DELIVERY IN WOMEN WITH ACTIVE REPLICATION OF CAUSATIVE AGENTS OF VIRAL HEPATITIS DURING GESTATION AND CORRECTION OF COMPLICATIONS USING PROTEFLAZID

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Introduction. Despite medical advances and constant introduction of new medical technologies to control infectious diseases, viral hepatitis (HV) with the parenteral route of transmission is a significant cause of increased morbidity and mortality [6, 9].

Acute viral hepatitis B (AHVB) is a real threat to the life of the woman, fetus and newborn. The state deterioration in the second half of pregnancy may be complicated by acute liver failure with encephalopathy and coma with a high mortality rate (mortality rate except pregnancy is 0.4-2%, in pregnant women it is 3-fold higher) [2, 5].

HVC is the most common liver disease in the world, the carriers of the pathogen are 150 to 500 million people on the Earth [4]. Chronic HVC (CHVC) took the first place in the incidence and severity of complications in the last 5 years. In the course of pregnancy, HVC, as well as HAV, has no special effects on the gestational process [5, 10]. This is what we cannot accept along with many other scientists. [8] For example, German researchers proved that in positive anti-HVC women the incidence of preterm birth is 29% [7]. The constant increase in the number of patients with HVB and HVC confirms the urgency and the need for a deeper study of the issue.

The **objective** of the presented study is to investigate the influence of proteflazid on the course of delivery in pregnant women with active replication of HV pathogens during gestation.

Study material and methods: analysis of 64 pregnancies and childbirth in women with active replication of HV pathogens during pregnancy and giving birth was carried out on the basis of the maternity hospital No.4 in Kyiv and 100 pregnancies in women who gave birth in the physiological department of the hospital of Uzhhorod. In each case designed study card was filled in. The reference documentation for a set of material were individual cards of pregnant women and birth stories.

During the study the incidence of premature births in the maternity hospital No.4 ranged from 4.9% to 6.2%, while it was 1.9% - 2.9% in physiological office in Uzhhorod. Number of births by abdominal delivery was greater in women from a physiological department - 12% -18%, while 8.4% - 11.5% in observational department. Lower rate of perinatal mortality was registered at childbirth in Uzhhorod - about 7,4-9%, with 10.6-14,6% in observational hospital of Kyiv.

To eliminate disorders caused by HV we used domestic product proteflazid as the one that has no teratogenic effects and is available in terms of price for the country's population. Proteflazid is a rare alcoholic extract of wild grass Deschampsia caespitosa L. and Calamagrostis epigeios L. In its formula it contains flavonoids with biologically active molecules and radicals, which cannot be synthesized in humans, as well as amino acids, chlorophyll, minerals. Proteflazid antiviral action is based on active induction of endogenous alpha- and gamma-interferon, as well as direct blocking of virus-specific thymidine kinase, DNA polymerase. At the same time, the drug has significant bioregulatory properties at the level of pathogenetic mechanisms of hepatitis B by stimulating macrophage apoptosis and non-specific modulation of antioxidant activity with the restoration of metabolic cycles, positive neurotropic action. The positive impact of proteflazid on the course of HV has been proven in studies conducted at the Gromashevsky Research Institute of Epidemiology and Infectious Diseases of the Academy of Medical Sciences of Ukraine [3].

The women were divided into 3 groups:

I - control (CG) - comprised the subjects from physiological department;

II - comparison (CompG) - comprised 38 women with active replication of HV pathogens during gestation;

III - experimental (EG) - comprised 26 women with active HV replication during gestation, whose treatment was supplemented with Proteflazid.

CompG comprised 38 women affected by HVC, 20 of whom experienced persistent chronic hepatitis C in phase of biochemical activity and in 18 pregnant women active replication of HVC virus was detected for the first time. Up to 10 weeks of pregnancy 1 case was registered of newly diagnosed active HVC replication from 11 to 20 - 3; from 21 to 30 - 11 and 3 cases in gestational age from 31 to 40 weeks, 3 of them at the point of delivery. In 10 pregnant women mild cases of hepatitis C were diagnosed and in 8 women moderately severe cases.

EG included 20 women with chronic persistent HVC at the stage of biochemical activity, as well as the six women with newly detected virus replication - 3 HVB and 3 HVC cases, moderately severe hepatitis was diagnosed in all six cases.

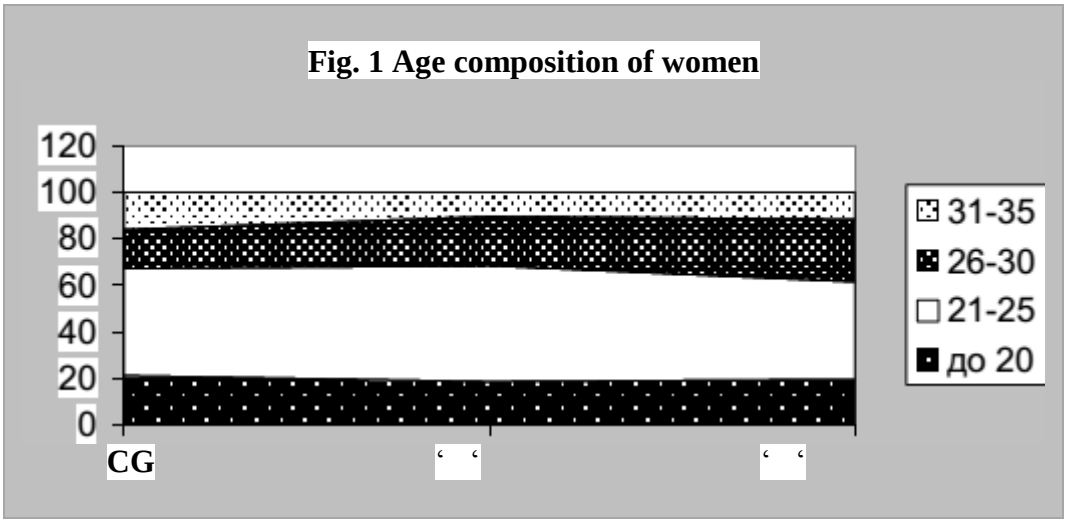
These groups were homogeneous in age, social status, to some extent, in occupation (housewives, or those whose work is not related to physical activity and exposure to teratogenic substances), they reside within the same time zone and in a temperate continental climate.

The HV diagnosis was made based on anamnesis, epidemiological, clinical and laboratory data. Comprehensive laboratory tests included biochemical tests, identification of HV markers by enzyme-linked immunosorbent assay (performed on programmable thermostats, shakers T-CY and ST-3L using test systems produced by "Vector-Best", Novosibirsk) and polymerase chain reaction (thermocycler "Terziy" TP-4PCR-01 was applied). The HV diagnosis was verified by infectious diseases specialist.

Statistical analysis of the results of the clinical study carried out with the help of STATISTICA 5.0 and Excel 5.0 software packages. To assess the reliability of the results used t-criteria Student in modification by Amosov N.M. et al. [1]. The critical level of significance was assumed to be 5%.

Results and their discussion. The study included the most active category of fertile women. Therefore, the age category 15-49 by WHO was modified and divided into intervals, and we have not examined women younger than 17 and older than 35 years. The age composition of women is shown in Figure 1 (data are in %):

Fig. 1 Age composition of women



In all subgroups significance level $p<0.05$ was reached as indicated by digital data: to 20 years - 21% in CompG with 18.4% in CG (t=0.34) and 19.2% in EG (t=0.2); from 21 to 25 years - 46% in the CG at 50% in CompG (t=0.42) and 42.3% in EG (t=0.34); 26-30 years - 17% in the CG with 21.1% CompG (t=0.53) and 26.9% in EG (t=1.01); 31-35 years - 16% in CG with 10.5% in CompG (t=1.04) and 11.6% in EG (t=0.62).

In CG the ratio of women giving birth for the first time to the multipara women was 65% to 35% at 68.4% to 31.6% in CompG and 84.6% to 15.4% in EG. Delivery analysis in the study groups is presented in tabular form:

Table 1

The labor in women of the studied groups

Complication	CG		CompG		EG	
	n	%	n	%	n	%
Metrypercinesia	2	2	8	21.1	3	11.5
Premature birth	-	-	5	13.2	-	-
Primary uterine inertia	3	3	1	2.6	1	3.8
Secondary uterine inertia	1	1	-	-	-	-
Labor stimulation	4	4	1	2.6	1	3.8
Labor induction	14	14	2	5.3	-	-
Prenatal amniorrhea	18	18	8	21.1	5	19.2
Early rupture of membranes	19	19	12	31.6	13	50
Big fetus	6	6	2	5.3	1	3.8
Preeclampsia I-II st.	2	2	-	-	1	3.8
Cesarean section	9	9	3	7.9	2	7.7
Dense placentation	2	2	-	-	-	-
Manual removal of placenta	3	3	-	-	-	-
Manual inspection of the uterine cavity	5	5	-	-	-	-
Instrumental inspection of the uterine cavity	2	2	5	13.2	4	15.4
Defect of the placenta and membranes	4	4	4	10.5	4	15.4
Uterine hypotension	4	4	1	2.6	-	-

According to the study, Metrypercinesia occured in 2% in CG members while tenfold increase in the frequency occured in CompG (21.1%, $p<0.05$, $t=2.82$) and fivefold increase in the members of EG (11.5%; $p<0.05$, $t=4.3$). When comparing the incidence of this complication in CompG and EG a strong tendency was determined to decrease of their number in women who applied proteflazid in the course of pregnancy ($p>0.05$, $t=1.04$). Premature births were only in members of CompG (13.2%).

The frequency of the primary weakness of labor force is reported at the same level in all groups - 3% in CG; 2.6% in CompG ($p>0.05$, $t=0.12$) and 3.8% in EG ($p>0.05$, $t=0.2$). Secondary uterine inertia of labor force was reported in only one case, in a member from Uzhhorod. While frequency of birth complications with labor stimulation was also almost at the same level in all groups - 4% in the CG; 2.6% in CompG ($p>0.05$, $t=0.42$) and 3.8% in EG ($p>0.05$, $t=0.04$), then labor induction was used more often in CG -14% when 5.3% in EG ($p>0.05$, $t=1.74$) and in the absence in EG.

Prenatal amniorrhea was reported in 18% of CG at 21.1% in CompG ($p>0.05$, $t=0.42$) and 19.2% in EG ($p>0.05$, $t=0.42$). Early rupture of membranes was significantly more often reported in EG (50%, $p<0.05$, $t=0.42$) and more often in CompG ($p>0.05$, $t=1.48$), with 19% in the subjects from the physiological department.

Caesarean section accomplished 9% of births in CG, 7.9% in CompG ($p>0.05$, $t=0.21$) and 7.7% of births in women who took proteflazid ($p>0.05$, $t=0.22$). Dense placentation, followed by manual separation and removal was reported only in the subjects from the physiological department. Instrumental inspection of the uterine cavity completed 2% of births in CG, 13.2% in CompG ($p<0.05$, $t=1.97$) and 15.4% in EG ($p>0.05$, $t=1.87$). Defects in placental tissue or membranes accompanied 4% of births in CG, 10.5% in CompG ($p>0.05$, $t=1.12$) and 15.4 in EG ($p>0.05$, $t=1.55$). Neither in the cases of instrumental inspection of the uterine cavity ($p>0.05$, $t=0.23$), nor in the cases of defects of the placenta or membranes ($p>0.05$, $t=0.56$) there was no statistically significant difference between EG and CompG detected.

The average duration of arid periods was 3 h. 17 min. in CompG ($p>0.05$, $t=0.57$), for 5 h. 2 min. in EG ($p>0.05$, $t=1.52$) while it was 3 h. 45 min. in CG. When comparing the value of this indicator, a tendency to its increase was detected in women from EG ($p>0.05$, $t=1.89$). The

average blood loss during labor in the subjects from CG was 237.3 ml (mean square deviation (MSD) 132.92) with 306.5 ml (109.6 MSD) in CompG ($p<0.01$, $t=2.96$), and 286.5 ml. (MSD 108.7) in EG ($p>0.05$, $t=1.77$). When comparing the magnitude of blood loss between CompG and EG a trend is determined to increase the blood loss in the subjects from CompG ($p>0.05$, $t=0.92$).

It is clear that the comparison of the frequency of obstetric complications, especially when the number of observations is not equal, is somewhat subjective. The positive dynamics of the level of bilirubin, ALT and AST, as well as other biochemical markers of liver function when taking proteflazid is well known and proven in the studies of specialists from the Gromashevsky Research Institute of Epidemiology and Infectious Diseases of the Academy of Medical Sciences of Ukraine, no numeric data on these indicators are given in the article. Perhaps the study of the biochemical composition of the amniotic fluid could be a marker for successful application of proteflazid in terms of pregnancy, as it is the amniotic fluid that is the link that provides unity of morphological and functional units that the parent organisms and the fetus are formed into.

But even the assessment of the frequency of main perinatal complications enables a practitioner to use proteflazid in women with active replication of HV pathogens during pregnancy, as a means of reducing the number of premature and fast delivery, as well as the volume of blood loss during delivery.

Conclusions. Application of Proteflazid in pregnant women with active replication of HV pathogens leads to lower rates of preterm and fast delivery, as well as the reduction of blood loss volume during childbirth.

It is clear that the number of women studied is not enough and the study requires to be continued using both the testing of effective application of proteflazid and biochemical test of the composition of the amniotic fluid.

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