Liver cirrhosis: clinical picture, pathogenesis, treatment and monitoring of patients

T. N. Hristich, D. A. Gontsaryuk

Bukovinian State Medical University, Chernovtsy, Ukraine

Key words: liver cirrhosis, pathogenesis, clinic, hepatic encephalopathy, treatment

In economically developed countries, cirrhosis of the liver is one of the six leading causes of death in patients 35 to 60 years, accounting for 14-30 per 100,000 of population. It is believed that cirrhosis is the ultimate stage of chronic liver disease. By definition of the International Society for the Study of Liver Diseases, cirrhosis is characterized by diffuse fibrosis process and a violation of architectonic hepatic lobule, vascular network forming structurally abnormal nodes. Thus, it is considered as a disease of collaptoid character, not only due to fibrosis of the liver, but to the vascular obstruction. It should be emphasized that this cirrhosis is able to regress, especially in the early stages, when there is no adjustment of cytoarchitectonics in portal tract and extensive vascular thrombosis. This approach is important for clinicians, since the main task then becomes to control the activity of the disease and ensure venous outflow, which determines the lower tissue pressure.

Regression of fibrosis is confirmed by clinical and histological data. In favor of the cirrhosis, venous obstruction, arterialization and nodular hyperplasia may indicate. In cirrhosis of the liver, the structure of the nodes slices changes, slices are surrounded by fibrous tissue. These nodes are called regeneration ones, however, full recovery of the liver tissue does not occur. The nodes in the liver without fibrosis (Felty's syndrome), congenital diffuse liver fibrosis do not relate to cirrhosis because in these diseases lobular structure is not broken [1, 3, 6].

The main causes of the disease are divided into common, rare and very rare. To the common reasons chronic viral hepatitis B, C, D (about 25%), alcoholic liver disease (about 20%), cryptogenic — cirrhosis of unknown etiology (about 20-40%) are attributed. Rarely fixed leading causes are: autoimmune hepatitis, primary biliary

cirrhosis, the use of drugs and hepatotoxic substances (about 5%). In turn, hemochromatosis, Wilson's disease, deficiency of alpha-1-antitrypsin deficiency, secondary biliary cirrhosis (extra- and intrahepatic biliary tract obstruction), Budd-Chiari syndrome, severe right ventricular failure refer to a group of very rare causes of cirrhosis. The most common causes are considered to be hepatitis C and alcoholism, for which often develop portal hypertension and liver failure. Therefore, from the viewpoint of etiology, clinical manifestations, as well as the histological characteristics of changes in the structure of liver, disease is regarded as a heterogeneous condition [3].

In a study of patients can be palpated the left lobe of the liver (solid and knotted) and a reduced right, indicating cirrhosis. Splenomegaly is also a sign of portal hypertension. It can be installed by palpation and confirmed by ultrasound/CT (a combination of the presence of a nodular surface, collaterals) with radionuclide liver-spleen scan revealed a preferential accumulation of the radioisotope in the spleen. Even a slight decrease in platelet count (less than 175 x 10^9/l) is considered as an important diagnostic feature. Furthermore, the level of albumin at least 38 g/l or international normalized ratio of less than 1.3, the specific features which are small, may indicate the presence of cirrhosis.

There are compensated and decompensated cirrhosis. It is believed that the stoppage lasts for many years (9-12) until the decompensation and should be considered as a state, regardless of cirrhosis, with a different treatment, prognosis, and causes of death. Patients don't have jaundice, and ascites has not yet developed, as well as encephalopathy, and bleeding from esophageal varices. The objectives of medical supervision in such cases are to treat the underlying disease and to prevent and early diagnose the complications. At this stage of cirrhosis primary prevention of bleeding from esophageal varices, stomach is important, because their presence and frequency of bleeding correlated with the severity of the disease. Endoscopy of the esophagus is necessary to determine the degree of varicose veins: if you press the endoscope, and the size of the veins decreases, one can think of the first degree, in the absence of reducing the size of the veins you should be thinking about the second

degree, and when the veins merge to surround the esophagus, the third degree of esophageal varices can be verified. The first bleeding is always a surprise for the patient and the doctor is required the decision on the forecast, which is dominated by the risk factors. These include the large size of varices, dark cherry color of nodular walls, class B/C cirrhosis by Child-Pugh, alcohol abuse, history of thrombosis of the portal vein. Bleeding from varices refers to urgent conditions, and patients require an intensive care [6].

Decompensated cirrhosis is characterized by the development of jaundice, bleeding from varicose veins of the esophagus and stomach, ascites or encephalopathy. Jaundice occurs due to liver failure. As preventive measures thus acts elimination or treatment of concomitant risk factors (for example, alcoholic hepatitis, sepsis, receiving hepatotoxic drugs). The causes of other complications are often a portal hypertension and hyperdynamic circulation, which requires the appointment of symptomatic therapy [1]. So, esophageal varices is a consequence of portal hypertension, and hyperdynamic circulation increases varices and bleeding. Upon increase in blood volume diuretics are prescribed (spironolactone, furosemd, torasemide). By increasing cardiac output nonselective beta-blockers are administered (propranolol), in the case of visceral arterial vasodilation it is expedient to administer vasoconstrictors (vasopressin, somatostatin, octreotide), and upon constriction of the portal collateral veins nitrates, molsidomine and calcium channel blockers are assigned. Prokinetics, increasing the tone of the lower esophageal sphincter, are used for increasing blood flow through the veins of varicose esophagus.

Ascites is caused by sinusoidal hypertension and sodium retention, in connection with what is necessary to observe a low-salt diet, the appointment of spironolactone (aldosterone antagonist like) in combination with loop diuretics.

Hepatorenal syndrome is a result of severe peripheral vasodilation, which causes vasoconstriction in the kidney until the development of acute renal functional insufficiency (because it is believed that the structure of the kidney is not affected). An important role is played in the pathogenesis of renal decline (glomerular) blood flow due to vasoconstriction background kidney vasodilation abdomen. Furthermore,

autoimmune mechanisms are important, damaging the renal tubules. There are two types of hepatorenal status: the first type is characterized by fast-flowing of renal failure (less than 2 weeks). It is typical for patients with acute liver failure, or alcoholic cirrhosis, and the prognosis is poor. The second type in most cases occurs in patients with less severe disorders of the liver, can be caused by refractory ascites. Renal failure develops slowly at the same time [1].

Hepatopulmonary syndrome runs rare, but extremely difficult. It is characterized by the presence of pathological changes in the lung, which can lead to the development of respiratory insufficiency. The components of the clinical triad of hepatorenal syndrome are a chronic liver disease (often cirrhosis), remodeling (expansion) of intrapulmonary vessels and reducing the partial pressure of oxygen in arterial blood. The primary task simultaneously with the treatment of the underlying disease is the use of drugs that inhibit the synthesis of nitric oxide. However, a promising method of treatment in respect of life is considered a liver transplant.

Hepatocellular carcinoma may cause the decompensation of cirrhosis, and it, in turn, is considered to be an independent predictor of death in hepatocellular carcinoma. Therefore, hepatocellular carcinoma should be considered as a prognostic indicator at any stage of the disease, rather than as the stage of cirrhosis, predetermining decompensation.

The development of hepatic encephalopathy (HE), which is necessary to meet the doctor quite often, is primarily the result of shunting of blood through portosystemic collaterals, which developed because of portal hypertension, the result of brain edema (due to vasodilation) and liver failure [7]. It should be emphasized that the term "encephalopathy" means that changes in the nervous system are not of inflammatory origin. It is most often found in patients suffering from liver cirrhosis and fulminant hepatic failure, in case of poisoning with paracetamol, hepatotropic poisons. However, it may develop in diseases initially not accompanied by clinically obvious signs of hepatic decompensation — chronic hepatitis, fatty liver [5]. It is important to know that the symptoms of HE are potentially reversible (except in cases

of terminal liver failure). With proper management of patients symptoms of HE regress within a few hours or days.

Precipitating factors, usually in 70-80% of cases promote occurrence of HE, although its episodes may occur spontaneously. These factors include:

- bleeding from varices extended veins of esophagus at liver cirrhosis;
- bacterial infection (e.g., pneumonia, pyelonephritis, spontaneous bacterial peritonitis);
- any operation or injury, anesthesia, episodes of falling blood pressure;
- constipation (accompanied by the accumulation of ammonia and other products the intestinal microflora in the body);
- excessive intake of protein, in particular animal (leads to increased production of ammonia);
- receiving hypnotics and tranquilizers, alcohol (having an excessive effect in terms of endogenous benzodiazepine substances);
- diuretics overdose that leads to electrolyte shifts and aggravate disorders of the nervous system. It should be noted that the dose of diuretic drugs, against which can develop disorders of electrolyte balance, may not necessarily exceed the therapeutic.

It is important to realize that HE is a continuum from minimal (subclinical) to apparent violations of liver failure, coma manifested in varying degrees of severity.

Depending on the reasons leading to the development of HE, distinguish its types. Tthe type A (Acute) can be assumed when the HE is associated with liver failure, type B (Bypass) indicates that the HE is associated with portosystemic shunting blood, liver disease available. Type C (Cirrohosis) presupposes that HE is associated with liver cirrhosis, portal hypertension and portosystemic shunt.

HE usually divided into episodic (acute episode with fixed or unspecified (spontaneous) precipitating factor); recurrence (2 episodes within a year); persistent (with cognitive deficits, disrupted social and professional activities) or relapsed after treatment interruption.

Furthermore, there are 5 stages in the clinical picture of HE. The main criterion for determining the stage is a state of consciousness. At the minimum (latent) stage neurologic symptoms do not appear, but the cognitive deficits evident in psychometric tests. Upon stage I (mild) rhythm disturbance of sleep is detected, attention is reduced, difficulty in orientation, forgetfulness, changes in handwriting, fine tremor. In stage II (moderate) appears apathy, possible lethargy, disorientation, inappropriate behavior, ataxia, asterixis. III (severe) stage is characterized by disorientation, somnolence, aggression, deep amnesia, asterixis, increased reflexes, spasticity. Stage IV (coma) includes the lack of consciousness and response to pain, the presence of areflexia, and loss of tone.

Today it is assumed that HE has a complex origin. Some issues of pathogenesis remain unclear. In chronic liver diseases, such as cirrhosis or active hepatitis, in the pathogenesis of HE mechanism of shunting of blood from the system of the portal vein into the systemic circulation is predominant. An important role is played not only by formed anatomical portosystemic shunts (in the lower third of the esophagus, rectal venous plexus, etc.), but also in the metabolism of blood sinusoids by changing their walls (i.e. functional bypass).

One of the basic mechanisms of HE is considered a toxic effect of ammonia on the brain and the whole body is apparently caused by inhibition of amino acid, transamination reaction that disrupts the detoxification of ammonia and other substances that cause brain dysfunction.

Ammonia is produced in the body by natural catabolism, deamination of amino acids in the liver, as well as during bacterial degradation of protein in the intestine. Under physiological conditions, the principal amount of ammonia is subjected to detoxification in periportal hepatocytes, where biochemical reactions occur ornithine cycle. The ornithine cycle toxic ammonia binds with amino acids to form a non-toxic urea. In the decomposition of ammonia hepatocytes are also involved, located in the central parts of the liver lobules, skeletal muscle cells and glia. Ammonia binds glutamate there. The end product of the reaction is low toxic glutamine. In the

context of liver failure muscle mass in part compensates the function of detoxification of ammonia [5].

Because of the intensity of liver ornithine cycle operation (main process of detoxification of ammonia) is significantly reduced. In cirrhosis of the liver due to thickening (capillarization) of sinusoidal wall and development of portocaval anastomoses (portosystemic shunting) also occurs direct leakage of ammonia into the systemic circulation. As a result of these pathophysiological changes hyperammonemia develops.

An increased content of ammonia in the liver failure shows a negative nitrogen balance (prevalence of catabolic processes); muscle wasting, characteristic of severe liver disease; hyperglucagonemy (to increase the rate of deamination of amino acids); increasing ammonia reabsorption in the kidneys (with concomitant hypokalemia); malnourished patients (energy deficit).

High concentrations of ammonia can have both direct and indirect damaging effect on cells of the nervous system, promoting the predominance of inhibitory processes. Excessive accumulation of glutamine, especially in the absence of vitamin B_6, prevents the formation of gamma-aminobutyric acid and causes the increase of osmotic pressure in the cytoplasm, intracellular edema and astrocyte dysfunction, disturbance generation of ATP molecules. Clinically it is manifested by insomnia, oppression, panic attacks, anxiety, tremor, tachycardia. These features of the relationship hyperammonemia in violation of the amino acid (and therefore protein) exchange should be considered when treating such patients.

The functions of proteins in the body are diverse, they are involved in the construction of the whole body from the cell membrane to blood vessels, through them functioning immune and endocrine systems. It is known that the liver synthesizes transport proteins for a large number of substances and trace elements (e.g., iron, lipids). A part of proteins are amino acids, many of which are synthesized in the liver (alanine, serine, arginine, cysteine, tyrosine, glutamic acid, aspartic acid, proline, glycine). Some amino acids come from food. Amino acids are divided into essential and nonessential. It is absolutely indispensable include lysine and threonine,

a conditionally fungible — tyrosine, arginine, proline, glycine, cysteine. Absolutely surrogate is glutamic acid and serine, in case they can be synthesized from the keto acid. Each of the amino acids is essential for human life.

Such amino acids are valine, isoleucine, leucine, protect tissue from disintegration during physical exertion, stress, dietary protein deficiency. Isoleucine is involved in hemoglobin synthesis, regulates the level of blood glucose. Leucine is involved in the restoration of bone, skin and stimulates the synthesis of growth hormone. Threonine is involved in the synthesis of antibodies, elastin, collagen formation in tissues of the cardiovascular, nervous and muscular systems. Tryptophan is indispensable in the synthesis of albumin, carnitine, hemoglobin, serotonin, vitamin PP. Glycine has a special place in the synthesis of collagen, elastin, heme, creatine, and participates in the conjugation of bile acids and has lipotronym and antidepressive action. Histidine contributes to the restoration of myelin fibers, growth and renewal of tissues, the synthesis of red blood cells, white blood cells and hemoglobin. Methionine and active form methionine (ademethionine) plays an important role in the metabolism of amino acids and is traditionally used in the treatment of liver diseases. Ademetionine due to the conversion of choline in the liver involved in the synthesis of phosphatidylcholine and glutathione, which "advocates" the cell from the toxic, including xenobiotic exposure. Choline is also a source of synthesis of acetylcholine — one of the most important mediators of synaptic nervous system. Ademethionine acts as an antidepressant in the case of a high level of histamine, however, contraindicated in patients with depression and schizophrenia, which occur at low levels of histidine and hyperhomocysteinemia [2].

Therefore, on the basis of the foregoing, the violation of the amino acid balance of the blood serum contributes to the pathogenesis of HE. Changes in amino acid composition of serum are very characteristic of decompensated liver disease. Liver failure is characterized by the processes of catabolism with a predominance of the deamination in which carboxylic acids are formed from the amino acids with branched side-chain. As a result, excessive consumption of amino acids with branched side-chain (their structure in formula can be expressed as COH-CH-R-CH3)

indicates the relative dominance of aromatic amino acids (COH-CH-). The quantitative ratio of a branched amino acid side chain (leucine, isoleucine, valine) and aromatic amino acids (phenylalanine, tyrosine, tryptophan) expressed by the Fischer coefficient. The normal ratio is 3.0-3.5 by Fisher. In hepatic failure it is reduced to 1.5 or less.

Under physiological conditions, phenylalanine, and tyrosine in the central nervous system are the sources of the excitatory neurotransmitters synthesis advantageously — dihydroxyphenylalanine, dopamine, and catecholamines. In terms of the predominance of aromatic amino penetration through the blood-brain barrier is greatly simplified [2]. Under the conditions of excess aromatics their metabolism is an alternative way: there is an accumulation of so called false neurotransmitters (octopamine, phenylethylamine, tyramine), depressing neuronal activity. Role of false neurotransmitters in hepatic failure is also played by endogenous substances produced by the action of intestinal microflora — mercaptans, derivatives of methionine, short- and medium-chain fatty acids, phenols, amines. These substances are not only the products of bacterial processing sulfur containing amino acids, and dietary fat in the colon.

It should be remembered that due to pathological changes in the composition of the microflora develops endotoxemia. Penetration of toxins into the bloodstream and contribute to enteric colonopathy, developing due to lack of bile acids, cholestasis, liver failure, portal hypertension. The wall of the intestine becomes permeable, that even more increases the likelihood of translocation of intestinal bacteria into the mainstream of the portal vein, resulting in numerous systemic effects, that can cause bleeding from esophageal varices, gastric, refractory ascites, hepatorenal syndrome and HE. Indirect evidence of falling coliform bacteria in the patient’s blood may serve as the detection of Enterococci and Escherichia in the urine. The severity of dysbiosis varies depending on the etiology of cirrhosis and class. Impaired bowel function requires the restoration and maintenance of the normal composition of intestinal microflora, which implies the appointment of antibiotic rifaximin. It is a semisynthetic antibiotic which inhibits DNA-dependent RNA polymerase, inhibits

RNA synthesis and bacterial proteins, possessing broad spectrum of activity. It does not interact with P-450 system, which makes it the drug of choice for the treatment of pathological contamination microflora to prevent spontaneous bacterial peritonitis [3, 6].

Furthermore, it is shown that increases in hepatic failure susceptibility of benzodiazepine receptors in the brain to the effects of inhibitory neurotransmitters. The reasons for this phenomenon are not well understood. It is assumed that upon liver failure benzodiazepine endogenous substances are accumulated, that aggravates the clinical course of HE.

Drug treatment of HE is carried out in several pathogenetic directions. This is, primarily, reduction of ammonia production and absorption, increasing metabolism of ammonia in tissues, reducing the production of false neurotransmitters blockade of GABA-benzodiazepine receptors. If possible, the effect of allowing factors is eliminated, which helps to stabilize the patient's condition [5].

However, for the successful and rapid elimination of the patient from the HE there must be the appointment of the special non-drug measures and medications. Speaking of food the patient is able upon HE, it should be emphasized the need to ensure sufficient energy intake (2000 kcal). This is required to maintain natural energy-ammonia detoxification reactions in the liver and muscle. Rapid and prolonged limiting the content of protein in the diet has been recently recognized as inappropriate, since it promotes the deficit of amino acids — the substrates for binding of ammonia, and muscle atrophy. During the period of exacerbation of symptoms of HE it is advisable limit protein intake to 10-20 grams per day for 1-2 days. In a coma enteral and parenteral nutrition are preferable [4].

If we consider the principles of treatment from the standpoint of clinical forms, they can be divided by the total treatment of specific and alternative therapies. For example, a common approach to the treatment of episodic HE is to eliminate the precipitating factors, including important gastrointestinal bleeding, infection, azotemia, constipation, use of hypnotics. Upon severe HE there must be short-term (less than 72 hours) limited use of proteins. True positive effect in treating HE

possess measures to facilitate the removal of protein decomposition products from the intestines: high cleansing enemas, which is useful to combine the reception osmotic laxatives, in particular lactulose, having the property of lowering the production and absorption of ammonia in the gut. Such measures are especially shown for a few days after the gastrointestinal bleeding. In chronic recurrent HE it is desirable to achieve mushy stool frequency of 2-3 times a day.

As a specific therapy for patients who are unable to take the drug per os, lactulose enema should be prescribed (300 ml per 1 liter of water). In other cases, the dose of lactulose in 30 ml is administered per os every 1-2 hours before emptying the intestine, then applied dose causing discharge in 2-3 hours (typically 15-30 ml, 2 times a day). Use of the drug is stopped upon elimination of the provoking factor.

General principles of treatment of persistent HE recommendations are to protein intake of vegetable or dairy origin, and not to resort to long-term restriction of protein, fight constipation, do not take sedatives and hypnotics. The use of lactulose in a dose conducive to 2-3 times the bowel (15-30 ml, 2 times daily) is referred to the specific therapy. Patients who can't tolerate lactulose are assigned with rifaximin 400 mg per os 3 times a day to 14 or more days under the supervision of a physician (alternative therapy). Appointment of antibacterial drugs, that suppress the growth of the intestinal microflora, contributes to the oppression of protein decomposition processes in the gut — one of the sources of the formation of ammonia. Examples of these drugs include neomycin, ciprofloxacin, metronidazole, vancomycin, rifampicin. Antibiotics are necessarily shown in the HE stage III or IV.

Special means for the treatment of symptomatic HE are the preparations including L-ornithine-L-aspartate, amino acid preparations with branched side chain and benzodiazepine receptor antagonist flumazenil. Preparations of L-ornithine-L-aspartate are produced in the form for oral and intravenous administration. The mechanism of action of L-ornithine-L-aspartate stimulation is based on the binding of ammonia in the biochemical synthesis of the urea cycle, which flows in the periportal hepatocytes. High efficiency in the correction and treatment of hyperammonemia in HE is proven in randomized controlled trials. L-ornithine-L-aspartate is a reliable

means of treating severe manifestations of HE — precoma and coma, as it enhances the protein-synthetic liver function, increases the production of energy in the Krebs cycle, reduces the production of lactic acid and the body's need for oxygen by enhancing the anaerobic oxidation [2]. Oral administration of L-ornithine-L-aspartate is especially indicated in chronic undulating course of HE; receiving a maintenance dose can improve the functional reserves hepatocyte detoxification of ammonia and to prevent the buildup of neurological manifestations. L-ornithine-L-aspartate is well tolerated even during many months of receipt.

Since there is increased consumption of amino acids with branched side chain (leucine, isoleucine, valine) in catabolic processes deamination and relative predominance of aromatic amino acids (phenylalanine, tyrosine, tryptophan, histidine), amino acids with the formulations branched side chain are special means for parenteral nutrition at liver failure. Recently, application prospects in hepatology drugs of this class received much attention as solutions for intravenous administration containing predominantly branched amino acid side chain, and only a minor amount of aromatic amino acid structure, are the suppliers of plastic material and the energy deficit which, as was highlighted above, underlies many pathophysiological changes in hepatic failure, HE, asthenic syndrome, muscle wasting, and others.

Among the drugs with a branched amino acid side chain there is Hepasol-Neo. It contains eight essential, two conditionally essential and five replaceable amino acids: valine, isoleucine, L-leucine, L-lysine as L-lysine acetate, L-methionine, L-threonine, L-alanine, L-arginine, glycine, L -gistidin, L-proline, L-serine, L-cysteine in the form of N-acetyl-L-cysteine, L-phenylalanine, L-tryptophan. Very important is the fact that the L-form of amino acids enables direct incorporation into protein biosynthesis. When administered intravenously, the amino acid components of Hepasol-Neo are distributed throughout the body, which are used in the process of protein synthesis and serve to provide energy costs.

The concentration of the solution was 8%. The drug does not contain carbohydrates and electrolytes.

The drug, according to the literature, significantly reduces the level of bilirubin, transaminase activity, reduces the mesenchymal-inflammatory syndrome, cytolysis [4].

The content in the formulation of conditionally essential amino acids (L-arginine and L-histidine) provides for eliminating their deficiency which is often observed in hepatic insufficiency. L-arginine acts as a substrate in the synthesis cycle of urea, and thereby reducing the severity of hyperammonemia. In addition, its use reduces hepatocyte steatosis, necrosis, inflammation, which is very important in the treatment of such patients. The selected dosage does not cause severe vasodilation.

Introduction of L-alanine and L-proline reduces the body's need for glycine and indirectly reduces the production of ammonia, i.e. glycine actively undergoes deamination with release of ammonium ions.

Introduction of L-isoleucine, L-leucine and L-valine (essential amino acids with branched side chain) not only eliminates the deficiency in the peripheral tissues, but also reduces the flow of aromatic amino acids in the central nervous system, reducing the symptoms of HE.

Introduction of amino acids with branched side chain is administered as a component of the partial or total parenteral nutrition to patients with liver failure, including the syndrome of HE, in the presence trophological failure. By their use the Fisher coefficient increases significantly, protein tolerability is improved in hepatic failure, severity of encephalopathy is reduced.

If Hepasol-neo is used as a component of total parenteral nutrition, it is administered together with glucose solutions and fat (carbohydrates and fats ratio 70:30). The infusion rate is 10.5 mg of nitrogen per 1 kg body weight for 1 hour. With the introduction of Hepasol-Neo percentage of assimilation of essential acids is 99% and the non-essential — 97%.

It is necessary to observe speed drip infusion of Hepasol-Neo — 1-1.25 ml per 1 kg body weight for 1 hour (0.08-0.1 g amino acids respectively for 1 kg of body weight for 1 hour). Dose and duration of the administration are set individually depending on the level of ammonia in the blood, severity of the clinical picture and

dynamics of neurological manifestations. The maximum daily dose for adults is 18.75 ml per 1 kg of body weight (1300 ml for patients weighing 70 kg).

Using Hepasol-Neo is contraindicated in disorders of amino acid metabolism, renal failure, in a state of hydration, hyponatremia, hypokalemia, decompensated heart failure.

In the case of a combination of hepatic and renal failure, deciding on the introduction of Hepasol-Neo should be guided by the severity of renal failure, the dynamics of serum creatinine.

The appointment of the drug for children and adolescents up to 18 years, pregnant and nursing mothers is not recommended due to insufficient clinical experience with the drug in these patients.

Side effects of Hepasol-Neo aren’t known. It is necessary to observe a slow infusion rate, as the rapid introduction of the drug may cause nausea, vomiting, sweating, chills, tachycardia, and increased transaminase levels. These side effects are transient in nature and resolved after discontinuation of the infusion. An excessive amount of solution can lead to the appearance of pulmonary edema and fluid overload, therefore the need to monitor the water balance. You also need periodic monitoring of electrolyte and acid-base balance.

Consequently, Hepasol-Neo is correcting stages of HE, including primary ones, it has a combined mechanism of action, providing detoxification, hepatoprotective and metabolic effects, which is very important for improving the quality of life of patients suffering from cirrhosis of the liver with the presence of amino acid imbalances and hyperammonemia.

References

1. Буеверов А. О. Трудные вопросы диагностики и лечения печеночной энцефалопатии / А. О. Буеверов, М. В. Маевская // Клин. перспект. гастроэнтерол. и гепатол. — 2005. — № 1. — С. 25–30.
2. Гепатопротектори в лікуванні захворювань печінки: клініко-біохімічні механізми дії / Н. В. Харченко, Г. А. Анохіна, С. І. Чекман [та ін.] // Здоров'я України. Тематичний номер. — 2013. — № 1. — С. 28–29.
3. Губергриц Н. Б. Печеночная энцефалопатия: клиника, диагностика, лечение : учебное пособие для врачей / Н. Б. Губергриц. — Донецк, 2008. — С. 29.
4. Звягинцева Т. Д. Хронические диффузные заболевания печени: патогенетические подходы к лечению / Т. Д.Звягинцева, С. В. Глущенко // Здоров'я України. Тематичний номер. — 2010. — № 1. — С. 46–47.
5. Особливості патогенезу, діагностики та лікування печінкової енцефалопатії на фоні цирозу печінки / В. О. Мойсеєнко, Е. Г. Манжалій, О. С. Солонович, Т. Д. Никула // Лік. справа. — 2014. — № 11. — С. 39–47.
6. Скрипник І. М. Клінічна гепатологія : навчальний посібник / І. М. Скрипник, Т. В. Мельник, М. М. Потяженко. — Полтава : Дивосвіт, 2007. — 424 с.
7. Шульпекова Ю. О. Печеночная энцефалопатия и методы ее коррекции / Ю. О. Шульпекова // Consilium medicum. — 2005. — № 1, Прилож. — С. 26–31.

Liver cirrhosis: clinical picture, pathogenesis, treatment and monitoring of patients

T. N. Hristich, D. A. Gontsaryuk

Bukovinian State Medical University, Chernovtsy, Ukraine

Key words: liver cirrhosis, pathogenesis, clinic, hepatic encephalopathy, treatment

The authors highlight the course of a clinical syndrome in liver cirrhosis with a focus on a hepatic encephalopathy and the principles of management of such patients. This review examines the treatment of hepatic encephalopathy in detail with Hepasol-Neo correcting stages of hepatic encephalopathy, including primary, having a combined mechanism of action (detoxification, hepatoprotective and metabolic), improving the quality of life of patients suffering from liver cirrhosis with a presence of amino acid unbalances and hyperammonemia.