Physiology and pathology of the liver in pregnant women

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“Vivamedica”

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During pregnancy it can be stated curatio some deflection mainly in the III trimester obusl copulating normal ee over due fetal waste products and mobilization of functionalreserves future mother liver. Among the relevant clinical and laboratory parameters palmar erythema her and spider veins on the skin, in the blood increased content triglycerides, cholesterol, phospholipids, bile acids, α_1- and α_2-globulins, a moderate increase in the activity of alkaline phosphatase, a decrease in the level of albumins, antithrombin andhaptoglobin. These changes can increase in parallel with the increase in the period of pregnancy. Cholesterolemia leads to an increase in the lithogenicity of bile. An increase in lipid fractions in the blood causes an increase in the fat content in the liver tissue.

Pregnancy can be accompanied by its associated liver disease (acute fatty liver s pregnant, cholestasis of pregnancy, preeclampsia syndrome, complications syndrome as hemorrhages in the liver and ee discontinuities) developed against the background ee disease (chronic hepatitis and cirrhosis of the liver, Wilson's disease, benign hyperbilirubinemia, etc.) or liver diseases can arise against pregnancy. out of communication with her (often acute hepatitis, mostly viral).

Acute fatty liver of pregnant women — Shihan syndrome

A rare idiopathic disease. It develops in the third semester of pregnancy. The disease is part of the mitochondrial group cytopathy. It occurs at a frequency of 1 per 13,000 births. The risk of development is higher in the primiparous, with multiple pregnancy and in cases when the male fetus [2, 3].

It is suggested that the disease is associated with genetic deficiency of 3-hydroxy-acyl-CoA dehydrogenase. It is involved in the oxidation of long-chain fatty acids. The disease develops in mothers-heterozygous carriers of the gene encoding this enzyme, if the fetus is homozygous for this feature [5].

Clinical manifestations x arakterizu th tsya weakness, nausea, vomiting, headache, pain in the right upper quadrant or epigastric.

After 1 — 2 weeks there are signs of liver failure — jaundice and hepatic encephalopathy. Further progress is possible with the development of fulminant hepaticinsufficiency, coagulopathy, renal insufficiency.

With direct examination, soreness in the liver region is revealed, jaundice, edema and the progression of signs of hepatic encephalopathy are possible.

Laboratory and instrumental tests reveal leukocytosis, features syndrome dissiminirovannogo intravascular coagulation (DIC), increased prothrombin and partialthromboplastin time, the content of I degradation products of fibrinogen, a decrease in the platelet count, increase ivaetsya blood levels of bilirubin, creatinine, uric acidaminotransferase activity and alkaline phosphatase. Determine th tsya hypoglycemia, hyponatremia.

With ultrasound and CT of the liver — signs of fatty degeneration. Although, they may be absent. Liver biopsy reveals the microvesicular obesity of the centrolobularhepatocytes.

In 20 — 40% of developing pre-eclampsia and eclampsia.

BSE should be differentiated from acute viral hepatitis. However, with it, the level of aminotransferases in the blood is higher and the DIC syndrome is not characteristic.

The means of choice is immediate delivery by caesarean section. Correction of platelet level, prothrombin and partially thromboplastin time is carried out: intravenously injected solution of glucose, freshly frozen plasma, platelet mass. If there is no effect, the question of liver transplantation [2, 3, 5].

The prognosis for the mother and fetus is unfavorable. Maternal mortality — 50% (with immediate delivery — 15%), infant mortality — 50% (with immediate delivery — 36%).In women who have recovered from BALF, the liver function after the delivery is rapidly improving and there are no signs of liver disease in the future. Subsequent pregnancies usually occur without complications. Rarely, there is a possible relapse of heart failure [3].

Cholestasis of pregnant women

The disease is associated with insufficient excretion of bile acids from the liver (intrahepatic cholestasis) due to the high content of female sex hormones (estrogens), possibly on the basis of a genetically determined defect in their metabolism. Nutripechenochn cause in th cholestasis and pregnant women may be a defect gene MDR 3, responsible for the transfer of phospholipids in the bile ducts [18]. Zabol e in and of oznikaet in at 0.1 — 2% of pregnant women, usually in the III trimester and less II trimesterin [11].

In the liver, focal cholestasis with biliary thrombi in dilated capillaries and deposition of bile pigment in neighboring hepatic cells in the absence of signs of inflammation and necrosis, the preservation of the structure of lobules and portal fields [14, 25].

Clinical manifestations characterized by pronounced skin itch, yellow skin and sclera, discolored feces, te me with urine. Possible nausea, vomiting, minor pain in the right upper quadrant. Erythema of the palms can be determined, on the skin are vascular asterisks, traces of scratching. The liver and spleen are not enlarged.

Laboratory studies reveal hyperbilirubinemia, mainly due to direct bilirubin, increased blood bile acid content, cholesterol, phospholipids, triglycerides, activity excretory liver enzymes (alkaline phosphatase, gamma glutamyl transferase, 5-nucleotidase) under normal neous values of transaminases (ALT, AST). S feasible reduction of prothrombin in the blood due to malabsorption of vitamin K on the basis of violation of resorption of fat, steatorrhea [6, 15].

Treatment. Preference should be given drugs ursodeoxycholic acid (rsofal Y k, Y rsohol et al.) At the rate of 10-15 mg / kg of body weight per day, which has a positive effect put e m oppression generating body and improving excretion t oxic bile acids [25]. For reduction of itchiness m gu m X olestiramin used, which binds bile acids in the gut and thus helps to reduce their accumulation in the body [9, 12], in the III trimester T eptral [12].

In connection with the violation of absorption of fat-soluble vitamins (A, D, E, K) shows their use mainly parenterally.

The prognosis for mothers is favorable. Most take e nnyh disease is benign and does not require ee interruptions [12, 23]. After giving birth for 1 to 2 weeks, there is a regression of symptoms. Although there may be delays syndrome fetus, abortions, premature births (30%), post-partum bleeding, placental insufficiency and even n erinatalnaya mortality (at 11-13%). In the postpartum period, the risk of cholelithiasis increases. In subsequent pregnancies intrahepatic cholestasis can recur.

Preeclampsia

The defeat of the liver with severe preeclampsia is associated with spasm of the arteries on the basis of their hypersensitivity to endogenous vasopressors and catecholamines. As a result of damage to the vascular endothelium, deposition of platelets and fibrin occurs with the development of ischemia, which can lead to necrosis and hemorrhages.

Along with arte ble hypertension, Kami of e and proteinuria characteristic for preeclampsia are marked symptoms associated with hepatic involvement in the process.Among them, soreness in the right upper quadrant, icterus of the skin and sclera (40%), hyperbilirubinemia, increased activity of serum transaminases, the appearance of bile pigments in the urine. Thus, the number of pregnant women preeclampsia may progress to HELLP-syndrome.

Accession of seizures indicates a transformation of preeclampsia into eclampsia.

HELLP-syndrome

It is an option for the severe course of pre-eclampsia. The term consists of the first letters of the designation of the main clinical manifestations: hemolysis, increased activity of hepatic enzymes in the blood, a decrease in the number of platelets in it. He proposed in 1982, J. Weinstein [1]. III develops in three Mestre (usually 35 weeks) of 0.2- 0.6% of pregnant women with severe eclampsia more commonly in women and white Chinese race, mainly in povtornorozhayuschih.

Suggest a mechanism in toimmunny endothelial damage from blood clots by increasing the platelet aggregation with the involvement of the collagen fibers, fibrin, complement system, followed by formation of microthrombi fibrinolysis. The destruction of platelets leads to a disruption of the thromboxane-prostacyclin system with the formation of multisystemic autoimmune dysfunction with DIC syndrome. Possible participation in the formation of thrombocytopenia, a decrease in the content ofthrombopoietin in the blood. The liver develops primarily per and portal and, to a lesser extent, focal parenchymal necrosis with the presence of microthrombi and the deposition of fibrin in sinusoids.

Clinical manifestations This turns into a headache, nausea, vomiting (possibly bed th), pain in the epigastric and right upper quadrant, icteric sclera and skin staining (rare),the presence of hemorrhage at the injection sites. There is an increase in the liver. With the progression of pathology, convulsions and coma are possible.

Laboratory research in yya vlyayut in kro vi expressed thrombocytopenia, features microangiopathic hemolytic anemia (toothed, wrinkled, small, irregularly shaped erythrocytes shistotsity, polihromoziya shadow cells as a result of the decay of erythrocytes with the loss of hemoglobin), hyperbilirubinemia, reduced content of I of fibrinogen, prothrombin, antithrombin, marked increase in the activity of transaminases, lactate dehydrogenase, in urine protein [7].

A positive D — dimer test, which testifies to active fibrin lysis due to an increase in thrombin production in response to tissue damage [5], deserves attention.

Computed tomography (CT) of the liver reveals sites of reduced density, ascites.

Differential diagnosis should be made with severe pre-eclampsia, acute fatty th Pechen yu pregnant women, thrombocytopenic purpura, obstetric sepsis, hemolytic-uremicsyndrome. When HELLP — syndrome, as opposed to acute fats th th liver of pregnant CT does not reveal signs of fatty liver infiltration.

The treatment provides for severe progressive course of HELLP-syndrome, the need for an emergency delivery, which can be performed vaginally with prepared cervical this, while untrained birth canal — put e m caesarean section.

Against the backdrop of moderate preeclampsia with the presence of HELLP — syndrome without complications is possible expectant management with prolongation of pregnancy up to a natural delivery [1].

Showing plasmapheresis replacement donor fresh frozen plasma, platelet transfusions (with a decrease of blood platelets less than 100×10^9/L), the introduction ofantithrombin glucocorticoid drugs.

Among the possible *complications* in HELLP-syndrome ICE — syndrome, placental abruption, acute renal failure, from e to the lungs, *subcapsular hematomas* due todraining liver necrosis and at the same time *liver ruptures* with the formation of hemoperitoneum [20].

Subcapsular hematomas are detected on CT and ultrasound examination in the form of focal changes. Liver ruptures manifest acute pain in the right hypochondrium, vomiting, collapse, anemia, the presence of local peritoneal symptoms.

At the same time among the possible benefits after cesarean section — drainage of the hematoma, stitching of the damaged area of the liver, application of local hemostaticmeans, ligation of the hepatic artery or e embolization during angiogr afii, removal of liver lobe.

Forecast. Maternal death during HELLP — syndrome is 1.5-5%, perinatal — 10-60% [2]. The manifestations of this syndrome can reach a maximum flow and 24-48 hours after delivery. With a favorable outcome, they quickly regress. The risk of relapse HELLP-syndrome in future pregnancies is low (4%).

Hereditary hepatitis

In carriers of hepatitis A virus (HAV), hepatitis C (HCV), hepatitis E (HEV) and hepatitis D (HDV) increased the risk of abortion, the likelihood of fetal infection is low (viruses do not penetrate the placenta). Nevertheless, the possibility of contracting the fetus of HCV is high enough in HIV — infected pregnant women and in pregnant women with a high HCV titer in the blood (> 2 million copies in 1 ml) [9, 12]. Breastfeeding does not infect children [24].

In viral hepatitis C, the risk of perinatal mortality is high, and in viral hepatitis E, due to its more severe course, mortality is high in pregnant women (up to 20%) and the risk of early childhood death [1]. Fortunately, viral hepatitis E is mainly found in hot countries.

In viral hepatitis B infection likely fetal sootvets m vuyuschimi viruses. Infection occurs in 15% in utero and in 90% during labor, if the mother of HBeAg

or HBV DNA -positive. D ore feeding of children born to such mothers are not contraindicated, since HBV is not outside the E tsya mother's milk. Nevertheless, infection is possible in the presence of nipple cracks in carriers of HBV and HCV. Pregnant with H in V infection is not rarely observed miscarriages, premature births, stillbirths I, complications during childbirth (delayed rupture of membranes and uterine inertia). A fter this, the possibility of the development of acute liver failure leading to high maternal mortality. The probability of process chronology increases. Premature babies born to mothers with acute viral hepatitis B die 2 times more likely than full-term.

Interruption of pregnancy in viral hepatitis leads to a weighting of their course. So the main thing in viral hepatitis carrying out activities aimed at abortion.

Babies born to HBSAg — positive mother shown for passive immunization against hepatitis B immunoglobulin B (hyper munnogo gammaglobulin m) at the rate of 0.06 ml / kg of weight. In parallel, vaccination against hepatitis B [4] at the rate of 10 μg HBSAg (0.5 ml) intramuscularly into the anterolateral lateral surface of the thigh on the first day after birth, and then twice with an interval of respectively 1 and 6 month warranty. Vaccination against HBV also protects against HDV infection. Recombinant vaccine against HBV is safe for pregnant women and can be used for the purpose of post-exposure prophylaxis, along with passive immunization immuno noglobulinom against hepatitisB within 14 days of exposure (HBsAg-positive blood transfusion, accidental needle stick after HBsAg positive patients, getting to HBsAg-positive material in the eyes or on broken skin, ingestion of HBsAg-positive material, sexual contact).

In children born with anti- HCV, the latter are defined up to 1.5 years. But, this does not mean that the child is infected with hepatitis C.

Specific antiviral treatment in pregnant women with active viral hepatitis B and C should be postponed for the postpartum period, as the antiviral agents shown in these diseases have a teratogenic effect or can be the cause of malformations.

Female carriers of HBSAg in treatment do not need.

Pregnant, contact with HAV carriers (infected within 2 weeks before the appearance of jaundice), it is necessary to maintain immune globulin intramuscular rate of 0.02 ml / kg within 14th day after contact [3].

Non-viral and chronic liver disease

With *chronic hepatitis, the* onset of pregnancy is mainly possible with low activity with the absence of amenorrhea. The presence of pregnancy, although rare, can make chronic chronic hepatitis worse. After the termination of pregnancy, an exacerbation of chronic hepatitis may occur.

Autoimmune hepatitis can have a negative effect on the course and outcome of pregnancy (late toxicosis, miscarriage, stillbirths, life-threatening complications during childbirth). The frequency of pregnancy loss is about 30%. Therefore, autoimmune hepatitis is a relative contraindication for pregnancy. However, at the request of a patient with autoimmune hepatitis, pregnancy can be preserved [7].

Using glucocorticoid drugs pregnant during auto m unnom hepatitis should be continued. Immunosuppressants are contraindicated.

Cirrhosis prevents the development of pregnancy due to the frequent presence of amenorrhea and anovulation. In rare cases, the development of pregnancy in patients with cirrhosis of the liver may contribute to the activation process and in the liver, uterine bleeding in the postpartum period due to a violation of clotting factors, bleeding holes ofesophageal varices, usually late in pregnancy. Spontaneous abortion in pregnant patients with cirrhosis is 15 — 20%, often in the I — trimester. They are less likely to occur with compensated liver cirrhosis [12]. Reduce the risk of bleeding from varicose dilated esophagus helps systematic use of small doses propranolol or carrying a patient with cirrhosis of the liver before deciding to become pregnant of the transu-gular intraphepatic port system bypass. Therefore, pregnant women with liver cirrhosis should be offered e e interruption in the early stages. It is allowed to bear pregnancy only with the woman's insistence in cases of absence of signs of decompensation and severe portal hypertension.

When *primary biliary cirrhosis of the liver* pregnancy and childbirth often proceed relatively smoothly. Although, itching is possible, worsening of the functional state of the liver, spontaneous abortions and stillbirths. Possible to use during pregnancy ursodeoxycholic acids [22].

When *alcoholic liver disease* women often suffer from infertility. In rare cases of pregnancy and continued use of alcohol, the risk of fetal development anomalies, physical and mental underdevelopment of children.

In case of illness *Wilson-Konovalov* (hepatocerebral dystrophy), pregnancy develops rarely due to a violation of ovulation and infertility. The onset of pregnancy can be facilitated by the use of D-penicylamine (DPA), linking excess free copper in the blood. During pregnancy, treatment with DPA is necessary continue. It follows that keep in mind that the content ceruloplasmin in the blood for and pregnancy can increase. Therefore, during the last 6 weeks of pregnancy about STI ADP dose may be reduced [2]. In most cases, the disease does not have a significant effect on the course of pregnancy and childbirth. B Variability in the background of Wilson-Konovalov's disease usually ends safely. Using DPA not presenting a great risk to the fetus [27th]. However, in some cases it is possible

miscarriage pregnancy (miscarriages, premature births). And alternative is the use of zinc sulfate, which is less toxic than DPA, which inhibits the absorption of copper in the intestine. Pregnancy is contraindicated in the neurological stage of Wilson-Konovalov's disease and in severe liver damage (active ny hepatitis, cirrhosis) and kidney.

When breastfeeding DPA is recommended to cancel.

Availability *hepatic block* (portal vein thrombosis) is the absolute indication for abortion.

Benign hyperbilirubinemia Do not pose a risk to pregnant women and are not a contraindication for pregnant women. e preservation, since the prognosis for the mother and the child is favorable.

With the syndrome Gilbert the use of small doses is acceptable phenobarbital, which facilitates the synthesis of enzymes that carry out conjugation of bilirubin.

Development *syndrome Budd Chiari* in 20% of cases associated with pregnancy. Maternal smarts In this case, the value reaches 70%.

Hemangiomas liver in the course of pregnancy can increase and in rare cases tear. This requires immediate surgical intervention.

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The deviations of the liver in normal pregnancy are described, as well as clinical picture, diagnostics and treatment of liver disease associated with pregnancy, which appeared on the background of pregnancy and preceding chronic liver disease.