, the current result that gestational age was an independent predictor for the delivery interval in dinoprostone-induced labor supports these previous studies.

Parity is one of the most important parameters affecting the success of induction. Induction of labor is easier in multiparous women than in primiparous women.[17,18] We found that multiparous women were more likely to undergo labor in a shorter time than primiparous women when a PGE2 vaginal insert was used for induction of labor. This finding is consistent with previous studies, which suggested that parity is an independent predictive factor for the induction to delivery interval.[8,19] However, unlike the results of our study and the above-mentioned studies, Laencina et al.[20] found that the average induction to delivery time interval was not significantly different among women with different parities, although this time was comparatively longer in nulliparous women. This conflicting result between studies may be partially explained by the population selected, the constituent ratio of our population (primipara: mutilpara = 7.9:1), and different agents used for induction of labor. Nevertheless, our study showed that parity was an independent factor that can be used to predict the induction to delivery time interval.

The cervical state is an important factor in predicting successful induction of labor and reducing the likelihood of delivery. The Bishop score summarizes the cervical condition and represents the phenotype of cervical histological changes. This score is considered as the best tool to assess cervical status.[21] A Bishop score <6 defines an unfavorable cervix and predicts a high rate of failed inductions and a high cesarean birth rate, which may cause a long delivery time.[22,23] A comparative study of cervical length and the Bishop score suggested that the Bishop score provided better prediction of the induction to delivery time interval.[24] Only doctors with more than 10 years of work experience are qualified to evaluate the Bishop score. However, we did not find any significant effect of the Bishop score on the delivery time. The potential reason for this lack of finding is unclear. The selected population and the fact that the Bishop score is a continuous variable may have played a role. Future studies are required to clarify this issue.

Birth weight is a significant factor in predicting successful induction of labor.[10] A direct correlation was observed between lower birth weight and delivery within 24 hours.[25] The delivery time was significantly prolonged with increasing birth weight in our study. This finding is consistent with the results of a previous study, which showed that fetal weight was an important variable for predicting the delivery time.[16] However, another study showed that birth weight was related to the delivery time in univariate analysis, but it was not significant after adjustment in multivariate analysis.[14] Additionally, maternal weight was found to be a predictor of the induction to vaginal delivery time.[26] However, our study and other studies showed that BMI has no obvious effect on prediction of the delivery duration.[16] This variation appears to be caused by the population that is selected.

This study has some limitations. The retrospective nature of this study might have caused some biases in data collection and interpretation. However, the data of our study were obtained from the Hubei Maternal and Child Health Hospital, which is the oldest tertiary maternity hospital in Hubei Province. All pregnant women who presented for labor/delivery between January and August 2016 were reviewed. Our study provided reliable clinical evidence for induction of labor with dinoprostone in a large sample of the Chinese

population. The findings of our study add to current information on induction of labor, which will be helpful in guiding the clinical use of dinoprostone.

In conclusion, our study provides evidence that dinoprostone is an effective method for achieving vaginal delivery in our study population. Gestational age, fetal weight, and parity are significant factors that can be used to predict the induction to delivery time in dinoprostone-induced labor.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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