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TACTICS OF MANAGEMENT AND TREATMENT OF VIRAL HEPATITIS B IN PREGNANT WOMEN

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✓ ***Resume***

The etiological role of hepatitis B /HBV/, C/HCV/ and delta/HDV/ viruses has been proven in the development of chronic viral hepatitis. Chronic viral hepatitis, as is known, is characterized by the latency of the course, the predominance of inactive and inactive forms; only a part (up to 1/4) of those infected on average for 20-30 years have the development of cirrhosis of the liver and there is a risk of developing hepatocellular carcinoma. At the same time, combined infection with two (HBV and HDV, HBV and HCV) or three hepatitis viruses accelerates the rate of disease progression. The effect of pregnancy on the course of chronic viral hepatitis has been studied in a number of studies, including a study conducted in our clinic. It has been shown that in most patients pregnancy does not affect the course of the disease and does not pose a risk to the mother.

The course of chronic viral hepatitis in pregnant women is characterized, as a rule, by low activity and the rarity of exacerbations, which are manifested by an increase in laboratory signs of cytolysis and are observed more often in the first half of pregnancy or after its resolution.

This article extensively covers the issues of management, treatment and prevention of viral hepatitis B in pregnant women.

Keywords: hepatitis B, pregnancy, virus, cirrhosis of the liver.

ТАКТИКА ВЕДЕНИЯ И ЛЕЧЕНИЯ ВИРУСНОГО ГЕПАТИТА В У БЕРЕМЕННЫХ ЖЕНЩИН

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✓ ***Резюме***

В развитии хронического вирусного гепатита доказана этиологическая роль вирусов гепатита В /HBV/, С /HCV/ и дельта /HDV/.

Хронический вирусный гепатит, как известно, характеризуется латентностью течения, преобладанием неактивных и малоактивных форм; лишь у части (до 1/4) инфицированных в среднем в течение 20-30 лет наблюдается развитие цирроза печени и имеется риск развития гепатоцеллюлярной карциномы.

При этом сочетанная инфекция двумя (HBV и HDV, HBV и HCV) или тремя вирусами гепатита ускоряет темпы прогрессирования заболевания.

Влияние беременности на течение хронического вирусного гепатита изучалчось в ряде исследований, в том числе в исследовании, проведенном в нашей клинике. Показано, что у большинства больных беременность не оказывает влияния на течение заболевания и не представляет риска для матери.

Течение хронического вирусного гепатита у беременных характеризуется, как правило, низкой активностью и редкостью обострений, которые проявляются нарастанием лабораторных признаков цитолиза и наблюдаются чаще в первой половине беременности или после ее разрешения.

В данной статье широко освещаются вопросы ведения, лечения и профилактики вирусного гепатита В у беременных женщин.

Ключевая слова: гепатит В, беременность, вирус, цирроз печени.

ҲОМИЛАДОР АЁЛЛАРДА ВИРУСЛИ ГЕПАТИТ В НИ БОШҚАРИШ ВА ДАВОЛАШ ТАКТИКАСИ

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✓ ***Резюме***

Сурункали вирусли гепатитнинг ривожланишида гепатит В /HBV/, С /HCV/ и дельта /HDV/ вирусларининг этиологик роли исботланган.

Сурункали вирусли гепатит, маълумки, курснинг кечикиши, ҳаракациз ва ҳаракатсиз шаклларнинг устунлиги билан тавсифланади; ўртача 1-4 йил давомида юқтирганларнинг фақат бир қисми (20-30 қисмигача) жигар циррози ривожланади ва гепатоцеллуляр карсинома ривожланиш хавфи мавжуд.

Шу билан бирга, иккита (HBV и HDV, HBV и HSV) ёки учта гепатит вируси билан бирлаштирилган инфекция касалликнинг ривожланиш тезлигини тезлаштиради.

Ҳомиладорликнинг сурункали вирусли гепатитнинг кечишига таъсири бир қатор тадқиқотларда, жумладан, клиникамизда ўтказилган тадқиқотда ўрганилган. Кўпгина беморларда ҳомиладорлик касалликнинг ривожланишига таъсир қилмайди ва онага хавф тугдирмайди.

Ҳомиладор аёлларда сурункали вирусли гепатитнинг кечиши, қоида тариқасида, ситолизнинг лаборатория белгиларининг кўпайиши билан намоён бўладиган ва ҳомиладорликнинг биринчи ярмида ёки уни ҳал қилгандан кейин тез-тез кузатиладиган паст фаоллик ва қўзғалишларнинг камлигининг камлиги билан тавсифланади.

Ушбу мақолада ҳомиладор аёлларда вирусли гепатит В ни олиб бориш, даволаш ва олдини олиш масалалари кенг ёритиб берилган.

Калит сўзлар: гепатит Б, ҳомиладорлик, вирус, жигар циррози.

Relevance

Chronic viral hepatitis (CVH) B and C are socially significant infections that have become widespread at the present time. More than 350 million people worldwide have CVH B, and more than 1 million people die every year from chronic liver diseases, including cirrhosis of the liver (LC) and hepatocellular carcinoma (HCC), caused by viral hepatitis B (HBV). In endemic areas where carrier rates are >5%, most individuals become infected perinatally, through vertical transmission, or in early childhood [1]. Hepatitis C virus (HCV) infection is the most significant public health problem worldwide. It is estimated that more than 200 million people worldwide are currently infected with HCV, most of them have a chronic infection [2].

Individuals infected with HCV serve as a reservoir for transmission to others and are at risk for developing chronic liver disease, cirrhosis, and HCC. It has been established that HCV is determined at 27% of CP and 25% of HCC worldwide. The rise in morbidity and mortality due to HCV that we are now seeing is the result of the unprecedented spread of this pathogen in the 20th century. Responsible for this increase is the prevalence of two factors: invasive therapy and injecting drug use [3]. Although the most likely route of transmission is direct percutaneous exposure to HCV, several studies demonstrate that sexual, familial, occupational, and vertical transmission may also play a role [4].

The clinical picture of CVH B during pregnancy is characterized by a few symptoms [10, 11, 12]. According to our data, during the examination of 80 women with CVH, CVH B was confirmed in 22 (27.5%) and CVH C in 58 (72.5%). Clinical manifestations in the form of hepatomegaly and extrahepatic signs (telangiectasia, spider veins), within the absence of complaints, were detected in 28% of women with CVH B and in 39% of women with CVH C, an increase in transaminase activity was observed only in 6.1% and 5.6% of women with CVH B and CVH C, respectively.

Ultrasound examination of women with CVH B and CVH C reveals moderate diffuse changes in the liver (55.4%), signs of chronic cholecystitis (41.9%), in isolated cases with CVH C, fatty hepatosis is detected. 70% of women had a history of various medical and parenteral interventions.

When studying the obstetric and gynecological history, it was found that the majority of women had repeatedly performed induced abortions: in 34% of women with CVH B and in 63% of women

with CVH C. Cases of spontaneous miscarriages at various stages of pregnancy occurred in 22% and 31% of pregnant women with CVH B and CVH C, respectively.

The course of this pregnancy was complicated by the threat of miscarriage in 36.8% of pregnant women with CVH B and in 49.1% of pregnant women with CVH C.

In the Doppler study of uteroplacental blood flow and fetal cardiotocography in the third trimester of pregnancy, placental insufficiency (PI) was diagnosed in 52.2% of women with CVH B and in 68.4% of women with CVH C.

Premature birth ended in 39.1% of women with CVH B and 24.6% with CVH C. When studying the characteristics of the course of labor, it was found that in 56.5% of cases with CVH B and in 43.8% with CVH C childbirth was complicated by premature rupture of the membranes. In 7.2% of the surveyed women with CVH B and 6.3% with CVH C, an anomaly of labor was diagnosed in the form of primary weakness.

When determining the virus genome using polymerase chain reaction in the third trimester of pregnancy, positive results were diagnosed in 28% of women infected with HBV, and in 60% of women infected with HCV [4]

Purpose of the study. To evaluate the effectiveness of the optimized complex prevention of pregnancy complications in chronic viral hepatitis B with the inclusion of the hepatoprotector of domestic production "Geptrong".

Materials and methods

The study involved 95 women whose pregnancy proceeded against the background of CHB. The control group consisted of 60 pregnant women without hepatitis B. The age gradation of pregnant women with HB varied from 18 to 40 years (Fig. 1), with a predominance of the frequency of detection of HB at the age of 25 to 29 years (40%; 44 pregnant women). The average age of pregnant women with hepatitis B was 28.5±0.3 years.

The diagnosis was established by infectious disease doctors and hepatologists based on the results of a clinical examination, data from laboratory and instrumental research methods.

Result and discussion

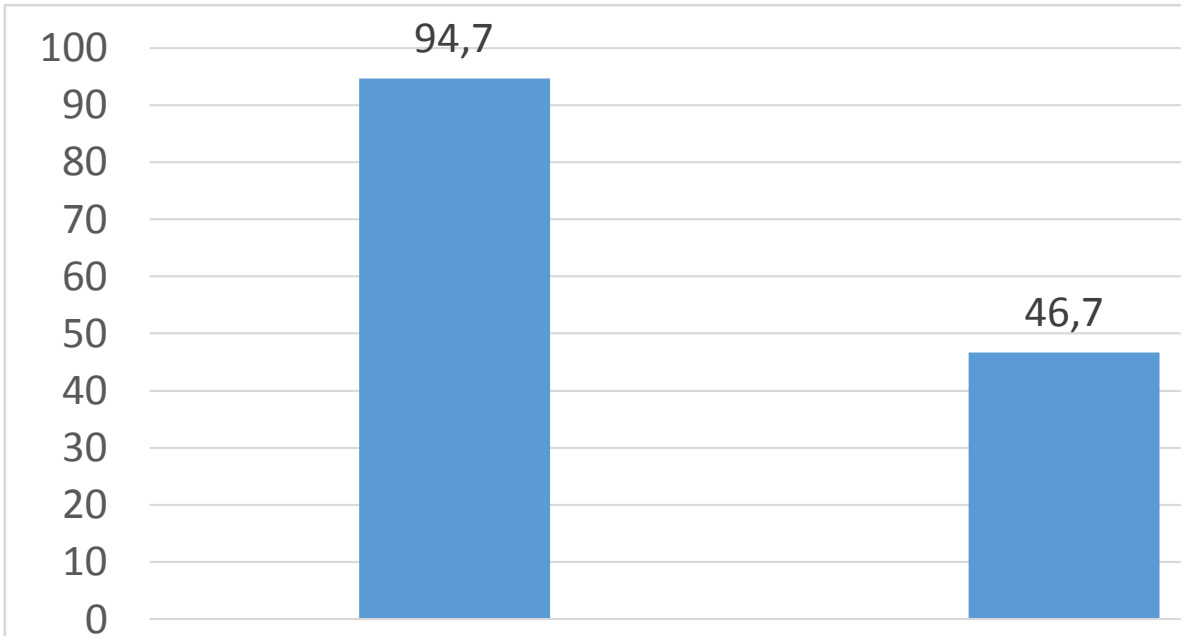
As is known, dysfunction of the hormonal status during pregnancy, impaired capillary permeability, which directly affect the decrease in the detoxification and protein function of women, in some cases cause the development of toxicosis in pregnant women. The presence of a history of CHB in pregnant women aggravates the severity of these disorders, which subsequently leads to the development of cholestatic hepatosis in pregnant women and preeclampsia.

When analyzing gestational complications, we drew attention to the relatively high incidence of early toxicosis - 2.2 times more in pregnant women with CVH than in healthy women (25.4% vs. 11.7% in the control group; $P<0.05$).

One of the key roles in the pathophysiological processes in CHB in pregnant women is the presence of hypoxia. So according to Antonova T.V. “... that in chronic hepatitis B, at the peak of metabolic disorders, a combination of signs of hypoxic, hemic, circulatory and histotoxic (tissue) hypoxia is revealed, which, in turn, leads to anemia” [1]. According to various authors, the progression of HB contributes to the development of an imbalance in red blood parameters [3, 4].

When analyzing the data obtained, we found that anemia in pregnant women with CHB was observed in 64.7% of cases (90 patients out of 95 women), while among pregnant women with a normal pregnancy, anemia was 2 times less common, amounting to 46.7% (28 out of 60 pregnant women) (Fig. 2).

The presence of anemia in pregnant women with CHB indicates the presence of violations of compensatory mechanisms in the cells of the red germ, in the future, these mechanisms trigger pathological changes in the liver. In this connection, anemia can be one of the main risk factors that lead to the development of liver dysfunction, and can also be a marker of the development of the bottom pathological process.



Picture. 2. The incidence of anemia in pregnant women with CHB in a comparative aspect (%)

Laboratory examination of pregnant women with chronic hepatitis B revealed moderate hyperbilirubinemia, unexpressed hypertransferasemia, dysproteinemia due to a decrease in albumin (Table 1).

In the study of the protein-forming function of the liver, a decrease in the average indicators of total protein by 1.4 times was noted in relation to the indicators of the control group (P<0.05).

The ALT and AST levels in the main group significantly exceeded those in the control group by 2.1 and 2.0 times (P<0.05), respectively.

ALP is tightly bound to the membrane of hepatocytes, and its high values in blood serum are the result of impaired function of hepatocytes, the phenomenon of hepatotoxicity, damage to the liver parenchyma. The average values of ALP in the main group increased by 1.6 times in relation to the data in the control group (P<0.05).

The average level of bilirubin in the blood of pregnant women in the main group was 16.34±0.5 μmol/l and was 1.6 times higher than similar indicators in the control group (P<0.05).

Table 1.

Biochemical indicators of liver function among pregnant women with CHB

Indicators	Control group (n=60)	Main group (n=95)	Reliability of data between groups
Total protein, g/l	70,5±2,8	50,12±1,1	P<0,05
Albumin, g/l	53,5±1,6	44,18±0,9	P<0,05
Bilirubin total, μmol/l	10,1±4,2	16,34±0,5	P<0,05
ALT, U/ml	23,9±7,52	50,58±1,9	P<0,01
AST, U/ml	20,4±8,3	40,17±1,8	P<0,05
ALP, U/l	186,2±17,6	288,93±2,8	P<0,05
GGTP, mmol/l	28,9±4,6	48,05±2,3	P<0,05
LDH, U/L	308,1±22,6	497,31±6,2	P<0,05
Glucose, mmol/l	3,8±1,06	4,55±0,07	-
Creatinine, μmol/l	76,5±19,8	80,41±0,6	-
Urea, mmol/l	4,15±0,8	5,79±0,8	P<0,05

Albumin indices in the main group of pregnant women decreased by 1.2 times compared to the control group (44.18±0.9 versus 53.5±1.6 g/l; P<0.05).

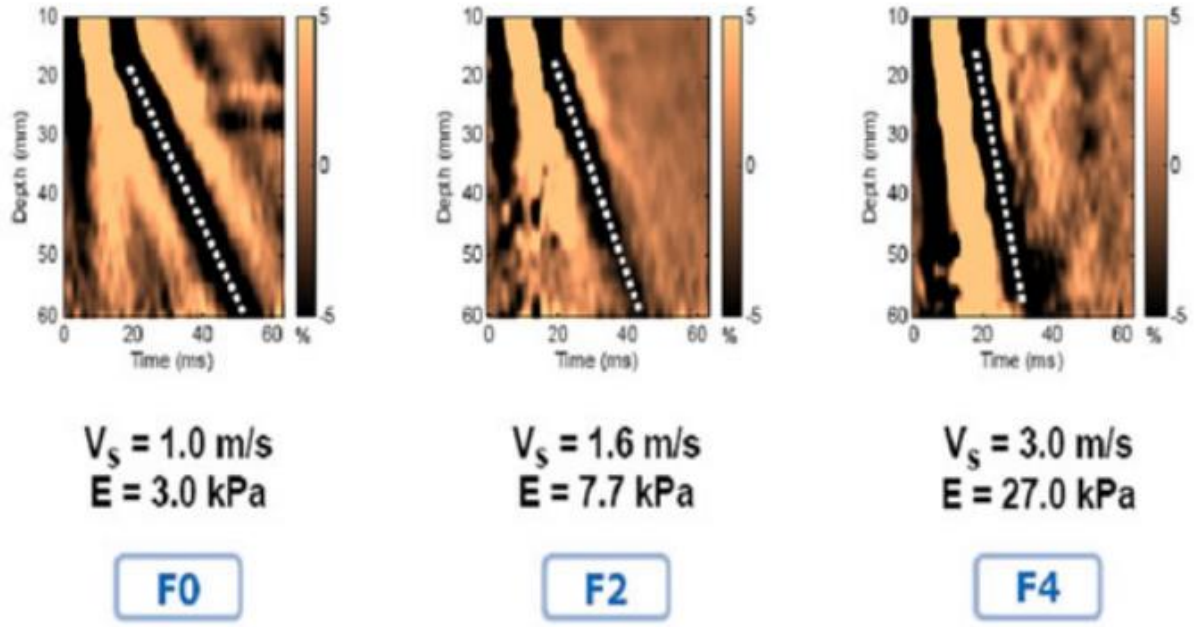
In the main group, GGTP and LDH also exceeded the control values by 1.7 and 1.6 times (P<0.05).

An increase in the activity of ALT, AST, LDH enzymes confirms the syndrome of cytolysis and hepatocellular insufficiency in pregnant women with CHB.

Thus, the analysis of the clinical and laboratory features of the course of CHB in pregnant women indicates a mild deviation from the norm of liver function tests.

The study of liver density by ultrasound (ultrasound elastography) was carried out in 30 pregnant women with CHB in the main group and in 20 pregnant women with normal pregnancy showed. The results of liver fibroscanning - according to the results of elastometry, the following conditions are diagnosed: F0 - healthy liver; F1 - F3 degree of fibrosis; F4 - cirrhosis of the liver (Fig. 3).

When analyzing the data obtained, we managed to establish (Fig. 4) that the F0 stage was noted in 16.7% of pregnant women (5 out of 30), F1 stage in 53.3% (16 out of 30), while F2, F3 degrees of fibrosis were recorded in 20% (6 of 30) and 6.7% (2 of 30), F4 - cirrhosis of the liver was noted in 3.3% of pregnant women with CHB (1 of 30).



Picture. 3. Degree of liver fibrosis

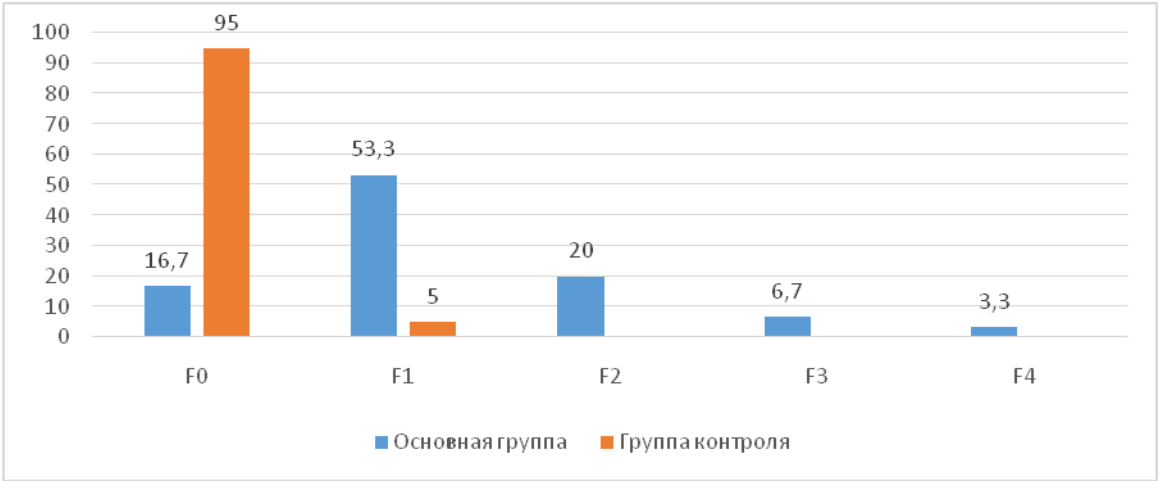


Figure 4. Distribution of examined women during pregnancy depending on the stage of liver fibrosis according to ultrasound data

The average liver density in the compared groups was 10.1±4.9 kPA (variation range from 4.2 to 25.1 kPA) in the main group, which was 2 times higher compared to the control group - 5.0±0 .5 kPa (P<0.05).

Thus, in pregnant women with CHB, in most cases, not only functional disorders in the liver were established, but also morphostructural changes in its parenchyma.

At a further stage, we evaluated the effectiveness of hepatoprotective therapy among pregnant women with CHB. The choice fell on the domestic drug "Geptrong", a drug with a proven component as hepatoprotectors (in the instructions for drugs in the list of indications, fatty toxicosis and hepatitis of various origins are indicated), and also due to the small number of publications on their clinical effectiveness.

To assess the effectiveness of obstetric tactics in the main group developed during the study (n=55), a comparative analysis of the course of pregnancy was carried out with a comparison group of 40 pregnant women with CHB. The features of the course of pregnancy in the main group were also analyzed in comparison with physiological pregnancy in the control group (n = 60).

When assessing the level of enzymes ALT, AST, alkaline phosphatase, GGTP, LDH in the dynamics of monitoring pregnant CHB, we found that these indicators reached the upper limits of the norm in the main group, while in the comparison group these indicators were not significant in relation to the initial data (Table 2)

Table 2

Dynamics of biochemical indicators of liver function among pregnant women with CHB

Indicators	Control group (n=60)	Main group (n=95)		Comparison group (n=40)	
		Outcome	After treatment	Outcome	After treatment
Total protein, g/l	70,5±2,8	49,5±1,2	68,2±2,1*	50,1±1,1	51,6±1,5^
Albumin, g/l	53,5±1,6	43,8±0,9	54,1±1,7	44,2±0,9	46,5±0,8
Bilirubin total, μmol/l	10,1±4,2	16,5±0,4	11,3±0,5	16,3±0,5	15,6±0,6
ALT, U/ml	23,9±7,52	50,7±1,8	29,2±2,3	50,6±1,9	42,3±1,8
AST, U/ml	20,4±8,3	39,8±1,4	22,5±3,2	40,2±1,8	35,6±1,7
ALP, U/l	186,2±17,6	286,5±2,2	191,3±7,6	288,9±2,8	165,3±3,2
GGTP, mmol/l	28,9±4,6	47,9±1,8	32,3±2,6	48,1±2,3	41,3±2,4
LDH, U/L	308,1±22,6	498,2±5,6	307,5±4,9	497,3±5,2	435,6±4,9

In the dynamics of observation, we found that the inclusion of the drug "Geptrong" improves liver function in the main group in 92.7% of pregnant women with CHB, as evidenced by biochemical parameters characterizing liver function. In the comparison group, improvements in liver function were recorded in 47.5%.

A differentiated approach to pregnancy management in the main group made it possible to reduce the incidence of gestational complications in relation to the comparison group. Thus, the frequency of threatened abortion decreased by 1.63 times by 29.1% (16 out of 55 pregnant women with CHB) in the main group versus 47.5% (19 out of 40 pregnant women with CHB) in the comparison group. PE was detected 1.2 times less often, and 2 times more often manifested in mild form - 85.5% (47 of 55 pregnant women) of mild forms in the main group versus 42.5% (17 of 40 pregnant women) in the comparison group. In the main group, 61.8% had independent urgent delivery, 21.8% of pregnant women were delivered by CS. In the main group, timely operative delivery was performed 1.6 times more often (p=0.0018) in a planned manner (96.3%) than in the comparison group (60%).

Table 3

Pregnancy outcomes in observed pregnant women with CHB

Outcome of pregnancy	Main group n=55		Comparison group n=40		Control group n=60	
	n	%	n	%	n	%
Term delivery	34	61,8	21	52,5*	60	100
preterm birth	5	9,1	11	27,5*	0	0
C-section	12	21,8	8	20*	0	0
Spontaneous miscarriage	4	7,3	0	0	0	0

*Note: *p<0.05 compared to the main group*

In the comparison group, 27.5% of pregnant women were delivered prematurely, which is 3 times more often (p = 0.0098) than in the main group (9.1%), of which 75% - the main indication for early delivery was the progression of placental insufficiency (FI), which was not observed in the main group (p=0.0014) (Table 3).

The frequency of PE acted as one of the causes of premature operative delivery in the comparison group was 16.4%, which is 4.6 times more often than in the main group (3.6%).

Conclusion

In all observations, both in the main and in the comparison group, live newborns were born. Height-weight indicators and assessment of the condition of newborns in the main group were significantly higher than in the comparison group (p>0.05).

In the comparison group, 17.5% of newborns had a body weight at birth less than 2500 g with individual fluctuations from 820 to 2430 g and prematurity by weight from I to IV degree, which is 3.2 times more often than in the main group (5.5 %). All premature newborns in the comparison group were diagnosed with respiratory distress syndrome (SDR) and ischemic-hypoxic CNS damage, which required transfer to mechanical ventilation and further treatment in the intensive care unit. In newborns of the main group, it was 2 times less likely to require mechanical ventilation and resuscitation.

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