Postpartum period in women with replication of pathogens of viral hepatitis during gestation and correction of complications using

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The effect on Proteflazid during the postpartum period in women with HV pathogens replication during gestation was studied. The analysis was made of post-partum periods in 99 women with HV pathogens replication during pregnancy and 100 women with physiological course of gestation using clinical laboratory, instrumentation and statistical methods. Women with HV pathogens replication taking Proteflazid during pregnancy, decrease of hyperthermia frequency was detected (31.4 with 35.9% in CompG) and of the total number of anemia of varying severity (28.6 with 36.0% in CompG). In the same postpartum women in the postpartum period in 51.4% of cases was uneventful with 32.8% in CompG. Use of Proteflazid in pregnant women with replication of pathogens of viral hepatitis leads to a decrease in the frequency of complications in the postpartum period.
Keywords: *post-partum period, viral hepatitis, complications*.

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 post-partum period in women with active replication of HV pathogens during gestation.

MATERIALS AND METHODS

Analysis of 99 post-partum periods 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 was individual cards of pregnant women and birth stories.

During the study the frequency of premature births in the maternity hospital No.4 ranged from 4.9 to 6.2%, with 1.9-2.9% in physiological department in Uzhhorod. Number of abdominal deliveries was higher in women from a physiological department - 12-18% with 8.4-11.5% in observational department. Perinatal mortality rate registered at childbirth in Uzhhorod was lower - about 7.4-9% with about 10.6-14.6% in observational Kyiv maternity hospital.

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]. Before prescription of Proteflazid pregnant women were selectively tested at a laboratory for susceptibility to the drug *in vitro* by means of the dynamics of thiol-disulfide ratio in the blood (clinic of individual medicine "Medica Nova", Kyiv).

The women were divided into 3 groups:

- I - control (CG) - comprised the subjects from physiological department;
- II - comparison (CompG) - comprised 64 maternity patients with chronic hepatitis C (CHVC);
- III - experimental (EG) - comprised 35 women with active HV replication during gestation, whose treatment was supplemented with Proteflazid.

EG included 28 women with chronic persistent HVC at the stage of biochemical activity, as well as 6 women with newly detected virus replication - 4 HVB and 3 HVC cases, moderately severe hepatitis was diagnosed in all 7 cases.

CompG was also formed of the subjects with chronic hepatitis C, since maternity patients with this very pathological state comprised the bigger part of EG (80%). In all 64 cases, CHVC had the nature of persistent infection with low-replicative pathogen activity. In 6 women the diagnosis with chronic hepatitis C was made 1 year prior to the pregnancy, in 8 postpartum women this period was 1-2 years, in 12 - from 3 to 5 years, in 2 - from 6 to 10 years, 2 women suffered from this nosology more than 10 years. In 34 subjects from Kyiv the starting time of the disease in general has not been found out.

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 %):

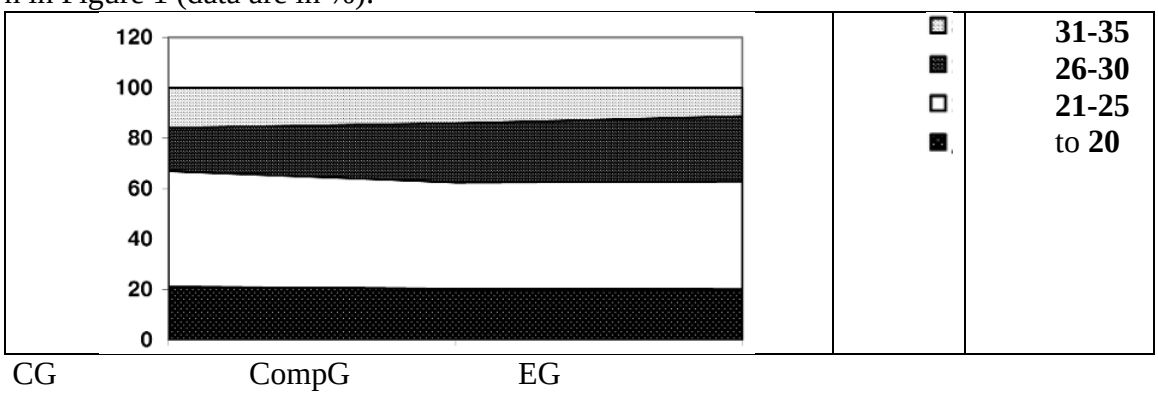

Fig.1 Age composition of the women

In all subgroups significance level p<0.05 was reached, as indicated by numeric data: to 20 years - 21±4.1% in CG with 20.3±5.0 in CompG (t=0.11) and 20±6.8 in EG (t=0.13); from 21 to 25 years - 46±5.0 in CG with 42.2±6.2 in CompG (t=0.48) and 42.9±8.4 in EG (t=0.32); 26-30 years - 17±3.8 in CG with 23.4±5.3 in CompG (t=0.99) and 25.7±7.4 in EG (t=1.1); 31-35 years - 16±3.7 in CG at 14.1±4.3 in CompG (t=0.34) and 11.4±5.4% in EG (t=0.7). The correlation coefficient of the age parameters of CG and CompG was 0.95 with 0.91 between CG and CompG, and 0.99 between CompG and EG, that is, there is a high degree of linear relationship between the represented groups.

For a more complete display of the course of postpartum period and its connection with childbirth a decision was made to present here the data on the duration of time between rupture and delivery and volume of blood loss. In women of CG, 54% of births were accompanied by duration of time between rupture and delivery to 2 hours, with 32.8% in CompG (p<0.01, t=2.75) and 14.3% in EG (p<0.01, t=2.75). At the duration of this time from 2 to 5 hours the ratio of the indicators was 16% in CG to 26.6% in CompG (p>0.05, t=1.59) and 34.4% in EG (p<0.05, t=2.1) and 19% in CG to 32.8% in CompG (p<0.05, t=1.96) and 48.6% in EG (p<0.01, t=3.18) with an interval from 5 to 10 hours. 11% of births were accompanied by increase of the time between rupture and delivery of more than 10 hours in women in CG with 7.8% in CompG (p>0.05, t=0.7) and 2.9% in EG (p>0.05, t=1.93). The obvious is to increase the frequency of the duration of anhydrous interval from 2 to 5 hours, and from 5 to 10 hours in observational department representatives. The average duration of time between rupture and delivery was 3 h 45 min in CG with 4 h 39 min in CompG (p>0.05, t=1.4) and 4 h 55 min in EG (p>0.05, t=1.62).

81% of births in a physiological department were accompanied by loss of blood in volume to 250 ml with 46.9% of births in women with CHVC (p<0.001. t=4.63) and 57.2% for maternity patient who took Proteflazid during pregnancy (p<0.01, t=2.58). Blood loss from 251 to 500 ml was reported more frequently in subjects from Kyiv - 40.6% in CompG (p<0.001. t=5.1) and 37.1% in EG (p<0.001. t=3.52), with 7% in women from Zakarpattia. The rate of loss of blood in volume from 501 to 1000 ml is almost the same in CG and CompG - 12.0 and 12.5% (p>0.05, t=0.1) with 2.9% in EG (p>0.05, t=1.23). Average blood loss in CG was 237.3 ml (mean square deviation (MSD) - 127.8) with 301.25 ml (MSD - 208.37) in CompG (p<0.05, t=2.44) and 298 ml (MSD - 130.45) in EG (p<0.05, t=2.44).

The course of the post-partum period is presented in Table 1

Table 1

Characteristics of the post-partum period

Complication	CG		CompG		EG	
	n	%	n	%	n	%
Postpartum without complications	57	57	21	32.8	18	51.4
Hyperthermia 1 time	22	22	15	23.4	6	17.1
Hyperthermia 1-3 times	4	4	5	7.8	3	8.6
Hyperthermia is more than 3 times	3	3	3	4.7	2	5.7
Anemia I degree	6	6	18	28.1	7	20
Anemia II degree	3	3	4	6.3	2	5.7
Anemia III degree	-	-	1	1.6	1	2.9
Postpartum endometritis	1	1	1	1.6	-	-
Hemometra	1	1	-	-	-	-

Particular attention in the analysis of the course of postpartum period was paid to an increased risk of suppurative inflammation complications which is displayed in registration of cases of hyperthermia syndrome. If in the cases of occasional increase in body temperature, the least amount thereof were found in EG - 17.1% (p>0.05, t=0.64) with minor differences in CG (22.0%) and CompG (23.4%; p>0.05, t=0.21), then in the cases of hyperthermia from 1 to 3 times a tendency was determined to increase of frequency in women from the observational department - 4% in CG

with 7.8% in CompG ($p<0.05$, $t=0.98$) and 8.6% in EG ($p>0.05$, $t=0.89$). Increase in body temperature more than 3 times was also more often reported in the subjects from the capital of Ukraine - 3% in CG with 6.3% in CompG ($p>0.05$, $t=0.94$) and 5.7% in EG ($p>0.05$, $t=0.63$).

According to the study, there is no significant difference between groups in the incidence of anemia of II degree, 3% in CG with 6.3% in CompG ($p>0.05$, $t=0.94$) and 5.7% in EG ($p>0.05$, $t=0.63$) but the subjects from Kyiv suffered from anemia of I degree significantly more often - 6% in CG with 28.1% in CompG ($p<0.001$. $t=3.63$) and 20% in EG ($p<0.05$, $t=1.96$); when comparing CompG and EG tendency to decrease was reported in EG ($p>0.05$, $t=0.92$). Anemia of III degree was reported in one case in CompG and EG. Postpartum endometritis was a complication in 1 post-natal period in CG and CompG, but was not the case in women who took Proteflazid.

Length of stay in a hospital bed in CG was 4.65 days (MDS 1.97) with a statistically significant increase in CompG - 6.2 days (MDS 2.8) ($p<0.001$. $t=4.2$) and 6.7 days (MDS 2.18) in EG ($p<0.001$. $t=4.0$). In subjects from CG in 57% of cases post-partum period was uneventful, with 32.8% in women of CompG ($p<0.01$, $t=3.15$) and 51.4% in the subjects from EG ($p<0.05$, $t=0.63$). When comparing this indicator between the subjects from the observational department a strong tendency to increase the number of post-natal period without complications was detected in the subjects from EG ($p>0.05$, $t=1.81$).

It is clear that the comparison of the frequency of obstetric complications, especially with unequal number of observations, 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 of the Gromashevsky Research Institute of Epidemiology and Infectious Diseases of the Academy of Medical Sciences of Ukraine, so the article does not give the numerical data on these indicators. Perhaps the study of the biochemical composition of the amniotic fluid could be a sign of success or failure of 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 which is constituted by the mother's body and the fetus.

But even the basic assessment of the frequency of perinatal complications enables a practitioner to use Proteflazid in women with replication of HV pathogens during pregnancy as a means of reducing the number of complications in the postpartum period.

CONCLUSIONS

Application of Proteflazid in maternity patients with replication of HV pathogens reduces the frequency of complications in the postpartum period.

It is clear that the number of women subjects is not enough for a study, and this study requires to be continued using both a test for efficacy of Proteflazid application and biochemical test of composition of the amniotic fluid.

Postpartum period in women with replication of pathogens of viral hepatitis in the course of pregnancy and correction of complications using proteflazid

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The influence of proteflazid on the course of postpartum period in women with replication of pathogens of viral hepatitis during gestation was studied. Postpartum period in 99 women with replication of pathogens of viral hepatitis during gestation and 100 women who gave birth in physiological compartment was assessed, using clinical and laboratory, instrumental and statistical methods. In pregnant women with active replication of pathogens of viral hepatitis that took proteflazid, a decrease of the incidence of hypertermia was detected (31.4 with 35.9% in CompG) and of the total number of anemias of varying severity (28.6 with 36.0% in CompG). In the same maternity patients the postpartum period in 51.4% of cases proceeded without complications with 32.8% in CompG. Application of Proteflazid in pregnant women with replication of pathogens of viral hepatitis contributes to reduction of the incidence of complications in the postpartum period.

Keywords: *postpartum period, viral hepatitis, complications.*

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