

ANALYSIS OF THE FACTORS AFFECTING THE DURATION OF THE LATENT PERIOD FROM THE MOMENT OF PRELABOR RUPTURE OF MEMBRANES TO THE ONSET OF LABOR

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▪ **Introduction.** Premature rupture of membranes during full-term pregnancy represents an increased risk of septic complications for both the mother and the fetus due to the prolongation of the latency period, the period from the discharge of amniotic fluid till the onset of labor.

Purpose of the study: to assess the factors affecting the duration of the latent period (from the moment of discharge of amniotic fluid to the development of labor) during full-term pregnancy.

Materials and methods. A prospective analysis of the labor of 136 patients with premature rupture of membranes and full-term pregnancy (37-42 weeks) of low and moderate risk groups, without contraindications for vaginal birth was carried out. Patients with Bishop's cervical score less than or equal to 7 points made up the main group (70 pregnant women). Patients with "mature cervix" were included in the comparison group (66 cases). The analysis of the duration of the latent period was carried out with the use of correlation and regression analysis.

Results. The time from the moment of discharge of amniotic fluid to the onset of regular labor in the group with a cervix ≤ 7 Bishop points was 7.82 ± 4.53 hours, while in the group with a cervix ≥ 8 Bishop points it was 4.4 ± 3.23 hours ($T = -5.02$; $p < 0.001$). The most significant effect on the duration of the latency period was the assessment of the cervix according to Bishop scale ($r = -0.48$; $p < 0.001$), the gestational age was in the second place ($r = -0.23$; $p = 0.08$). In patients who didn't take mifepristone, the main factors influencing the duration of the latency interval were fetal weight ($r = -0.31$; $p = 0.004$) and gestational age ($r = -0.29$; $p = 0.008$); the increase in these parameters led to the decrease in the latency interval. Women who received 200 mg mifepristone in labour had a significant positive correlation with maternal age ($r = 0.36$; $p = 0.04$), negative with maternal weight ($r = -0.42$; $p = 0.01$) and cervical Bishop score ($r = -0.48$; $p = 0.004$). Women in labor with the longest latency interval, who received mifepristone in a daily dosage of 400 mg, have an inverse correlation for the gestational age ($r = -0.39$; $p = 0.09$), connection with the degree of cervical maturity, age, constitutional features, gestational age was not revealed.

Conclusion. The main predictors of the duration of the latency period of premature rupture of membranes at full-term pregnancy were the degree of cervical maturity according to Bishop scale, gestational age and fetal weight at birth.

▪ **Keywords:** pregnancy; premature rupture of membranes; caesarean section; labor abnormalities; amniotic fluid; oxytocin.

АНАЛИЗ ФАКТОРОВ, ВЛИЯЮЩИХ НА ПРОДОЛЖИТЕЛЬНОСТЬ ЛАТЕНТНОГО ПРОМЕЖУТКА ОТ МОМЕНТА ОТХОЖДЕНИЯ ОКОЛОПЛОДНЫХ ВОД ДО РАЗВИТИЯ РОДОВОЙ ДЕЯТЕЛЬНОСТИ

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▪ **Введение.** Преждевременный разрыв плодных оболочек при доношенной беременности представляет собой повышенный риск септических осложнений как для матери, так и для плода за счет увеличения продолжительности безводного периода, основную долю в котором составляет латентный период — время от момента преждевременного разрыва плодных оболочек до начала родовой деятельности.

Цель исследования — оценить факторы, влияющие на продолжительность латентного периода (от момента отхождения околоплодных вод до развития родовой деятельности) при доношенной беременности.

Материалы и методы. Проведен проспективный анализ течения родов у 136 пациенток с преждевременным разрывом плодных оболочек и доношенной беременностью (срок 37–42 недели) низкой и умеренной групп риска, без противопоказаний к родам через естественные родовые пути. Пациентки с оценкой шейки матки ≤ 7 баллов по Бишопу составили основную группу (70 беременных). Пациентки со «зрелой шейкой матки» составили группу сравнения (66 случаев). Анализ продолжительности латентного периода выполнен с помощью корреляционного и регрессионного анализа.

Результаты. Время от момента отхождения околоплодных вод до начала регулярной родовой деятельности в группе с оценкой шейки матки ≤ 7 баллов по Бишопу составило $7,82 \pm 4,53$ ч, тогда как в группе с оценкой шейки матки ≥ 8 баллов по Бишопу — $4,4 \pm 3,23$ ч ($T = -5,02$; $p < 0,001$). Наиболее значимо на продолжительность латентного периода влияли оценка шейки матки по Бишопу ($r = -0,48$; $p < 0,001$), на втором месте — срок беременности ($r = -0,23$; $p = 0,08$). У пациенток, не получавших мифепристон, основными факторами, влияющими на продолжительность латентного промежутка, являлись вес плода ($r = -0,31$; $p = 0,004$) и срок беременности ($r = -0,29$; $p = 0,008$); увеличение этих параметров приводило к сокращению латентного промежутка. Роженицы, получившие мифепристон 200 мг, имели значимую положительную корреляцию с возрастом матери ($r = 0,36$; $p = 0,04$), отрицательную с весом матери ($r = -0,42$; $p = 0,01$) и оценкой шейки матки по Бишопу ($r = -0,48$; $p = 0,004$). У рожениц с максимально длительным латентным промежутком, получивших мифепристон в суточной дозировке 400 мг, выявлена обратная корреляция для срока беременности ($r = -0,39$; $p = 0,09$), связи со степенью зрелости шейки матки, возрастом, конституциональными особенностями, сроком гестации выявлено не было.

Заключение. Основными предикторами, влияющими на продолжительность латентного периода при преждевременном разрыве плодных оболочек и доношенной беременности, можно считать: степень зрелости шейки матки по Бишопу, срок беременности и масса плода при рождении.

■ **Ключевые слова:** беременность; преждевременный разрыв плодных оболочек; кесарево сечение; аномалии родовой деятельности; околоплодные воды; окситоцин.

Introduction

According to various authors, the incidence of premature rupture of membranes during full-term pregnancy ranges from 8.2% to 19.6% [7, 20]. The main problem with this complication lies in choosing the optimal approach for managing female patients, since long-term expectant approaches are hazardous for the development of septic complications in the mother and fetus [1, 3, 19, 23]. With the active management of labor, the probability of labor abnormalities, obstetric injuries, surgical interventions, and signs of fetal distress increases [11, 25].

The prolongation of the rupture to delivery interval often leads to labor complications (metroryxia or accelerated labor and poor and disorganized uterine contraction strength), which aggravates the condition of the fetus and in some cases requires surgical delivery [3, 4, 6, 19].

The duration of an anhydrous interval largely depends on the duration of the latent period, which is the period from the moment of amniotic fluid leak to the onset of active labor. Analysis of factors affecting the latent period and the search for options for modifying these factors are urgent tasks of modern obstetrics.

According to most international guidelines, premature rupture of membranes (PROM) is

considered an indication of labor induction [17, 21, 22, 24]. However, the expectant time can vary in different countries from 6 to 48 h. In Russia, currently, no clinical protocol is approved by the Ministry of Health of the Russian Federation, governing the management of childbirth in patients with full-term pregnancy and PROM. Accordingly, most obstetric institutions are guided by the clinical guidelines of the Academician V.I. Kulakov Scientific Center for Obstetrics, Gynecology and Perinatology “Premature rupture of membranes. Premature leak of amniotic fluid” [2], in which two variants of the approach are available, depending on the degree of maturity of the cervix. With a mature cervix, the expectant approach for 6 h is applied, after which labor is induced with oxytocin. With an immature or insufficiently mature cervix, its preparation starts with using fepristone antigestagens at a dose of 200 mg, followed by an assessment of the obstetric situation and, if necessary, repeated administration of mifepristone after another 6 h.

The study aimed to assess the factors influencing the duration of the latent period from the moment of amniotic fluid leak to labor onset in full-term pregnancy.

Materials and methods

We performed a prospective analysis of the course of labor in 136 patients with PROM and full-term pregnancy (37–42 weeks), admitted from home with amniotic fluid leak. Thus, the criteria for the inclusion of patients in the study were full-term singleton pregnancy, cephalic presentation, absence of contraindications for vaginal delivery, and pre-labor leakage of amniotic fluid.

The exclusion criteria from the study were high-risk pregnant women, according to the procedure for providing care in “Obstetrics and Gynecology” No. 572 dated 11/01/2012 [8], a scar on the uterus after surgery and a cesarean section, and gynecological diseases. During the previous 2 days, vaginal examinations and any interventions on the cervix were excluded.

According to the clinical protocol “Premature rupture of membranes. Premature leakage of amniotic fluid” [2], in case of PROM with full-term or close to full-term pregnancy and “mature” cervix (≥ 8 points according to Bishop), the expectant approach for 4–6 h is recommended, with further assessment of the situation and oxytocin induction, if necessary. As for the immature and insufficiently mature cervix (≤ 7 points according to Bishop), an active expectant approach was adopted in the study group, which included the administration of 200 mg mifepristone twice, immediately upon admission of the pregnant woman and 6 h after the first dose. Before the second drug dose and another after 6 h, the state of the cervix was assessed. Depending on the nature of the structural changes in the cervix, oxytocin labor induction was applied. Pregnant women with mature cervix made up the comparison group ($n = 66$, 48.5%), and patients with immature and insufficiently mature cervix were included in the main group ($n = 70$, 51.5%). The division of groups according to this principle was based on international guidelines, which represent two gradations depending on the presence of structural changes in the cervix, i.e., unfavorable in case with up to 8 points, and favorable in case with ≥ 8 points [10, 14]. In the absence of changes at the time of cervical maturation after the intake of mifepristone (total dosage of 400 mg) or in the absence of adequate labor at 4 h after intravenous infusion of oxytocin, delivery by cesarean section was raised. Patients with delivery by cesarean section were excluded from the study.

According to previous studies, the prolongation of membrane rupture to delivery interval is fraught with an increased risk of septic complications in both the mother and newborn. Accordingly, the choice of the optimal approach for the management of patients with pre-labor leak of amniotic fluid in full-term pregnancy includes identifying a balance between the optimal moment of the onset of labor induction and a decrease in its aggressive effect on the fetus and myometrium. In this study, we assessed the most significant factors affecting the duration from the moment of amniotic fluid leak to the onset of active labor, namely, age, anthropometric parameters of the pregnant woman, number of previous pregnancies, parity of births, condition of the cervix, and fetal weight.

Statistical analysis. The study results were processed using the Statistica 10.0, SPSS 13 software. The mean (M) was used to describe quantitative data, and the standard deviation (σ) was used as an interval estimate. In case of correspondence to the normal distribution, the means were compared using Student's t -test. In the absence of correspondence with the normal distribution, the means in the groups were analyzed using the Mann–Whitney test. Qualitative parameters were given as absolute frequencies and percentages. Qualitative parameters were analyzed using contingency tables, using chi-square test and two-tailed Fisher's test. The analysis of relationships between quantitative parameters was performed using Pearson's correlation analysis, and a multivariate regression model was also constructed. Differences were considered significant at $p < 0.05$.

Study results

The analysis results revealed no significant differences between the compared groups (Table 1). The average age values of pregnant women in the main and comparison groups were 28.37 ± 5.51 and 28.28 ± 4.77 years, respectively ($T = 0.10$; $p = 0.91$). Height and weight indicators were also comparable, and 14 (20%) and 12 (18%) women had a body mass index of >30 , respectively ($\chi^2 = 0.07$; $df = 1$; $p = 0.78$). The reproductive history did not differ significantly in the groups; primiparous patients were predominant in both groups, with 49 (70%) and 46 (69.6%) patients, respectively ($\chi^2 = 0.001$; $df = 1$; $p = 0.97$).

The gestational age in the groups was not significantly different. There were 14 (20%) and 14 (21.2%) patients with gestational age up to

Table 1 / Таблица 1

Characteristics of the study groups
Характеристика исследуемых групп

Sign	Main group (n = 70)		Comparison group (n = 66)		Note
	m	σ	m	σ	
Age, years	28.37	5.44	28.28	4.77	T = 0.10; p = 0.91
Body mass index, kg/m ²	27.03	3.92	27.15	4.37	T = -0.18; p = 0.85
Gestational age, weeks	38.73	1.14	39.00	1.34	T = -1.27; p = 0.20
Average number of pregnancies per woman	1.77	1.09	1.88	1.18	Z = -0.33; p = 0.73
Average number of therapeutic abortions per woman	0.17	0.45	0.24	0.56	Z = -0.42; p = 0.67
Average number of ectopic pregnancies per woman	0.03	0.17	0.03	0.17	Z = -0.01; p = 0.98
Average number of spontaneous miscarriages per woman	0.16	0.40	0.12	0.33	Z = 0.23; p = 0.81
Average number of births per woman	0.41	0.71	0.48	0.83	Z = -0.18; p = 0.85

38 weeks, 15 (21.4%) and 22 (33.3%) patients with gestational age >40 weeks; pregnant women at 38–41 weeks of gestation recorded the highest number ($\chi^2 = 2.91$; df = 2; p = 0.23).

The time from the amniotic fluid leak to the onset of active labor in the main group was 7.82 ± 4.53 h, while this indicator was 4.4 ± 3.23 h in the comparison group (T = -5.02; p < 0.001). In the majority of patients in the main group (41 cases, 58.5%), labor developed after ≥ 6 h from the rupture of membranes (Fig. 1), and in the comparison group, in 50 patients (75.7%), labor activity developed earlier than 6 h of the rupture to delivery interval ($\chi^2 = 21.03$; df = 3; p < 0.000).

In the main group, 16 (22.8%) patients had spontaneous active labor, without mifepristone, after 6.33 ± 1.25 h, but the cervix had an average Bishop score of 4.5 ± 1.6 points. In four of them, the Bishop cervical score was <4 points, but this is an exception to the rule, since the duration of the latent period from the moment of amniotic fluid leak to labor onset had a significant inverse correlation with the Bishop cervical score (r = -0.48; p = 0.000). The remaining 54 (77.1%) patients of the main group received the first tablet of mifepristone, and only 20 (28.8%) patients received the second tablet after 6 h, since the majority of patients after the intake of the first tablet of mifepristone had active labor (Fig. 2). Thus, in patients who

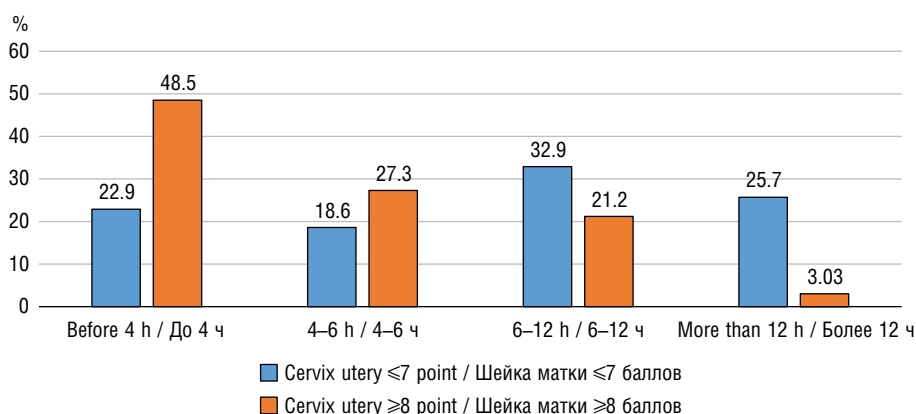


Fig. 1. The time from the moment of the prelabor rupture of membranes to the onset of labor in groups of patients

Рис. 1. Время от момента отхождения околоплодных вод до начала родовой деятельности в группах

received one tablet of mifepristone, labor started after 6.20 ± 2.82 h, and in those who received two tablets, labor commenced 11.76 ± 2.72 h after the amniotic fluid leak. In 12 patients, intravenous administration of oxytocin was required for labor induction.

To identify the factors that affect most significantly the duration of the latent period from the moment of amniotic fluid leak to labor onset, we constructed a correlation matrix (Table 2).

As regards the strength of the relationship and significance, the assessment of the cervix on the Bishop scale at the time of amniotic fluid leak ($r = -0.48$; $p < 0.001$) with an inversely proportional relationship ranked first. The weight of the fetus ($r = -0.22$; $p = 0.006$) ranked second because the greater the weight of the fetus, the shorter the duration of the latent period, which can be due to the more intense pressure of the fetus with a greater mass on the lower segment and cervix. That is, in the process of labor onset, the mechanical component of the pressure of the presenting part is extremely important. Gestational age is also significant, as the longer the gestational age, the higher is the probability that the cervix

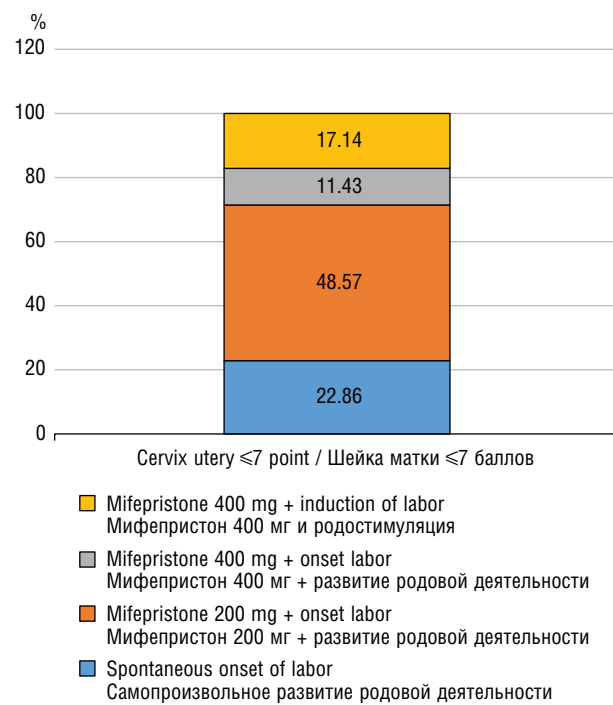


Fig. 2. The ratio of patients in the main group depending on the methods of labour induction

Рис. 2. Соотношение пациенток в основной группе в зависимости от методов индукции родов

Table 2 / Таблица 2

Correlation matrix of the main clinical and medical history indicators and latent period from the moment of pre-labor rupture of membrane to labor onset, $r(p)$

Корреляционная матрица основных клинико-анамнестических показателей и времени от момента излития околоплодных вод до начала родовой деятельности, $r(p)$

Sign	Age	Mother's height	Mother's weight	Birth parity	Fetal weight	Cervix (Bishop score)	Gestational age
Time of amniotic fluid leak to labor onset	0.04 (0.322)	0.19 (0.014)	0.00 (0.482)	-0.02 (0.431)	-0.22 (0.006)	-0.48 (<0.001)	-0.23 (0.008)
Age	1.00	-0.03 (0.374)	0.03 (0.375)	0.55 (<0.001)	0.08 (0.175)	-0.09 (0.147)	-0.098 0.256
Mother's height	-0.03 (0.374)	1.00	0.26 (0.001)	0.03 (0.355)	-0.07 (0.225)	-0.31 (<0.001)	-0.06 0.482
Mother's weight	0.03 (0.375)	0.26 (0.001)	1.00	-0.03 (0.378)	0.29 (<0.001)	-0.17 (0.027)	0.12 (0.156)
Birth parity	0.55 (<0.001)	0.03 (0.355)	-0.03 (0.378)	1.00	-0.03 (0.383)	0.02 (0.390)	-0.24 (0.005)
Fetal weight	0.08 (0.175)	-0.07 (0.225)	0.29 (<0.001)	-0.03 (0.383)	1.00	0.08 (0.184)	0.57 (<0.001)
Cervix (Bishop score)	-0.09 (0.147)	-0.31 (<0.001)	-0.17 (0.027)	0.02 (0.390)	0.08 (0.184)	1.00	0.10 (0.245)
Gestational age	-0.09 0.256	-0.06 0.482	0.12 0.156	-0.24 (0.005)	0.57 (<0.001)	0.10 (0.245)	1.00

Note. Bold font indicates significant correlations.

Примечание. Полужирным шрифтом выделены статистически значимые корреляции.

Table 3 / Таблица 3

Coefficients of the regression model indicating the dependence of the duration of the period from the time of premature rupture of membranes to labor onset in the entire cohort

Коэффициенты регрессионной модели, отражающей зависимость продолжительности периода от момента преждевременного разрыва плодных оболочек до начала родовой деятельности во всей когорте

Predictors	<i>b</i>	beta	<i>t</i>	<i>p</i>	<i>R</i> ²	SE regr
Constant	2095.09		6.48	<0.001	0.27	222.5
Assessment of the cervix according to Bishop (score) — <i>X</i> ₁	-43.92	-0.47	-6.24	<0.001		
Gestational age (weeks) — <i>X</i> ₂	-37.32	-0.18	-2.40	0.017		

Note. *b*, equation coefficient; beta, standardized ratio; *t*, data which are used to evaluate significance of coefficients of the regression equation; *p*, significance of coefficients of the equation; *R*², determination coefficient of the model; SE regr, standard mean square error of regression (minutes).

Примечание. *b* — коэффициент уравнения; beta — стандартизованные коэффициенты; *t* — статистика, по которой оценивается статистическая значимость коэффициентов регрессионного уравнения; *p* — статистическая значимость коэффициентов уравнения; *R*² — коэффициент детерминации модели; SE regr — стандартная ошибка регрессии (в минутах).

has a higher Bishop score. The duration from the moment of amniotic fluid leak to labor onset did not depend on the total number of pregnancies and parity of childbirth.

To construct a predictive model of the duration of the latent period from the moment of PROM to the onset of contractions, which was taken as the dependent variable, a regression analysis was performed. The above variables were included in the regression model as predictors. Mifepristone intake was excluded from the regression analysis due to the strong correlation (*r* = -0.74; *p* < 0.001) and logical connection with the cervix assessment.

As a result of the step-by-step analysis with ruling out, the most significant predictors were the assessment of the cervix according to the Bishop scale (score) and the gestational age at the time of amniotic fluid leak (Table 3).

Accordingly, the regression equation is as follows:

$$y = 2095.00 - 43.92X_1 - 37.32X_2.$$

where *y* is the latent period (time from PROM to the labor onset in minutes), *X*₁ is the assessment of the cervix according to Bishop (score), and *X*₂ is the gestational age (weeks).

Table 4 / Таблица 4

Correlation coefficients of the duration of the latent period from the moment of premature rupture of membranes to labor onset

Коэффициенты корреляции продолжительности периода от момента преждевременного разрыва плодных оболочек до начала родовой деятельности

Sign	Подгруппа 1 (n = 82)	Подгруппа 2 (n = 34)	Подгруппа 3 (n = 20)
Age	-0.18 (0.11)	0.36 (0.04)	0.26 (0.26)
Height	0.05 (0.66)	-0.11 (0.52)	0.32 (0.17)
Mother's weight	-0.16 (0.89)	-0.42 (0.01)	-0.23 (0.33)
Birth parity	-0.06 (0.61)	-0.73 (0.68)	-0.33 (0.16)
Fetal weight	-0.31 (0.004)	0.04 (0.81)	-0.08 (0.75)
Cervix (Bishop score)	-0.153 (0.169)	-0.48 (0.004)	-0.24 (0.32)
Gestational age	-0.29 (0.008)	-0.03 (0.87)	-0.39 (0.09)

Note. Bold font indicates statistically significant correlations.

Примечание. Bold font indicates significant correlations.

After stratification according to the characteristics of mifepristone intake, correlation and regression analyses were also performed (Table 4).

In patients who did not receive mifepristone (subgroup 1), the main factors influencing the latent interval duration were the weight of the fetus and gestational age; an increase in these parameters led to a reduction in the latent period. Puerperas who received 200 mg mifepristone (subgroup 2) had a significant positive correlation with maternal age and negative correlation with maternal weight and Bishop cervical score. As for the group with the longest latent period, these patients received mifepristone at a daily dosage of 400 mg (subgroup 3); an inverse correlation was revealed for gestational age at a significance level of $p = 0.09$.

Discussion of results

According to the review by Diguisto [13], spontaneous delivery without any intervention was registered in 71% of the patients, 26.3% underwent labor induction, and 2.7% had cesarean section. Given the high incidence of spontaneous labor, PROM can be considered a physiological duplicate mechanism for labor onset. Most international recommendations do not define clearly the duration of the latent period (from amniotic fluid leak to the spontaneous labor onset), which would be physiological, in case where no medical interventions would have been indicated. In different countries, the safe duration of both the latent interval (time from the amniotic fluid leak to labor onset) and rupture to delivery interval as a whole differs [2, 5, 21, 22, 24, 26]. Thus, the supreme health authority of France and an expert group proposed a 12-h interval of rupture to delivery as the boundary between physiological case and a potentially hazardous situation [13].

According to Chandra et al. [12], the average duration of the latent period is 18.94 ± 17.11 h without taking into account the degree of cervix maturity, exclusively under the condition of an expectant approach. In our study, the average duration of the latent period in the main group was 7.82 ± 4.53 h, while in the comparison group, this indicator was 4.4 ± 3.23 h, which we tend to associate with artificial limitation of the latent period and onset of labor induction.

As a result of the study, we did not reveal significant differences in age, anthropometric

data, reproductive history, including the parity of childbirth in patients with PROM and “immature”/“insufficiently mature” cervix (main group) and “mature” cervix (comparison group). According to the literature, the duration of the latent period reduces the high parity of births [15, 18], interval between previous births <2 years, as well as the mother’s age, and gestational age [27]. By contrast, a study revealed that the first birth is associated with a shorter latent period in case of PROM in preterm birth [9].

The main factor influencing the duration of the latent period in both full-term and preterm pregnancies is the degree of cervical maturity [9, 16]. This study confirmed this pattern. In most pregnant women in the comparison group, where the cervical maturity was ≥ 8 points according to Bishop (75.8%), labor developed <6 h after the amniotic fluid leak. In the main group, where the cervical maturity was ≤ 7 points according to Bishop (58.5%), >6 h passed from the amniotic fluid leak to labor onset. Thus, women with an unprepared birth canal need nearly two times more time for the development of active labor. A mature cervix is one of the main factors in assessing the prospects for labor induction; labor developed spontaneously in all patients in the comparison group. In 22.8% of pregnant women in the main group, labor developed spontaneously on average within 6 h, despite the initially unpromising cervix. As a result, a fifth of pregnant women with an unpromising cervix, labor still develops within the next 6 h.

Correlation and regression analyses showed that the cervix score according to Bishop and then the weight of the fetus and gestational age have the most significant effect on the duration of the latent period from the moment of amniotic fluid leak to labor onset. The variability of this indicator by 27% is caused by the above factors.

In patients with insufficiently mature and immature cervix, who received 200 mg of mifepristone for cervical maturation (subgroup 2), the degree of cervical maturation was the most significant predictor influencing the duration of the latent period, and an inverse relationship was noted between the body weight and age of a female patient.

In patients who required repeated administration of mifepristone (subgroup 3), no significant effects of any of the predictors studied were identified. Apparently, in this case, some other factors must be taken into account.

Conclusions

The main predictors influencing the duration of the latent period in PROM and full-term pregnancy were the degree of cervical maturity according to Bishop and gestational age. When stratified by the sign of induction of labor by mifepristone for patients who received a course dose of 400 mg mifepristone, no relation with the degree of cervical maturity, age, constitutional aspects, and gestational age was established.

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