

# Cervical ripening agent dinoprostone for delivery induction in late pregnancy mothers: experiences of 685 cases

C. Liang, D. Xu, J. He

Obstetrics and Gynecology Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang (China)

## Summary

The failure of labor induction often requires following cesarean section and suffering of patients. Cervical ripening is therefore critical in clinical care of pregnant mothers. The present study demonstrated the use of dinoprostone in cervical ripening for delivery induction in 685 cases of pregnancy mothers. The authors conclude that dinoprostone is a very useful and safe drug for delivery induction. The combined use of oxytocin and careful monitoring of all body symptoms are important for the clinical safety.

**Key words:** Dinoprostone; Delivery; Cesarean section; Vaginal delivery; Cervical ripening.

## Introduction

The failure of labor induction often requires following cesarean section and suffering of patients [1-3]. Cervical ripening is therefore critical in clinical care of pregnant mothers and the application of cervical ripening agents is with high usefulness [4-8]. The present study examined the use of cervical ripening agents in delivery induction for late pregnancy mothers, in order to provide the efficiency, safety, and clinical management of these agents.

## Materials and methods

### Clinical data

This study included 685 late pregnancy mothers admitted to the present hospital from April 30, 2009 to May 1, 2010, aged  $28.5 \pm 3.2$  years: 639 cases were first mother, while 46 cases were with experience. Subjects with head disproportion, abnormal birth canal, fetal distress, uterine scar, more than three times full-term pregnancy, and cervical Bishop score less than 6, were excluded. All subjects had no history of allergy to prostaglandin preparations, no asthma, no glaucoma, and no history of cardiovascular disease. The ripening agent was dinoprostone (prostaglandin E<sub>2</sub>) 10 mg.

All patients were informed with this drug administration and written consents were obtained. The study was approved by ethic committee of human medical studies in Zhejiang University School of Medicine (IRB No: ZJU0309-C-GB091).

Among all mothers, the gestational age was 37-42 weeks (mean gestational age  $40.2 \pm 1.1$  weeks), including 150 cases 37-40 weeks, 221 cases of 40-41 weeks, 279 cases of 41-42 weeks, and 35 cases more than 42 weeks. The main reasons for induced delivery include: 458 cases close or exceeding the predicted delivery phase, 125 cases of suspected oligohydramnios, 35 cases of premature rupture of membranes for 24 hours without delivery, 31 cases of suspected fetal distress, 18 cases of gestational hypertension, 13 cases of gestational diabetes, three cases of pregnancy-nephritis, and two cases of thyroid disease during pregnancy.

### Cervical ripening procedures

The cervical score was with improved Bishop Score: less than 6 suggests no ripening. Then 10 mg dinoprostone was placed in the posterior fornix, with the subject left for rest of 30 minutes. The dinoprostone was removed in case of (1) delivery or membrane eruption in 24 hours; (2) any overstimulation signs or stress of the babies; (3) no signs of regular contractions after 24 hours.

The following indices were monitored: (1) the Bishop score improvement: 3 was significant effective, and 2 was effective, with both counted for effective rates; (2) in case of any adverse effects such as nausea or vomiting, fever, hypotension, and tachycardia; (3) the time length of dinoprostone placement; (4) the time length since dinoprostone placement to delivery; (5) the approach used for delivery; (6) the mother conditions: postpartum hemorrhage, infection, and birth canal injury; (7) fetal conditions: fetal heart rate changes, amniotic fluid, and neonatal Apgar score.

If there were no signs of delivery 30 minutes after dinoprostone removal, the mothers were treated with intravenous oxytocin at 0.5% (2.5 mU/minute, eight drops per minute) for every half an hour until contractions appeared (maximum 30 drops/minute). The subjects without delivery after 72 hours of cervical ripening were evaluated as failure of induction.

### Statistics

The data were analyzed with SPSS13.0 software and the count data were compared with t test across groups. The measurement data were with  $\chi^2$  test, and  $p < 0.05$  was considered as significant. For paired split comparisons,  $p < 0.025$  was considered as statistically significant.

## Results

### The effects of cervical ripening by dinoprostone for mothers with different pregnancy weeks

The authors found that among 685 mothers with cervical ripening by dinoprostone treatment, 557 cases showed improved Bishop scores more than 3, 81 cases with more

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Table 1. — *The effects of cervical ripening by dinoprostone for mothers with different pregnancy weeks.*

Weeks	Cases	Improvement (cases, %)	Vaginal delivery (cases, %)	Cesarean section (cases, %)
37-40	150	131 (87.3%)	84 (56.0%)	66 (44.0%)
40-42	500	477 (95.4%)	324 (64.8%)	176 (35.2%)
> 42	35	30 (85.7%)	20 (57.1%)	15 (42.9%)
Total	685	638 (93.1%)	428 (62.5%)	257 (37.5%)

Table 2. — *The effects of cervical ripening by dinoprostone for mothers with different reasons.*

Reasons	Cases	Vaginal delivery (cases, %)	Cesarean section (cases, %)
Approaching or exceeding the expected delivery phase	458	289 (63.1%)	169 (36.9%)
Suspicious oligohydramnios	125	69 (55.2%)	56 (44.8%)
Premature rupture of membranes 24 hours without delivery	35	29 (82.9%)	6 (17.1%)
Suspected fetal distress	31	20 (64.5%)	11 (35.5%)
Pregnancy complications or comorbidities	36	21 (58.3%)	15 (41.7%)
Total	685	428 (62.5%)	257 (37.5%)

than 2, with a total effective rate 93.1%. Among these subjects, they found that the improvement rate for 40-42 weeks mother was significantly better than < 40 weeks group ( $X^2 = 12.423, p = 0.001$ ), while the improvement rate for 40-42 weeks mothers was also better than > 42 weeks group ( $X^2 = 6.187, p = 0.013$ ), suggesting for limited time window of this drug administration.

The modes of delivery included: 428 cases of vaginal delivery (62.5%, including 401 cases of normal delivery, 21 cases with prolonged delivery, and six cases with fetal distress and helper forceps), 257 cases of cesarean section delivery (37.5%). Among these subjects, the authors found that the vaginal delivery rate for 40-42 weeks mothers was significantly better than < 40 weeks mothers ( $X^2 = 3.824, p = 0.05$ ), but not > 42 weeks group ( $X^2 = 0.835, p = 0.361$ ) (Table 1).

#### *The effects of cervical ripening by dinoprostone for mothers with different reasons*

The reasons for induction of delivery included: 458 cases of approaching or exceeding the expected delivery phase, 125 cases of suspicious oligohydramnios, 35 cases of premature rupture of membranes 24 hours without delivery, 31 cases of suspected fetal distress, and 36 cases of pregnancy complications or comorbidities (Table 2).

#### *The effects of cervical ripening by dinoprostone on pre-delivery and final delivery*

The mean time length from dinoprostone placement to delivery induction was  $641.6 \pm 365.9$  minutes; average de-

Table 3. — *The success rate of vaginal delivery by Dinoprostone without or with oxytocin combined use*

Groups	Cases	Cesarean section (cases & %)	Vaginal delivery (cases & %)
Dinoprostone alone	530	170 (32.1%)	360 (67.9%)
Dinoprostone + 1 day oxytocin	96	46 (47.9%)	50 (52.1%)
Dinoprostone + 2 day oxytocin	59	41 (69.5%)	18 (30.5%)
Total	685	257 (37.5%)	428 (62.5%)

Table 4. — *The risk factors for failure of vaginal delivery.*

	Vaginal delivery (428 cases)	Cesarean section (257 cases)	t value (p value)
Age	$28.3 \pm 3.3$	$28.9 \pm 3.2$	-2.284 (0.023)
Body weight index (kg/m <sup>2</sup> )	$26.3 \pm 2.7$	$27.7 \pm 3.0$	-5.752 (0.001)
Pregnancy weeks	$40.3 \pm 1.1$	$40.1 \pm 1.2$	1.958 (0.051)
Bishop score	$4.4 \pm 1.1$	$4.3 \pm 1.0$	1.429 (0.153)
Bishop score improvement	$5.1 \pm 4.4$	$3.3 \pm 1.6$	6.323 (0.001)
Neonatal weight	$3.3 \pm 0.4$	$3.5 \pm 0.4$	-4.221 (0.001)

livery time was  $538.7 \pm 256.5$  minutes for vaginal delivery mothers ( $473.2 \pm 244.0$ ,  $55.8 \pm 44.7$ , and  $8.0 \pm 6.5$  minutes, respectively, for first, second, and third phase of delivery).

The authors further analyzed patients without or with oxytocin addition (one or two days) during delivery into three groups. Interestingly, they found that dinoprostone alone group ( $X^2 = 32.328, p = 0.001$ ) and dinoprostone + one day oxytocin group ( $X^2 = 6.908, p = 0.009$ ) showed higher success rate of vaginal delivery in compared to dinoprostone + two day oxytocin group (Table 3).

#### *The analysis for cases with failure of vaginal delivery*

The authors further explored the potential cases of failure of vaginal delivery in the 257 cases of cesarean section in order to isolate risk factors for failure of vaginal delivery (Table 4). They found that the failure of vaginal delivery can be associated with age of the mother ( $p = 0.023$ ), body weight index (kg/m<sup>2</sup>) ( $p = 0.001$ ), neonatal weight ( $p = 0.001$ ), cervical ripening improvement after dinoprostone application ( $p = 0.001$ ), and the weeks of pregnancy ( $p = 0.051$ ), but not the cervical ripening score before dinoprostone application ( $p = 0.153$ ).

#### *The adverse effects of dinoprostone induced cervical ripening*

All body symptoms of pregnancy mothers were carefully monitored. The authors found no signs of nausea, vomiting, hypotension, and tachycardia; without tonic contraction of the uterus and uterine rupture; the average postpartum hemorrhage was  $210.3 \pm 86.1$  ml, with 14 cases of postpartum hemorrhage (12 cases of vaginal delivery and two cases of cesarean section). Five cases showed puerperal infection and 100 cases showed newborn amniotic

fluid II degrees or more turbid. Six cases showed children bruising asphyxia, with one case of full-month RDS. No other complications were observed.

## Discussion

The increased percentage of cesarean section in recent years does not suggest improved neonatal conditions, especially in developing countries [1, 2]. The improperly performed cesarean section might lead to neonatal harm [9, 10]. The successful induction of delivery in prolonged pregnancy therefore is critical to reduce the percentage of cesarean section. The present study demonstrated that the administration of dinoprostone leads to cervical ripening improvement in 93.1% mothers, with 62.5% of vaginal delivery rate. These results proved the clinical usefulness of dinoprostone in cervical ripening induction and preparation for delivery.

It is critical to decide induction of delivery. The first cause was prolonged pregnancy as suggested, followed by suspicious oligohydramnios, and premature rupture of membranes for 24 hours without delivery. In some studies the induction was performed after 12-24 hours following membrane rupture [3, 11-14]; while for post-24 hours cases, the successful rate of induction was 82.9%. In cases of pregnancy complications, the authors believe that the pregnancy should be terminated when expected date is approaching while controlling the symptoms.

It is interesting that mothers at different weeks of pregnancy exhibited different responses to cervical ripening improvement and vaginal delivery rates. The association analysis showed that the age, body-weight index, and neonatal weight are important factors affecting the improvement rate, and therefore the successful rate of delivery induction. The authors further showed that with the addition of oxytocin for one day, the delivery induction was significantly improved [8, 12, 15]. Yet whether oxytocin should be provided further for one to two days when the induction failed is to be discussed.

Last but not least, the use of dinoprostone in cervical ripening induction showed few adverse effects and neonatal symptoms [9, 16-18]. The authors have provided consistent monitoring for contraction and body symptoms every two hours for any potential side effect detection. None of the present cases showed serious complications before and after delivery.

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Address reprint request to:  
J. HE, M.D.  
Obstetrics and Gynecology Hospital,  
Zhejiang University School of Medicine,  
Hangzhou, Zhejiang 310006 (China)  
e-mail: hej@zju.edu.cn