



Dinoprostone in the Induction of Labor in Women with Late and Term Preeclampsia

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Abstract: Preeclampsia in the structure of causes of maternal mortality occupy a leading position. It is known that only delivery cures preeclampsia. But until now, the success of induction depending on the method, the choice of medication for induction in preterm gestation, obstetric and perinatal outcomes depending on the method of labor induction in women with preeclampsia remain controversial. A comparative analysis of obstetric and perinatal outcomes of women with «de novo» preeclampsia whose used induction of labor with dinoprostone and women whose labor began after amniotomy was carried out. It has been shown that the use of dinoprostone does not increase the incidence of complications in childbirth and the postpartum period and does not worsen perinatal outcomes compared with mechanical induction by amniotomy. It has been established that the use of dinoprostone simulates the physiological process of delivery, when the maturation of the cervix precedes labor, and the duration of labor after induction with dinoprostone does not statistically significantly differ in women with full-term and late preeclampsia. The results of this study prove the clinical efficacy and safety of using dinoprostone for preinduction and induction of labor in women with late and term preeclampsia.

Key words: preeclampsia, induction, amniotomy, dinoprostone, efficacy, safety, obstetric and perinatal outcomes

Relevance

Until now, preeclampsia is a widespread complication of pregnancy, causing high rates of adverse obstetric and perinatal outcomes. In cases of severe preeclampsia, they are accompanied by dysfunction of organs and organ systems. Restoration of organ functions caused by preeclampsia occurs after childbirth. Therefore, complicated preeclampsia requires delivery. In some cases, there is a need for early delivery [5, 7, 8, 13, 14].

The method of delivery of women with preeclampsia depends on the condition of the mother and fetus, the severity of complications of preeclampsia, gestational age, and the state of utero-fetal-placental blood flow. In some cases, the timing and mode of delivery of women with severe preeclampsia require not only differentiated, but also individualized approaches. Programmed childbirth of women with preeclampsia is carried out in cases where the risk of prolonging pregnancy prevails over intervention for the purpose of delivery, since any medical intervention has its own risks [2, 4, 6, 9, 11].

Recovery of renal function and toxemia in women with preeclampsia after childbirth occurs more quickly if delivery is performed vaginally compared with delivery by cesarean section. One of the methods of vaginal delivery is induction of labor. Induction of labor involves preventing complications that may worsen as pregnancy progresses. Induction of labor prevents the deterioration of the condition of the mother and fetus in complicated preeclampsia and helps reduce the frequency of cesarean sections [1, 10].

At the same time, with induction of labor, the risks of increased frequency of operative vaginal birth, fetal distress, and hyperstimulation increase. The issues of induction for preterm gestation in women with preeclampsia remain controversial [3].

It is known that the onset, course and outcome of labor depend on two factors - the maturity of the cervix and myometrial contractions. Cervical maturity is considered the main indicator for successful induction of labor in both full-term and preterm pregnancy. During the physiological course of pregnancy and childbirth, ripening of the cervix precedes myometrial contractions. Therefore, when inducing labor, it is necessary to strive to ensure that cervical ripening precedes labor [12].

Today, different methods of pre-induction of labor are used. Of the pharmacological methods for pre-induction of labor, the most acceptable drug is dinoprostone, which is an analogue of prostaglandin E₂, which promotes shortening and dilatation of the cervix. At the same time, dinoprostone affects membrane calcium channels and the content of cyclic adenosine monophosphate, promoting the activation of myometrial contractions. Dinoprostone helps to increase the frequency of labor starting within 24 hours after its use and reduce the frequency of cesarean sections [12].

A large number of studies have been conducted regarding pre-induction and induction of labor at full-term pregnancy. Much less research has focused on the use of dinoprostone in preterm pregnancy.

The aim of this study was to evaluate the effectiveness and acceptability of dinoprostone for induction of labor in women with late-onset preeclampsia and term preeclampsia.

Research material. We examined 65 pregnant women with hypertensive disorders (de novo preeclampsia) during pregnancy from 34+6 to 38 weeks of pregnancy. Among them, 39 women underwent induction of labor with dinoprostone (main group). In the main group there were 20 women with late onset preeclampsia (subgroup 1) and 19 with full-term preeclampsia (subgroup 2). 26 women were admitted with a favorable cervix and labor began within 2 hours after amniotomy (comparison group). All subjects were diagnosed with uteroplacental dysfunction. The inclusion criteria for the

examined women were reproductive age, gestational age greater than 34+6, diagnosed de novo preeclampsia, cephalic presentation of the fetus, and blood flow disorders in the mother-placenta-fetus system. The exclusion criteria for women from the surveyed groups were fetal malposition, multiple pregnancies, uterine fibroids, hemolytic disease of the newborn, serious extragenital diseases, and critical disorders of the hemodynamic function of the placenta.

Obstetric and perinatal outcomes were analyzed in women with induction of labor with dinoprostone (main group) and in women with induction of labor by amniotomy (comparison group). The characteristics of the effectiveness of pre-induction and induction of labor with dinoprostone in women with pre-eclampsia were also studied depending on the gestational age (at 34+6 - 38 weeks and at full term).

Research methods: The diagnostic criteria for de novo preeclampsia were hypertension (chronic and gestational) and proteinuria (protein/creatinine ratio in a single morning urine sample of 30 mg/mmol). Cervical maturity was assessed using the modified Bishop scale (Table 1).

Table 1 - Modified Bishop scale for assessing the “maturity” of the cervix (RCOG, 2001)

Characteristics of the cervix	Modified Bishop scale			
	0	1	2	3
Opening (cm)	<1	1-2	3-4	>4
Length(cm)	>4	2-3	1-2	<1
Position of the presenting part relative to the ischial spines (cm)	3 sm higher (-3)	2 sm higher (-2)	1 sm higher or at the same level (-1/0)	1-2 sm lower (+1/+2)
Consistency	Dense	Moderately softened	Soft	-
Position relative to the wire axis of the pelvis	Posteriorly	Centered	Anterior	

Interpretation of the cervical maturity score:

1. “Immature”: 0–5 points;
2. “Mature, but not enough”: 6–7 points;
3. “Mature”: 8–13 points

The state of utero-fetal-placental blood flow was assessed by performing Doppler measurements of the uterine arteries, umbilical cord artery and fetal aorta before induction of labor. In each of these vessels, the systole-diastolic ratio, pulsation index, and resistance index were determined. The selection of women for induction of labor included subcompensated forms of blood flow disturbances in the “mother-placenta-fetus” system. In order to diagnose disorders of the functional state of the fetus, women underwent cardiotocography before induction of labor. Selection of women for induction of labor was carried out with the following cardiotocogram indicators: basal rhythm 120–160 per minute; amplitude of basal rhythm variability 10–25 per minute; no decelerations; the presence of two or more accelerations during 10 minutes of recording.

Statistical processing of the results was carried out using the processing of the obtained data, including classical methods of descriptive statistics: determination, methods of variation statistics, calculation of $M \pm m$ and the indicator of statistical significance. Statistical analysis of the obtained data

was carried out using the SPSS 17.0 application package (IBM SPSS Cstatistics, USA). Calculated for relative share values (%). Comparative analysis was carried out using the χ^2 criterion. Comparison of populations according to related quantitative characteristics was carried out using the Student's t-test, for small groups - using the Man-Whitney U test. The results were statistically significant at $p < 0.05$.

The results obtained and their discussion. Obstetric and perinatal outcomes were analyzed depending on the method of labor induction. A comparative analysis of the characteristics of the effectiveness of pre-induction and induction of labor with dinoprostone in women with pre-eclampsia was also carried out depending on the gestational age (at 34+6 - 38 weeks and at full term).

Clinical characteristics of the examined groups of women are presented in Table 2.

Table 2 – Clinical characteristics of the examined groups of women

User	Group	Main (n=39)	Comparisons (n=26)	P
Average age		29,1±1,8	28,3±7,6	P* > 0,05
Late preeclampsia		20	9	P > 0,05
Pre-eclampsia at term		19	17	P > 0,05
Anemia		5	6	P > 0,05
Kidney diseases		17	8	P > 0,05
History of ARVI		24	13	P > 0,05
Primipara		14	9	P > 0,05
Multiparous		15	11	P > 0,05
Multiparous		10	5	P > 0,05

Note: P - statistical significance of the difference in indicators between groups (P* - according to Student, P - according to Fisher's exact test)

A mathematical analysis of the clinical characteristics of the examined groups of women established that the difference in the characteristics (average age, timing of diagnosed preeclampsia, frequency of EHD, parity) of women in the main group and the comparison group did not have statistically significant differences (Table 1), which made it possible to conduct a comparative analysis of obstetric and perinatal outcomes of the above groups. When comparing the obstetric outcomes of women with preeclampsia who gave birth after amniotomy and after induction of labor with dinoprostone, isolated cases of labor weakness and fetal distress were noted. Of the 39 cases of induction of labor with dinoprostone, 1 birth ended in caesarean section; the indication for surgery was weakness of labor combined with fetal distress. Cases of hyperstimulation and bleeding in the postpartum period and cases of worsening preeclampsia after childbirth have not been recorded. The average blood loss during childbirth and during the first 2 hours after birth did not differ significantly in both groups of women examined (Table 3).

Table 3 – Frequency of complications during childbirth, in the postpartum period and surgical delivery in groups of examined women

User group	main (n=39)	Comparisons (n=26)	χ^2 with Yates correction	Significance level P
Weakness of labor	2	1	0,131	0,718
Fetal distress	2	1	0,131	0,718
C-section	1	0	0,042	0,838

Hyperstimulation	0	0		
Postpartum hemorrhage	0	0		
Vacuum extraction of the fruit	1	1	0,193	0,661
Complication after childbirth: ELLP, chronic renal failure	0	0		
Average blood loss during childbirth (ml)	287,7±17,6	319,6±34,5	$t = 0,82$	$P > 0,05$

Our results confirm that the use of dinoprostone does not increase the incidence of complications during childbirth and the postpartum period compared with such a mechanical method of induction of labor as amniotomy.

The assessment of newborns on the Apgar scale at the 5th minute after birth in women of the main group and the comparison group is presented in Table 4. As can be seen from the data presented in the table, in which newborns are distributed according to assessment scores, there are no statistically significant differences in the number of newborns with the corresponding assessment installed. The number of newborns born with asphyxia in the main group (5 newborns) did not statistically significantly exceed (χ -square with Yates correction 0.720; $p=0.397$) the corresponding indicator in the comparison group (7 newborns).

Table 4 - Distribution of newborns with different Apgar scores at 5 minutes after birth in the groups of examined women

Apgar \ Group	Main (n=39)	Comparisons (n=26)	χ^2 with Yates correction	Significance level P
10 points	0	0		
9 points	0	0		
8 points	8	6	0,004	0,951
7 points	22	17	0,216	0,642
6 points	6	1	1,127	0,289
5 points	1	2	0,131	0,718
4 points	1	0	0,042	0,838
3 points	0	0		
2 points	1	0	0,042	0,838

Note: P - statistical significance of the difference in indicators between groups according to the χ^2 criterion with Yates' correction

In the groups of women examined, no cases of stillbirth or early neonatal mortality were registered. Thus, the use of dinoprostone for induction of labor in women with late and full-term preeclampsia does not worsen obstetric and perinatal outcomes compared with the mechanical induction method of amniotomy.

The distribution of women with late-onset preeclampsia and full-term preeclampsia according to the degree of cervical maturity showed no statistically significant differences in the frequency of women with an “immature” and insufficiently “mature” cervix (Table 4).

Table 4 – Distribution of women in the main group by cervical maturity (Bishop scale)

Cervical assessment	Group	P
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	1st (n=20)	2nd (n=19)	
Immature (0-5 b)	12	13	>0,05
Not mature enough (6-7 b)	11	6	>0,05
Mature (8-13 b)	0	0	

Note: P - statistical significance of the difference in indicators between groups (according to the χ^2 criterion with Yates' correction)

The comparative effectiveness of pre-induction and induction of labor with dinoprostone in women with full-term preeclampsia and late-onset preeclampsia is presented in Table 5.

Table 5 – Efficiency indicators of pre-induction and induction using dinoprostone

User	Subgroup		Mann-Whitney U test	P
	1st (n=20)	2nd (n=19)		
Duration from start of induction to start of labor (hours)	from 7,8 to 18,3	from 5,3 to 17,4	90,5	<0,05
Duration of labor (hour)	from 4,8 to 16,2	from 5,4 to 17,4	193,5	>0,05

Note: P - statistically significant difference (The critical value of the Mann-Whitney U test for a given number of compared groups is 119)

A statistically significant increase in the duration from the start of induction with dinoprostone to the onset of labor was established in women with late-term preeclampsia compared with the corresponding indicator in women with full-term preeclampsia. However, the duration of labor in both studied groups did not have statistically significant differences.

Labor with a cervical score of 7 points on the Bishop scale began in 12 (30.8±7.4%), with a score of 8 points - in 27 (69.2±7.4%) women of the main group, who Dinoprostone was used for induction. In women after amniotomy, labor began with a condition of the cervix corresponding to 7 points in 10 (38.5 ± 9.5%) and 8 points in 16 (61.5 ± 9.5%) women, which did not have statistical significance compared with the corresponding indicators in women who underwent pre-induction and induction with dinoprostone (t=0.6; t=1.5).

Dinoprostone is an analogue of prostaglandin E2, which increases in the cells of the fetal membranes in the area of the internal pharynx towards the time of delivery, which contributes to the maturation of the cervix at the onset of labor. The action of dinoprostone is aimed at increasing the secretion of collagenase, elastase and hyaluronic acid in the cervix, which promotes cervical ripening. Dinoprostone also promotes the activation of uterine contractions. Our results indicate that when dinoprostone is used, the development of contractions occurs gradually and is associated with ripening of the cervix. The use of the PGE2 analog dinoprostone models the physiological process of childbirth, when cervical ripening precedes labor. This point is especially important for pre-induction and induction of labor in premature pregnancy. At 34-37 weeks of pregnancy, the maturation of the organs and organ systems of the fetus is completed. However, premature fetuses, even at these times, remain sensitive to hypoxia and obstetric aggression. Careful delivery when early termination of pregnancy is necessary is an important factor influencing perinatal morbidity and mortality rates.

Thus, the results of this study prove the clinical effectiveness and safety of the use of dinoprostone for preinduction and induction of labor in women with late and full-term preeclampsia.

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