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EARLY DIAGNOSIS OF CHANGES IN THE KIDNEYS OF HEPATORENAL SYNDROME DEVELOPED IN VIRUS ETIOLOGY OF LIVER CIRRHOSIS AND ASSESSMENT OF THE EFFECT OF COMPLEX TREATMENTS

(monograph)

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Annotatsiya

Monografiyada virus etiologiyali jigar sirrozida rivojlangan gepatorenal sindromning buyrakdagi o‘zgarishlarini erta tashxislash va kompleks muolajalar ta’sirini baholash bo’yicha olib borilgan tadqiqot natijalari ilmiy-amaliy dalillarga asoslangan holda muallif tomonidan keng yoritib berilgan.

Аннотация

В монографии автором на основе научных и практических данных широко освещены результаты исследований по ранней диагностике изменений почек при гепаторенальном синдроме, развившихся при циррозе печени вирусной этиологии, и оценке эффекта комплексного лечения.

Annotation

In the monograph, the results of research on early diagnosis of kidney changes in hepatorenal syndrome developed in liver cirrhosis of viral etiology and evaluation of the effect of complex treatments are widely covered by the author based on scientific and practical evidence.

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INTRODUCTION

PF of the President of the Republic of Uzbekistan dated February 28, 2023 on the state program for the implementation of the development strategy of New Uzbekistan for the years 2022-2026 in the "year of attention to people and quality education" Within the framework of Decree No. 27, a number of promising tasks and goals related to the further development of the health care system of our country and the strengthening of public health were determined. Including bringing primary medical services closer to the population and providing citizens with quality medical services, identifying diseases at an early stage, as well as creating additional amenities for patients, preventing non-communicable diseases among the population, forming a healthy lifestyle and physical activity in children among them is the wide-scale organization of measures to increase the level.

Within the framework of this decree, it was determined to further improve the quality of medical services to the population, to protect motherhood and childhood, to actively promote a healthy lifestyle among the population, and to implement preventive measures.

President Sh.M. Mirziyoev's promotion of the grand idea "Medicine of Uzbekistan - for human dignity" and based on this idea, a broad vision aimed at increasing the efficiency of the health care system of our country and bringing it to a new level. preventive measures have been developed and are being put into practice.

As a result of the reforms carried out over the past five years, the political-legal, social-economic, scientific-educational foundations necessary for the establishment of New Uzbekistan have been created in our country.

Decree No. PF-60 of the President of the Republic of Uzbekistan dated January 28, 2022 "On the strategy for the development of New Uzbekistan in 2022-2026" on improving the system of high-tech medical care for reproductive women tasks are defined. age, pregnant women and children, equipping perinatal centers with the necessary medical equipment and equipment and providing them with qualified personnel was defined as one of the main goals and tasks.

The signing of the Decree of the President of the Republic of Uzbekistan on December 7, 2018 "On comprehensive measures to fundamentally improve the healthcare system of the Republic of Uzbekistan" has led to the implementation of a number of promising plans in the medical higher education system. created the basis for its increase. Within this decree, the following broad development issues were defined:

- formation of an effective system of training, retraining and professional development of medical personnel, development of medical science, including certification (accreditation) of medical scientific and educational institutions according to international standards, introduction of modern educational programs, methods and technologies forming on the basis of achievement;

- reforming the system of secondary and higher medical education, revising curricula, programs, educational materials and theoretical training in terms of further optimization and increasing practical training, as well as aligning them with the universal achievements of medical science and practice;

- strengthening the role of clinics of medical higher education institutions in the integration of advanced scientific developments and technologies into practical health care;

- improvement of training of medical personnel in narrow specialties, optimization of training periods in master's degree and clinical residency based on the complexity of acquiring clinical skills;

-revision of the system of post-secondary education, the system of improving the qualifications of healthcare professionals and their retraining, introducing problem-oriented modular training programs, wide use of distance learning mechanisms lash;

- wide involvement of highly skilled and qualified foreign experts, scientists and teachers in the management and educational process;

- improving educational standards and curricula of higher education and post-higher education by gradually introducing the credit-module system of education and increasing their practical aspects;

- based on the complexity of obtaining a clinical specialty, optimizing the training period of highly qualified personnel in master's degree and clinical residency (residency) from 1 to 5 years in accordance with international standards;

- extensive cooperation with foreign medical educational institutions, including the opening of their branches and faculties, as well as the introduction of a dual diploma system;

- to expand educational opportunities due to the use of resources of foreign universities through the use of network cooperation and open courses in the implementation of educational programs, as well as the development of electronic national platforms of medical education and the formation of an electronic educational environment;

- to strengthen the role of clinics and educational bases of higher medical educational institutions in the integration of advanced scientific developments and technologies into healthcare practice;

- to increase the role of professors and teachers of medical higher education institutions and scientific institutions in the introduction of new scientific developments and technologies through financial incentives for training highly qualified personnel and their participation in the process of treatment and diagnosis;

- organization of simulation centers in medical educational institutions where training is conducted in virtual reality conditions, on medical simulators and mannequins;

- providing targeted support from the state to medical and scientific teams for basic and program-targeted financing of medical scientific and educational institutions, transfer of innovative developments and technologies, introducing them into health care practice;

- the educational programs of the departments of the medical and preventive direction of higher medical educational institutions are recognized by international organizations, including the Association of Schools of Public Health in the

European Region (ASPHER — The Association of Schools of Public Health in the European Region) to ensure accreditation by;

- development and introduction of the draft of the decision of the President of the Republic of Uzbekistan on the development of the medical education system and medical science, including the optimization of the structure and directions of educational institutions, the integration of "education-science-practice" and introducing continuity, defining new directions of higher and secondary medical education, establishing anatomical morgues and teaching-biological laboratories, providing for the opening of international faculties and branches of leading foreign higher educational institutions;

- improvement of educational standards and educational programs of higher education and post-higher education, including the introduction of the credit-module education system and increasing the practical component in them.

Liver disease is one of the six main causes of death in economically developed countries among 35-60-year-olds. There are 14-30 people per 100,000 inhabitants. Worldwide, 1.4 million people die each year from cirrhosis of the liver (JS) and its complications. One of the most dangerous complications is hepatorenal syndrome (GRS), which leads to death in most cases. Hepatorenal syndrome is a serious complication of the kidney in patients with liver failure due to acute or chronic liver disease, in addition, there are no other causes of kidney disease leading to kidney failure. In hepatorenal syndrome, the kidney almost does not change morphologically, the amount of mesangial cells is reduced.

There are some observations in the world dedicated to the study of GRS. According to them, approximately 18% of patients with JS develop GRS in the first years of the disease, reaching 39% by the fifth year. GRS was diagnosed in 17% of patients hospitalized for ascites, and in-hospital mortality in this group exceeded 50%. The development of GRS has been confirmed in patients with a compensated form of liver failure in the presence of predisposing factors such as bacterial infection or sepsis, high volume paracentesis, gastrointestinal bleeding, intensive use of nephrotoxic drugs or diuretics. Clinical symptoms of GRS are

growth, azotemia, edema syndrome, ascites, increased urine osmolality, and hyponatremia. Understanding the collected clinical data, new diagnostic criteria for GRS were developed at the San Francisco conference in 2005 and recommended by a special group of the International Ascites Club.

The medical workers of our republic have a number of tasks to further coordinate the field, including early detection and treatment of diseases of the gastrointestinal system, liver and kidneys, and adapt them to the requirements of international standards, and positive work is being carried out in this direction. "... To increase the efficiency, quality and popularity of medical care provided to the population in our country, as well as to introduce high-tech methods of early diagnosis and treatment of diseases, by creating a patronage service, to support a healthy lifestyle and prevent diseases Tasks such as ..." are defined. They allow early diagnosis of various diseases and complications caused by them among the population, their prevention and improvement of patients' quality of life.

This monograph is based on the Decree of the President of the Republic of Uzbekistan No. PF-60 of January 28, 2022 "On the Development Strategy of New Uzbekistan for 2022-2026", PQ-5124 of May 25, 2021 No. "On additional measures for the comprehensive development of the health sector" and No. PQ-215 of April 25, 2022 "On bringing primary medical and sanitary care closer to the population and improving the efficiency of medical services" serves to a certain extent the implementation of the tasks specified in the Decisions on additional measures and other regulatory legal documents related to this activity.

This study was carried out in accordance with the IV "Medicine and pharmacology" priorities of the republic's science and technology development.

Scientific observations on cirrhosis of the liver and its complications are being conducted in different countries of the world [28; pp. 58-88, 27; pp. 41-70, 54; p. 46-55, 68: p. 72-9, 92: p. 397-417, 97: p. 762-68, 160.; 138; pp. 116-122, 129; pp. 1426-1437, 111; pp. 438-445, 98; pp. 605-613, 94; p. 406-460. 95; p. 474-481] and is widely covered in publications of foreign countries.

However, in our republic, scientific work on complications of liver cirrhosis, including hepatorenal syndrome, which in most cases leads to death, has not been conducted.

Symptoms of cirrhosis of the liver are different - it can last for many years in the form of acute hepatitis and chronic inflammatory diseases of the liver. About 20% of patients are diagnosed with liver cirrhosis at autopsy after their death [9; p. 152, 42. p. 25-38].

Complaints of patients and clinical manifestations of the disease are related to liver cell failure, portal hypertension syndrome and its complications, and systemic, immune and metabolic damage observed under the influence of the etiological factor [52; 87-88-b]. In most cases, the disease is hidden and has minimal changes or symptoms that are not characteristic of cirrhosis.

Its decompensation stage is manifested by obvious clinical signs of the disease, and the average life expectancy of patients does not exceed two years. In the manifest state of this stage, a number of complications are observed and the prognosis of the disease is inextricably linked with them [87; 241-242-b, 94; 406-460-b]. These include hepatic encephalopathy, bleeding from esophageal and gastric varices, ascites (abdominal fluid with or without infection), hepatorenal syndrome, hyponatremia, and infection-related complications [9; p. 152, 22; pp. 24-31, 42; p. 25-38, 38; p. 16-21].

The Child-Pugh classification is used to assess the severity of liver cirrhosis. It is very convenient because it is possible to determine the indicators used to determine the severity of the disease in all systems of medicine.

In some cases, the combined effects of viruses and alcohol can cause liver cirrhosis in patients at the same time [43;. 57-65-b, 55;. pp. 6-13, 56; pp. 43-52]. In a series of observations, when these two negative effects come together, it is noted that the disease is severe before cirrhosis is formed, that is, at the stage of hepatitis. Some authors compared chronic hepatitis developed as a result of these two etiological factors. As a result of the harmful effects of alcohol (or drugs) with a viral infection, liver enlargement in almost all cases and splenomegaly and

jaundice have been noted in a large number of patients. Also, under the influence of the virus-alcohol double factor (hepatitis C virus 32.4%, B virus 53.8%), the disease was manifested by cytolysis syndrome in most patients.

In 1978, M. Wiese found out the following in his fundamental examination based on the observation of 420 patients with acute viral hepatitis C. After 20 years, 70% of them were anti-HCV, almost 50% had RNA HCV, and only 0.4% had liver cirrhosis [167; p. 295]. In the observation of a Spanish scientist in 78 patients with developed and complicated liver cirrhosis due to viral hepatitis C, 57.7% of them had liver failure, 30.8% had bacterial infection, 7.7% had gastrointestinal bleeding, and 3.8% had hepatocellular carcinoma [141; pp. 823-830]. In Japan, 38.6% of them had hepatocellular cancer, 34.1% had gastrointerstitial bleeding, and 6.8% had bacterial infection [160; pp. 1276-1283].

N. Toshikuni and co-authors observed patients with alcoholic (n=75) and advanced liver cirrhosis (n=152) due to chronic hepatitis C and found that survival increased significantly when patients stopped drinking alcohol [160; pp. 1276-1283].

In another observation, death was observed 3 times more in liver cirrhosis caused by viral infection (hepatitis C and B viruses) than in alcoholic cirrhosis. However, in both cases, patients developed liver cancer in the same way [34; 27-31-b, 37; pp. 63-68, 4; p. 45].

In all observations, when liver cirrhosis is caused by viral hepatitis and alcohol together, compared to monoetiological cases, the disease worsens rapidly and death occurs 50% more often, and liver cancer is also recorded in them. In almost all scientific observations, this opinion is confirmed and generally accepted [40; pp. 44-46, 1;5; 55; pp. 6-13].

Among the many complications of liver cirrhosis, hepatorenal syndrome is one of the least studied. About 15% of patients with it developed hepatorenal syndrome within 6 months after the first hospitalization due to ascites, and 40% within 5 years [140:1385–1394 p., 106:1279–90 p., 2; 71:17-30-b, 7; 12; 15; p. 90-

100, 16; 24-28 p]. Full-fledged scientific observations dedicated to it have not been conducted in our republic.

There are two types of hepatorenal syndrome. Its first type is associated with rapid deterioration of kidney function in response to increasing deterioration of liver function. This type is often observed in severe alcoholic hepatitis and in the terminal stages of liver cirrhosis with spontaneous bacterial peritonitis. A 100% increase (at least 221mmol/l) of blood creatinine levels in patients of this type is typical [164:11-17-p., 149:1241-8-p., 88:1-20-p., 39 ; p. 59-64, 73; 811-22-b].

The second type of hepatorenal syndrome is observed in liver cirrhosis with ascites and resistant to diuretics, is stable and slowly increases [26:71-102-p., 20; 86;].

In patients with obvious ascites, if there is no positive result of the procedures performed, if arterial hypotension and hyponatremia are detected, it indicates the development of hepatorenal syndrome. At this point, this syndrome, which develops in liver cirrhosis, should be distinguished from acute tubular necrosis, glomerulonephritis, toxic nephropathy, and nephropathies developed in chronic heart failure.

30 years ago, creatinine levels of 150 mmol/l and higher were accepted as criteria for kidney failure in hepatorenal syndrome. This corresponds to glomerular filtration rate (GFR) of 40 ml per minute and below [76; 164-176-b].

In a number of scientific works, the changes in the kidney observed in cirrhosis of the liver were considered as a functional condition [p. 26:71-102], but at the same time, modern tests used to detect nephropathy in the early stages were not used. Apart from that, in all cases, KFT is determined using creatinine. Most hospitals in the world, including Uzbekistan, use creatinine to assess kidney function.

Considering the above, M.G. Shlipak and co-authors proposed a new term "preclinical kidney disease". This phrase is used in cases where the KFT is preserved when determined using creatinine, but the cystatin-S values are high, and the expediency of its use is noted [54; 46-55 p].

Numerous scientific studies have confirmed that not only in certain physiological conditions, but also when excess protein enters the body (orally or intravenously), it leads to a temporary increase in KFT and an acceleration of plasma flow [63; pp. 81-88].

Depending on the protein used, the filtration rate can be different [48; pp. 396-402, 54; p. 46-55, 63; pp. 81-88, 64; pp. 15-26]. After loading with meat protein, CFT, renal plasma and blood flow in the spleen increase for one hour and remain for several hours [19; 114; pp. 1296-1309]. Based on the mentioned data, the renal functional reserve (RBF) consensus and its evaluation tests were created. BFZ is understood as its ability to increase KFT from the basal, i.e., primary state to a maximum high level. To achieve it, all nephrons, not only deep, but also superficial, take part in the process.

In most of the literature, in the presented data, BFZ was studied in patients with diabetes in most cases. However, there is almost no information on the use of this test in a number of other diseases, including hepatorenal syndrome. However, the study of BFZ in hepatorenal syndrome developed on the basis of liver cirrhosis provides an opportunity for early diagnosis of nephropathy.

In addition to the above, one of the markers of kidney damage is the excretion of type IV collagen in the urine. It forms the basis of the basal membrane of balls and tubules. According to some authors, the appearance of this protein in urine is one of the early morphological signs of nephropathy [120; 885-893-b].

The above confirms that no scientific observations have been made regarding the early diagnosis of hepatorenal syndrome, which is a serious complication of cirrhosis, one of the common liver diseases among the population in the whole world, including our republic, using modern markers. Taking this into account, we set the following goals and objectives for the study.

To study the characteristics of hepatorenal syndrome in liver cirrhosis with viral etiology (developed on the basis of hepatitis B and C viruses) and to evaluate the effect of early diagnosis of kidney dysfunction and complex treatments.

Tasks of the research:

- Study of renal glomerular filtration rate in order to early diagnosis of hepatorenal syndrome in patients with developed liver cirrhosis due to hepatitis B and C viruses;
- Comparative study of renal functional reserve for the purpose of early diagnosis of hepatorenal syndrome in patients with liver cirrhosis developed on the basis of hepatitis B and C viruses;
- Assessment of type IV collagen excretion in urine in liver cirrhosis developed on the basis of hepatitis B and C viruses;
- Evaluation of the effect of complex treatments with the addition of glutathione and eplerenone on the functional reserve of kidneys in liver cirrhosis developed on the basis of hepatitis B and C viruses;
- Evaluation of the effect of complex treatments with the addition of glutathione and eplerenone on the secretion of type IV collagen in urine in liver cirrhosis developed on the basis of hepatitis B and C viruses.

The object of the study. For this purpose, 124 patients with liver cirrhosis were selected. In 60 of them, chronic viral hepatitis V and in 64 of them the disease developed as a result of chronic viral hepatitis C.

Venous blood, serum and urine of patients were collected for immunological and biochemical studies.

Research methods. General clinical, instrumental, laboratory, including biochemical, immunological and statistical methods were used.

The scientific novelty of the research is as follows: it has been proved that hepatorenal syndrome can be diagnosed in the early, hidden stage by determining the functional reserve of the kidneys with the help of a load of 0.45% sodium chloride solution in liver cirrhosis developed on the basis of viral hepatitis B and C;

It has been shown that the determination of glomerular filtration rate with the help of creatinine in liver cirrhosis developed on the basis of viral hepatitis B and C allows early assessment of changes in the functional state of the kidney in hepatorenal syndrome;

In hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of viral hepatitis B and C, fibrosis processes in the liver and kidney occur in common, for the first time it was confirmed by the examination of type IV collagen in urine.

The practical result of the research is as follows:

It has been confirmed that in the hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of chronic hepatitis B and C, it is possible to determine the amount of type IV collagen in the urine in the assessment of the effectiveness of complex procedures;

Addition of glutathione and eplerenone in the complex treatment plan of hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of chronic hepatitis B and C has been proven to stabilize pathological processes in the kidney due to their nephroprotective and antifibrosis effects;

It has been confirmed that the determination of its functional reserve is of great practical importance in controlling the effect of treatment on the changes in the kidney in the hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of chronic hepatitis B and C.

The approach and methods used in the work, the compatibility of the theoretical data with the obtained results, the methodological accuracy of the conducted examinations, the sufficient number of patients, processing using statistical methods, as well as international and local information of the research results. it is explained by the fact that it is compared with the data, the conclusion drawn and the results obtained are confirmed by the competent bodies.

The scientific significance of the research results is that the use of modern markers used in the diagnosis of hepatorenal syndrome developed on the basis of viral liver cirrhosis, which are used to determine the pathological process in the kidney, made it possible to identify the state of its functional reserve and fibrosis processes early.

The practical importance of the research results is that the implementation of the recommendations formed on the basis of the obtained results, the timely

detection of nephropathies observed in liver cirrhosis, and the use of monad treatment measures can moderate the pathological process in the kidney, reduce the number of patients being readmitted to the hospital, and lead to an increase in life expectancy.

The scientific significance of the research results is that the use of modern markers used in the diagnosis of hepatorenal syndrome developed on the basis of viral liver cirrhosis, which are used to determine the pathological process in the kidney, made it possible to identify the state of its functional reserve and fibrosis processes early. Taking into account that glomerular filtration rate increases with infusions or excessive fluid intake, high protein intake, and decreases with physical exertion and negative emotions, patients should be listed above to correctly assess this indicator. We made it free from the above factors. Stages of chronic kidney disease were determined according to modern recommendations. Stage 1 - markers of kidney damage are present and the glomerular filtration rate (GFR) is normal or 90 ml/min/1.73 m2. Stage 2 - when markers of kidney damage are present and GFR is 60-89 ml/min/1.73 m2. Stages 3a and 3b – when CFT decreases proportionally to 45-59 and 30-44 ml/min/1.73 m2. Stages 4 and 5 – when CFT decreases proportionally to 15-29 and <15 ml/min/1.73 m2. Glomerular filtration rate calculated using creatinine and renal functional reserve were determined using CKD-EPI (Cloronic Kidney Disease Epidemiology Collaboration) formulas. In order to determine the amount of creatinine in the blood and its use of KFT, venous blood was taken, and then it was ordered to drink sodium chloride solution with 0.45 - 0.50% of body weight (on average 400 ml). After that, the patient was observed in a quiet sitting position for 1 hour. One hour later, venous blood was taken again to determine the amount of creatinine, and renal functional reserve (RBF) was determined using the following formula. BFZ = (KFT2 – KFT1) / KFT1 × 100 %; KFT1 is its initial indicator; KFT2 - the indicator after the transfer; Depending on the results obtained, the BFZ is preserved (if the increase in KFT is more than 10%), decreased (if the KFT is in the range of 5-10%) and there is no reserve (increase is 5% and less lsa) [Ivanov D.D., 2019]. The economic efficiency

of the scientific innovation is as follows: it has been proven that hepatorenal syndrome can be diagnosed at an early, hidden stage by determining the functional reserve of the kidneys using a load of 0.45% sodium chloride solution in liver cirrhosis developed on the basis of viral hepatitis B and C, that is, unlike expensive immunoenzymatic methods, it is inexpensive biochemical determination of creatinine costs 35,000 soums and saves 120,000 soums per patient. Conclusion: The indicators of the functional reserve of the kidneys determined by the loading of 0.45% sodium chloride solution with the help of creatinine in the blood are 4.3±0.17% in liver cirrhosis developed on the basis of viral hepatitis V, and 4.1±0.12% in its C form. 'lib they were not reliably different from each other (R>0.05) and the indicators indicated no reserve.

It has been shown that the determination of the glomerular filtration rate in liver cirrhosis developed on the basis of viral hepatitis B and C using creatinine allows early assessment of changes in the functional status of the kidney in hepatorenal syndrome. It has been found that the timely detection and application of monad treatment measures moderates the pathological process in the kidney, reduces the number of re-admissions of patients to the hospital and prolongs life.

Social effectiveness of the scientific innovation: determination of glomerular filtration rate using creatinine in liver cirrhosis developed on the basis of viral hepatitis B and C allowed early assessment of changes in the functional state of the kidney in hepatorenal syndrome, and as a result of treatment, the functional reserve of the kidney improved by 18% from 4.1 ± 0.2% to 5.09 ± 0.14 ; The fact that in hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of viral hepatitis B and C, fibrosis processes in the liver and kidney occur in common for the first time was confirmed by the examination of type IV collagen in urine, the correct diagnosis and treatment of hepatorenal syndrome was not performed by several specialists, but only by a gastroenterologist. the pathogenetic therapy of liver cirrhosis is sufficient and the economy of excessive costs of treatment has been achieved; The economic efficiency of the scientific innovation consists of the following: 1) an algorithm for early diagnosis of hepatorenal syndrome developed

in viral liver cirrhosis has been developed, and the determination of the glomerular filtration rate in the functional state of the kidney in the hepatorenal syndrome developed in viral liver cirrhosis B and C with the help of creatinine allows early assessment of changes in the functional state of the kidney in hepatorenal syndrome was given, and as a result of not using other expensive examinations, the cost of diagnosing hepatorenal syndrome for 1 patient amounted to 35,000 soums and made it possible to save extra-budgetary funds by 120,000 soums; 2) determination of glomerular filtration rate using creatinine in liver cirrhosis developed on the basis of viral hepatitis B and C allowed early assessment of changes in renal functional status in hepatorenal syndrome, and as a result of treatment, renal functional reserve improved by 18% from 4.1 ± 0.2% to 5.09 ± 0.14%, which improved the patient's which led to a reduction in the days of inpatient stay and made it possible to save budget funds by 2,640,000 soums and extra-budgetary funds by 1,870,000 soums. Conclusion: The values of collagen IV in urine were 242.33 ± 3.85 μg in liver cirrhosis developed on the basis of viral hepatitis V, and 259.48 ± 3.55 μg in its S form, they were reliably different from each other (R<0.001) and After the indicators, it was confirmed that the group was higher in liver cirrhosis. This shows that fibrosis processes are accelerated in liver cirrhosis developed on the basis of viral hepatitis C, and provides information for timely pathogenetic therapy.

In hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of chronic hepatitis B and C, it has been confirmed that the determination of the amount of type IV collagen in the urine can be used to evaluate the effectiveness of complex procedures.

The social effectiveness of the scientific innovation consists of the following: the use of a modern marker used to identify the pathological process in the kidney in the diagnosis of hepatorenal syndrome developed on the basis of viral cirrhosis of the liver with the help of the examination of type IV collagen in urine made it possible to detect the state of its functional reserve and fibrosis processes early; in case of early diagnosis of hepatorenal syndrome in viral liver

cirrhosis and timely pathogenetic therapy, 4-10% improvement of patients without kidney transplantation was observed and reduction of complications was achieved; the use of proposed diagnostic algorithms and a comprehensive approach improved the quality of diagnosis and treatment of hepatorenal syndrome in viral liver cirrhosis. The economic efficiency of the scientific innovation is as follows: In hospitalization with hepatorenal syndrome with viral liver cirrhosis, following the diagnostic rules: hepatorenal syndrome developed in viral liver cirrhosis reduces the rate of early death in patients with 85%. Conclusion: The values of collagen IV in urine were 242.33 ± 3.85 μg in liver cirrhosis developed on the basis of viral hepatitis B, and 259.48 ± 3.55 μg in its S form, they were reliably different from each other (R<0.001) and After the indicators, it was confirmed that the group was higher in liver cirrhosis. It has been shown that the fibrosis processes are more rapid in liver cirrhosis developed on the basis of viral hepatitis C, and the determination of collagen IV in urine shows how the kidney fibrosis process progresses in liver cirrhosis of different etiologies, early assessment of the results of its treatment, hospitalization of a patient with hepatorenal syndrome developed in liver cirrhosis is economical and life expectancy is reduced by 4-10%.

Implementation of the recommendations formed on the basis of the obtained results, timely detection of nephropathies observed in cirrhosis of the liver, and the use of eplerenone + L-ornithine, L-aspartate and glutathione on the basis of the monand standard treatment can moderate the pathological process in the kidney, reduce the number of re-hospitalization of patients, and improve healing. accelerates the process, shortens the bed day.

The social effectiveness of the scientific innovation is as follows: in the complex treatment plan of the hepatorenal syndrome caused by cirrhosis of the liver developed on the basis of chronic hepatitis B and C, the addition of glutathione and eplerenone proved the stabilization of pathological processes in the kidney due to their nephroprotective and antifibrosis effects. The economic efficiency of the scientific innovation is as follows: for the period of the patient in the hospital: by reducing the length of the patient's stay in the hospital from 12

days to 8 days, the amount of payment for the stay in the hospital was saved from 1200,000 soums for 12 days to 850,000 soums for 8 days 350 reduced by one thousand soums (according to the price list of TTB, a 1-day stay in the hospital is 100,000 soums); reduces rehabilitation costs by 590,000 soums (an average of 120,000 soums is spent on drugs per day); Conclusion: Collagen IV values in liver cirrhosis developed due to hepatitis V virus increased from 245.37 ± 5.2 μg to 224.6 ± 6.4 μg after complex treatment with eplerenone + L-ornithine L-aspartate and glutathione. decreasing differences were reliable ($p<0.05$). In cirrhosis of the liver developed on the basis of hepatitis C, these numbers were 256 ± 4.2 μg and 224 ± 4.25 μg, respectively, and reliable changes were noted ($p<0.001$). This can be attributed to the antifibrosis effect of eplerenone and glutathione drugs.

The composition of the monograph consists of an introduction, 4 chapters, a conclusion and a list of used literature.

CHAPTER I. LITERATURE REVIEW

§ 1.1. Liver cirrhosis and its complications

Cirrhosis of the liver is considered a diffuse process and is characterized by the transformation of its normal structure into fibrous tissue and the formation of regeneration nodules. It is the final stage of a number of chronic liver diseases [8; p. 59-67, 79: p. 545-59, 130: p. 117-71. 26; p. 71-102]. Every year, 5-7% of patients with liver cirrhosis of various etiologies go to the stage of decompensation [94; 406-460-b]. At this stage, not only liver, but also multiorgan (systemic) damage is observed in patients. Before the decompensation stage, there is a compensation (asymptomatic) stage, during which, in most cases, the clinical symptoms of the disease are not clearly observed. Three periods of the compensation phase of liver cirrhosis are distinguished:

- Period 0. Signs of portal hypertension and varicose veins of the esophagus are not detected in patients. Liver stiffness score (liver St ffnees-LSM) greater than 15 but less than 20 or portal vein pressure 5 mm sim. higher than 20 below;
- 1st period. Varicose veins of the esophagus are not detected, significant portal hypertension (LSM≥20) or pressure in the portal vein is 10 mm sim. higher than above;
- 2nd period. Varicose veins of the esophagus and high portal hypertension.

The decompensation stage of liver cirrhosis is manifested by obvious clinical symptoms, and the average life expectancy of patients does not exceed two years. The manifest state of this stage is manifested by a number of complications, and the prognosis of the disease is inextricably linked with them [8; p. 59-67, 87; 241-242-b]. These include hepatic encephalopathy, bleeding from esophageal and gastric varices, ascites (abdominal fluid with or without infection), hepatorenal syndrome, hyponatremia, and infection-related complications [9; p. 152, 66; 24-31., 42;. pp. 25-38].

In most cases, cirrhosis of the liver develops as a result of viral hepatitis (mostly hepatitis B and C). According to information from various sources,

hepatitis causes liver cirrhosis from 40-50% to 70-80% [22; pp. 24-31, 41; pp. 5-8, 44; pp. 75-82].

The clinical manifestation of the disease is different - it can be asymptomatic for many years or in the form of acute hepatitis and chronic inflammatory diseases of the liver. About 20% of patients are diagnosed with liver cirrhosis at autopsy after their death[42;. pp. 25-38, 9; p. 152].

Complaints of patients and clinical manifestations of the disease are related to liver cell failure, portal hypertension syndrome and its complications, and systemic, immune and metabolic damage observed under the influence of the etiological factor [52; 87-88 p]. In most cases, the disease is hidden and has minimal changes or symptoms that are not characteristic of cirrhosis. At the stage of obvious clinical manifestation, i.e. decompensation, its symptoms are different - it shows that the pathological process has spread to all organs and systems. In most cases, patients complain of weakness, reduced work capacity, abdominal discomfort and heaviness, and dyspeptic disorders.

Later, skin itching, impotence in men, and menstrual cycle disorders in women are observed. When examining patients, palmar erythema, vascular asterisks on the chest and shoulders, alopecia in the armpits, lower abdomen, and gynecomastia in men are visible. These changes are associated with hyperestrogenemia observed in liver cell failure in liver cirrhosis. Weight loss of patients due to a decrease in muscle mass is also one of the symptoms of this disease. In the late stages of the disease, peripheral swellings (mostly in the legs), ascites, and venous collaterals appear in the anterior part of the abdomen. Subfebrile fever is observed in about 50% of patients due to continued necrosis processes in hepatocytes [140; p. 1385–1394, p. 106:1279–90].

According to the results of observations of Scandinavian scientists, less than 20% of women and 40% more men with cirrhosis of the liver retained their work. The above-mentioned varnished tongue, vascular asterisks, palmar erythema, gynecomastia occur in up to 75% of patients during the manifest period of liver cirrhosis. One of the most common symptoms in patients is the expansion of the

veins of the esophagus, stomach, intestines, and bleeding from them in most cases ends with death. As a result of reflux esophagitis caused by increased intra-abdominal pressure, patients experience gasping for air, sometimes belching. In addition to the above symptoms, mental disorders occur as a result of central nervous system intoxication and toxic encephalopathy [42;. 25-38., 9;].

In the initial stages of cirrhosis of the liver, the enlargement of both lobes is determined. Later, its left lobe becomes more enlarged. In one third of patients, the surface of the liver may be uneven. In the last stages, the size of the liver decreases, the hepatolienal syndrome is accompanied by hypersplenism [52; p. 87-88, 30;].

In the biochemical analysis of blood, approximately 40% of patients have a normal level of bilirubin, transaminases are slightly elevated. Elevated gamma transferases and presence of hypoalbuminuria are characteristic signs of liver cirrhosis. In the general analysis of blood, thrombocytopenia, sometimes post-bleeding anemia, increased erythrocyte sedimentation rate and leukocytosis are detected when infection is added [42;. 25-38., 67; pp. 13-17].

The Child-Pugh classification is used to assess the severity of liver cirrhosis. It is very convenient because it is possible to determine the indicators used to determine the severity of the disease in all systems of medicine (Table 1.1.).

Table 1.1

Description of the assessment of severity of liver cirrhosis according to the Child-Pugh classification

Indicators	**POINTS**		
	1	**2**	**3**
Ascites	No	in small quantities	medium\large amounts
Encephalopathy	No	few	Obvious
Bilirubin level (mg/dL)	<2,0	2-3	>3,0
Albumin indicator	>3,5	2,8-3,5	<2,8

(mg/l)			
Prothrombin time prolongation (seconds)	1-3	4-6	>6
Total points			Classes
5-6			A (compensation)
7-9			V (subcompensation)
10-15			S (decompensation)

If the cumulative score is less than 5, the average life expectancy of patients is 6.4 years, and if it is 12 or more, it is 2 months [10].

Also, in order to determine the etiology of the disease in cirrhosis of the liver, it is appropriate to use the following table 1.2. to analyze the laboratory parameters along with viral markers.

Table 1.2

Analysis of laboratory indicators recommended for detection in liver cirrhosis

№	**Laboratory indicators**	**Amount in blood**	**Clinical analysis**
1	Total and bound bilirubin	↑↓	Hepatocyte necrosis and cholestasis
2	ALT and AST	↑	Hepatocyte necrosis
3	ALT and AST	N	A decrease in the number of hepatocytes
4	IF, GGTP, cholesterol	↑	Cholestasis of bile ducts inside and outside the liver
5	IF, GGTP, cholesterol	↑↓N	Cholestasis accompanied by liver parenchymatous damage
6	GGTP	↑	Hepatocellular cholestasis, toxic liver damage
7	Albumins, prothrombin index	↓	Hepatocellular failure

8	Gamma globulins	↑	Immune (autoimmune) disorders
9	Serum iron content, ferritin	↑	Hepatocyte necrosis (hemachromatosis, secondary accumulation of iron in the liver)

Note: ALT - alanine aminotransferase, AST - aspartate aminotransferase, IF - alkaline phosphatase, GGTP - gamma-glutamyltranspeptidase.

As mentioned in the beginning of this paragraph, cirrhosis of the liver caused by viral hepatitis is common among the population.

At the same time, in some cases, the combined effect of viruses and alcohol can cause cirrhosis of the liver in patients at the same time [43;. 57-65-b, 55; pp. 6-13, 56; pp. 43-52]. In a series of observations, when these two negative effects come together, it is noted that the disease is severe before cirrhosis is formed, that is, at the stage of hepatitis. Some authors compared chronic hepatitis developed as a result of these two etiological factors. As a result of the harmful effects of alcohol (or drugs) with viral hepatitis, liver enlargement is noted in almost all cases, and splenomegaly and jaundice are noted in a large number of patients. Also, under the influence of the virus-alcohol double factor (hepatitis C virus 32.4%, B virus 53.8%), the disease was manifested by cytolysis syndrome in most patients. Long-term alcohol abuse (an average of 70 g of ethanol per day for 11 years) had a significant negative effect on the survival of viral hepatitis B and C. In this group of patients, severe liver fibrosis and cirrhosis (3 times more than those with viral hepatitis B, 2 times more than those with viral hepatitis C) were detected, in 57% of cases a rapidly worsening form of the disease was observed, the duration of cirrhosis was reduced by almost 2 times. [4; p. 45].

O.O.Znayko, who examined the liver puncture of 380 patients with viral hepatitis C (34 of them abused alcohol), found that alcoholics had significantly more liver fibrosis 3-4 according to the Knodell criterion (38.2±8, 3% and 12.5±20%, respectively) [23; 44-p]. Similar results are also presented in the observations of some other authors [43;. 57-65 p]. According to the observations of A.L. Bondarenko and S.V. Baramzina [11; Asthenia, dyspepsia, portal

hypertension, liver → cellular failure and cholestasis were reliably observed in patients with liver cirrhosis developed on the basis of viral hepatitis C (n=30). In most cases, the disease is hidden in them, and the first sign can be recurrent bleeding and repeated jaundice. According to the authors, in 75% of cases, the process developed slowly in patients, and 10 or more times passed before the development of cirrhosis, and in 25%, it was formed in less time. According to other observers, almost a quarter of patients with hepatitis C had cirrhosis when the disease was diagnosed [53; pp. 67-71, 45; 6-11 p].

In 1978, M. Wiese found out the following in his fundamental examination based on the observation of 420 patients with acute viral hepatitis C. After 20 years, 70% of them were anti-HCV, almost 50% had RNA HCV, and only 0.4% had liver cirrhosis [102; pp. 1616-1624, 167; 29; 13-18 p]. In the observation of a Spanish scientist in 78 patients with developed and complicated liver cirrhosis due to viral hepatitis C, 57.7% of them had liver failure, 30.8% had bacterial infection, 7.7% had gastrointestinal bleeding, and 3.8% had hepatocellular carcinoma (141; 823-830-b). In a study conducted in Japan, 38.6% of them had hepatocellular cancer, 34.1% had gastrointerstitial bleeding, and 6.8% had bacterial infection [85; 83; 160; pp. 1276-1283, 135;].

Belarusian scientists found that 64.1% of those who were followed up in 2002-2013 with HCV-associated cirrhosis of the liver died from liver-kidney failure, 25.6% from bleeding from esophageal veins, 10.3% of cases. caused by hepatocellular carcinoma [44; pp. 75-82, 112; pp. 55-68, 113; 136; 7544-7554-b, 137; 207-220-b].

M.V. According to Maevsky (n=51), the disease was insidious and averaged in class B according to the Child-Pugh classification. In most cases, liver cancer was observed in patients with combined viral and alcohol etiology. In comparison to cirrhosis of the liver developed only due to a virus, cases of death were observed much later in those who developed due to alcohol reasons (42; p. 25-38).

In 1996-2005, the etiology of the disease was studied in 947 patients with cirrhosis of the liver treated in the hospital. Alcoholic cirrhosis of the liver was

detected in 438 of them, 63.4% of deaths were recorded, and their life expectancy was equal to 54.9 years. Patients with advanced liver cirrhosis due to chronic hepatitis C (n=213) had a mortality rate of 2.8% and a longer life expectancy of 73.5±3.5 years [50; 6; pp. 19-24, 163; 443-459-b].

N. Toshikuni and co-authors observed patients suffering from alcoholic (n=75) and advanced liver cirrhosis due to chronic hepatitis C (n=152) and co-authors found that survival increased significantly when patients stopped drinking alcohol [160; pp. 1276-1283].

In another observation, the death rate was 3 times higher in liver cirrhosis caused by viral infection (hepatitis B and C viruses) than in alcoholics. However, in both cases, patients developed liver cancer in the same way [4, 158; pp. 6518-6528].

According to the results of M. Mutsira's observations (n=196), liver cirrhosis developed on the basis of chronic hepatitis C was dominated by patients of "C" class according to the Child-Pugh classification (41.8%), and they had more ascites (53.4 %), hepatomegaly (82.2%), splenomegaly (86%), dilation of esophageal veins (71%) was observed. In the biochemical analysis of blood, aminotransaminases were high in 90% of patients, alkaline phosphatase in 32.9%, and gamma-glutamyltransferase in 74% of cases. Hypoalbuminemia was noted in 2/3 of patients. In the general analysis of blood, anemia was found in 48.9% of patients, and thrombocytopenia in 85.7%. A decrease in the thrombin index was observed in 50.5% of patients [44; p. 75-82, 77; 80; 116; p. 9-14, 119; 737-41-b, 152; 1-12 p, 154; 36-66 p].

In all observations, when liver cirrhosis is caused by viral hepatitis and alcohol together, compared to monoetiological cases, the disease worsens rapidly and death occurs 50% more often, and liver cancer is also noted in them. In almost all scientific observations, this opinion is confirmed and generally accepted [40; 44-46 p].

As mentioned in the introduction of this paragraph, a number of complications observed in cirrhosis of the liver play a decisive role in the quality

and duration of the patient's life. Therefore, early detection of these complications and concomitant treatment are of great importance for scientific and practical medicine.

Among the many complications of liver cirrhosis, hepatorenal syndrome is one of the least studied. Full-fledged scientific observations dedicated to it have not been conducted in our republic.

§ 1.2. Hepatorenal syndrome in liver cirrhosis

Hepatorenal syndrome occurs as a result of kidney damage based on obvious clinical signs of liver disease, including cirrhosis, in the absence of other causes leading to kidney failure. In 1994, the international ascites club formulated the major criteria for hepatorenal syndrome, and in 2007 they were revised and partially changed. According to some information from scientific sources, approximately 15% of patients with cirrhosis of the liver develop hepatorenal syndrome within 6 months after the first hospitalization due to ascites, and 40% within 5 years [62; 72; 92; p. 397-417, 89; 90; 156; p. 364-375, 157; 1246-1255-b].

The above-mentioned club recommended the following diagnostic criteria for hepatorenal syndrome:

- Liver cirrhosis with ascites;
- Serum creatinine level of 133 mmol/l and higher;
- Absence of shock symptoms;
- The presence of hypovolemia (if no positive changes in kidney function are observed after the cancellation of diuretics for two days and after administration of 1 g of albumin per 1 kg of body weight);
- Not taking nephrotoxic drugs at the same time and in the recent past;
- Absence of kidney parenchymatous diseases (proteinuria is less than 0.5 g per night, microhematuria is not detected, there are no signs of kidney damage on ultrasound) [26:71-102-p., 166; 1047-81-b, 168; 55-64 p].

There are two types of hepatorenal syndrome. Its first type is associated with rapid deterioration of kidney function in response to increasing deterioration of

liver function. This type is often observed in severe alcoholic hepatitis and in the terminal stages of liver cirrhosis with spontaneous bacterial peritonitis. In this type of patients, a 100% increase (at least 221 mmol/l) of creatinine in the blood compared to the primary level is characteristic [47; 75; 600-610-p, 78:1505-13-p, 153; 1735-1744-b, 155; 578-581-b].

The second type of hepatorenal syndrome is observed in liver cirrhosis with ascites and resistant to diuretics, it is stable and slowly increases [26: pp. 71-102, 161; 352-9-b, 162; 43-8-b].

4 mechanisms are distinguished in the development of hepatorenal syndrome:

- Reduction of effective arterial blood flow due to expansion of vessels in the abdominal cavity;
- Due to the activation of the sympathetic nerve and the renin-angiotensin-aldosterone system, the development of renal vasoconstriction and violation of the mechanisms of vascular tone maintenance;
- As a result of the development of cirrhotic cardiomyopathy, heart failure and weakening of the compensatory mechanisms that maintain blood pressure (increased blood pumping activity of the heart due to the expansion of the vessels of the abdominal cavity);
- Increase in the synthesis of vasoactive mediators (cysteinyl, leukotrienes, thromboxane A2, F2-isoprostanes, endothelin-1), which cause blood flow and glomerular microcirculation disorders in the kidneys [126:543-52-p., 81:558-67-p, 165: pp. 55–69, pp. 100:313–6, pp. 88:1–20, pp. 71:17–30, pp. 145:439–47, pp. 26:71–102].

In some sources, it is noted that hepatorenal syndrome develops on the basis of bacterial infection in most cases (30%) [26:71-102-p., 25: 1074-92-p] and the average life expectancy of patients is 1-3 months shown.

There are no specific clinical signs characteristic of hepatorenal syndrome. Patients are disturbed by symptoms such as thirst, apathy, lethargy. In the objective examination, the abdomen is enlarged, blood pressure is reduced, and in some

cases, jaundice is increasing. Oliguria, decreased glomerular filtration rate and a slight increase in serum creatinine are detected. In rare cases, obvious proteinuria and minor changes in urine sediment are found [105:1819-27-b, 91; 93; 101].

If positive results are not observed in patients with obvious ascites, arterial hypotension and hyponatremia are detected, it indicates the development of hepatorenal syndrome. Here, this syndrome, which develops in liver cirrhosis, should be distinguished from acute tubular necrosis, glomerulonephritis, toxic nephropathy, and nephropathies developed in chronic heart failure [124; 69: p. 659-682, 121; 83-100 p. 139; p. 61-68].

30 years ago, creatinine levels of 150 mmol/l and higher were accepted as criteria for kidney failure in hepatorenal syndrome. This corresponds to an indicator of KFT of 40 ml per minute and below [17; pp. 36-38, 76; pp. 164–176, 122; 2017-26-p,103; 593-603-b, 138; pp. 116–122].

According to the new concept of the International Ascites Club (International Ascites Club), the amount of urine excreted in the diagnosis of acute kidney injury in patients diagnosed with liver cirrhosis is not taken into account. Oliguria is often caused by sodium retention in cirrhosis with ascites syndrome. They may have increased diuresis on the basis of diuretic drugs, even if the KFT is relatively normal [108; 317-24-p, 74; 968–974., 150; 1310-1318-b, 151; 715-32-b].

Classification of acute kidney injury in cirrhosis of the liver is based on the increase of creatinine compared to the basal (primary) indicator or the high (peak/peak) increase during hospitalization in the new system [123; 505-20-p, 146; 2087-107-p, 147; 1651-3].

According to the criteria of KDIGO, its I stage is 1.5-2.0 times the basal/primary indicator or 265 mmol/l and higher. Acute kidney injury in the 2nd stage is defined as cases where creatinine is 2 times more than the norm but less than 3 times. In stage 3, creatinine increases more than 3 times [118; 179–184 p].

Recent studies have shown that the efficiency of treatment in stage 1 of acute kidney injury developed on the basis of cirrhosis of the liver is inextricably linked with creatinine values. If it exceeds 132.6 μmol/l, it is not good because of

the disease [95; pp. 474–481, 111;]. Unlike the experts of KDIGO, the experts of the international ascites club recommended to divide the 1st stage of acute kidney damage observed in liver cirrhosis into two small groups, i.e. "a" and "b".

In subgroup 1a, creatinine is 132.6 μmol/l, and in subgroup 1b, the indicator is higher [74; pp. 968–974].

A new algorithm for the treatment of acute kidney injury in cirrhosis of the liver was recommended based on a number of prospective observations based on the new stages [74; p. 968–974]. In its 1a stage (increased creatinine up to 132.6 μmol/l), in some cases, a number of provoking factors (cancellation of hepatotoxic drugs, non-specific anti-inflammatory drugs, diuretics and β-blockers stopping, increasing plasma transfusion) will be sufficient to eliminate. In stage 1b, it is recommended to completely cancel diuretics and inject 1 g of albumin per 1 kg of body weight for two days [99; pp. 2064–2077, 74; pp. 968–974, 169; pp. 702–709]. It is necessary to titrate the dose of albumin during infusion [128; pp. 923–930, 82. pp. 983–992].

When hepatorenal syndrome is accompanied by ascites, it is necessary to inject albumin in order to prevent it. Therefore, if symptoms of bacterial peritonitis are observed in them, 1 mg of albumin per 1 kg of body weight is injected into the patient, this dose is reduced by 1 mg from the third day [134:529-537-p.,132:360-367-p., 144; pp. 955–961, 148; 424-9-b]. Also, 400 mg of norfloxacin per day is prescribed to prevent bacterial peritonitis in hepatorenal syndrome.

In a number of scientific works, the changes in the kidneys observed in cirrhosis of the liver were considered as a functional state (p. 26:71-102), but at the same time, modern tests used to detect nephropathy in the early stages were not used. In particular, as one of the diagnostic criteria of hepatorenal syndrome, the indicator of protein excreted in urine overnight is defined as 0.5 g or less. But according to the latest recommendation, if less than 10 mg of protein is excreted in the urine in one night, optimal albuminuria, if 10-29 mg is excreted, it is more than normal albuminuria (in the previous high norm), if 30-299 mg is excreted in the high norm (in the previous microalbuminuria), 300-1999 mg of excretion is very

high (former macroalbuminuria/proteinuria), in cases of excretion of 2000 mg and more, nephrotic albuminuria was considered [117; 1-150-b].

Creatinine is also used in Uzbekistan to assess kidney function. It should be noted that its indicators change depending on the age, gender, metabolic state of the body, muscle mass, balance of water-salt exchange [117; 1-150-b]. When the KFT is 40-90 ml per minute per body surface of 1.73 M2, there is no correlation between the increase in creatinine and the decrease of KFT. This is due to the increase in the secretion of creatinine in the tubules due to the decrease in KFT [117; 1-150-b].

§ 1.3. Importance of renal functional reserve and type 4 collagen in early detection of nephropathy symptoms

It is known that KFT can be determined using special formulas based on the level of endogenous creatinine in blood serum. One of the currently used formulas is the Cockroft-Gault formula, according to some data, the indicator is 23% higher than the original level when it is used to determine the KFT [57;62-66-b]. Also, MDRD (Modification of Diet in Renal Disease [58; 82-85-p.] CKD - EPI (Cloronic Kidney Disease Epidemiology Collaboration) formulas are used in practice to determine it [59; 259-298-p, 60; 77-80 -b].

Using the MDRD formula, KFT is calculated based on gender, age, nationality and the patient's body surface area of 1.73 m2. This will help him identify the stages of SBK. However, the formula increases the number of patients with SBK in screening examinations in people under 18 years old, pregnant women, people over 70 years old, in cases where kidney function is normal or slightly weakened [61; 425-428-b, 60; 77-80 p].

Currently, the CKD-EPI formula is used more when the KFT is 60-90 ml/min per 1.73 m2 body surface per minute. It can be applied to healthy people in the initial period of SBK. But using this method, KFT is determined based on creatinine indicators. The main causes of errors in determining KFT using

creatinine are detailed in the 2012 recommendations of Kidney Dysensei: Improving Outcomes (KDIGO) [117: 1-150].

It has been confirmed in numerous scientific studies that not only in certain physiological conditions, but also when excess protein enters the body (orally or intravenously), it leads to a temporary increase in CFT and an acceleration of plasma flow [63; pp. 81-88].

Filtration speed may vary depending on the protein used). After loading with meat protein, CFT, renal plasma, and blood flow in the spleen increase for one hour and remain for several hours [48; pp. 396-402, 54; p. 46-55, 63; pp. 81-88, 64; p. 15-26, 35;]. Based on the mentioned data, the renal functional reserve (RBF) consensus and its evaluation tests were created. BFZ is understood as its ability to raise KFT from the basal, i.e., primary state to a maximum high level. To achieve it, all nephrons, not only deep, but also superficial, take part in the process. The method of determining BFZ was first developed by J.P. Recommended by Bosch. Usually, the expression of the difference in the percentage of the filtration of the balls determined after the loading with the basal, that is, the initial KFT, is called BFZ. If this indicator is more than 10%, BFZ is preserved, between 5-10% it is reduced, and if it is less than 5% or negative, it is considered that there is no reserve [36; 112-118-b, 115; 260-272-b]. The absence of BFZ indicates that the glomeruli are in a state of hyperfiltration [49; pp. 48-53, 131; pp. 1138-1139, 133; pp. 11-17, 151; 5-10 p].

One of the simplest and most physiological methods for testing renal functional reserve is the use of a semi-diluted (0.45%) solution of NaCl. Initially, KFT is calculated based on the amount of creatinine in the blood. Then the patients drink 0.45% aqueous NaCl solution in the amount of 0.5% of body weight for 3-5 minutes. This volume and concentration of the solution is considered sufficient to remove excess sodium ions. After one hour, the concentration of keatinine in the blood is determined and the KFT is calculated. Its percentage increase indicates the presence of BFZ.

An increase in KFT after screening indicates that there is a reserve in the filtration fraction. According to the change in KFT, BFZ is evaluated as preserved (increased by more than 10%), decreased (if increased by 5 - 10%) or no reserve (in cases where it is less than 5%). BFZ may not be present even with preserved KFT, which indicates that the organ is undergoing a hyperfiltration process and the non-immune process is increasing. It confirms that the kidney is working in a state of hyperfiltration with high power in cases of reduced or absent scores.

In most of the literature, in the presented data, BFZ was studied in patients with diabetes in most cases. However, there is almost no information on the use of this test in a number of other diseases, including hepatorenal syndrome. However, the study of BFZ in hepatorenal syndrome developed on the basis of liver cirrhosis provides an opportunity for early diagnosis of nephropathy.

In addition to the above, one of the markers of kidney damage is the excretion of type IV collagen in the urine. It forms the basis of the basal membrane of balls and tubules. According to some authors, the appearance of this protein in urine is one of the early morphological signs of nephropathy [31; 32; 33; p. 87-93, 120; pp. 885-893, 143; 1473-80-b]. Compared to healthy people, patients with normoalbuminuria have a higher urinary excretion rate. It has been noted that IV collagen concentrations are high in the tissue of patients who underwent kidney biopsy and that it is directly related to the protein level in the urine of patients diagnosed with normoalbuminuria. In this study, urinary excretion of type IV collagen was detected even in individuals with normal albumin levels. The authors showed that type IV collagen was present in 26% to 45% of patients with a confirmed diagnosis of diabetes and normoalbuminuria in their urine based on another examination. In most cases, this condition can be noted more often when hypertension and diabetes occur together [142; pp. 3337-3344, 65; 552-560-b]. The given data confirm that urinary excretion of type IV collagen can be observed before the clinical symptoms of nephropathy appear, and that it is appropriate to use it in the diagnosis of fibrotic processes in the kidney even in hepatorenal syndrome.

It is known that the development of the fibrosis process in the kidneys greatly aggravates the course of the main disease, including cirrhosis of the liver. At this point, the use of effective anti-fibrosis drugs and the control of the process with the help of collagen IV are of great practical importance in liver cirrhosis.

In an experimental study conducted by Chinese scientists, a model of interstitial fibrosis in the kidney was called in rats. The effect of eplerenone on kidney damage was studied. According to the obtained results, eplerenone reduced the processes of interstitial fibrosis. Histological examination of eplerenone-treated rats on days 7 and later showed significantly higher amounts of fibrotic tissue in the kidneys of the latter group compared with those in the control group. Immunohistological tests conducted by the authors showed that eplerenone reduces inflammatory processes in the kidney, proliferation in interstitial tissues, and oxidative stress. Based on the obtained results, the researchers concluded that eplerenone reduces renal interstitial fibrosis by having an anti-inflammatory effect [p. 84:557-66].

In numerous studies, it has been confirmed that the deficiency of endogenous glutathione in liver diseases, including liver cirrhosis developed on the basis of viral hepatitis, by supplementing the body, gives positive results [3].

As we conclude the literature analysis chapter, it is necessary to note the following. Liver cirrhosis developed as a result of viral hepatitis B and C has not been compared in our republic. Also, type IV collagen, a marker of fibrosis, was not used in the early diagnosis of hepatorenal syndrome, one of the serious complications of liver cirrhosis. In addition, a reliable and early sign of kidney dysfunction is the calculation of its functional reserve, scientifically proven. But until now, this test has not been used to evaluate the functional changes in the kidneys observed in liver cirrhosis. However, its detection allows early detection of kidney dysfunction observed in liver cirrhosis.

The mentioned cases confirm that the goals and tasks planned to be fulfilled in this scientific research are one of the urgent problems.

CHAPTER II. RESEARCH MATERIAL AND METHODS

§ 2.1. Clinical description of the patients included in the study

In the scientific research work, 124 of the 350 patients treated at the clinic of the Andijan State Medical Institute, who were diagnosed with advanced liver cirrhosis on the basis of hepatitis B and C, were observed. The following criteria of hepatorenal syndrome, recommended by the "international ascites" club in 1994 and revised and partially amended in 2007, were used to separate them into a separate group [20].

- Liver cirrhosis with ascites;
- Serum creatinine level of 133 mmol/l and higher;
- Absence of shock symptoms;
- The presence of hypovolemia (if no positive changes in kidney function are observed after the cancellation of diuretics for two days and after administration of 1 g of albumin per 1 kg of body weight);
- Not taking nephrotoxic drugs at the same time and in the recent past;
- Absence of kidney parenchymatous diseases (proteinuria is less than 0.5 g per night, microhematuria is not detected, there are no signs of kidney damage on ultrasound examination) [20; 26; 71-102-b].

Patients who were diagnosed with hepatorenal syndrome and included in the study were divided into two groups. The first group consisted of 60 patients with liver cirrhosis caused by viral hepatitis B, 28 men (46.7%) and 32 women (53.3%), their average age was 46.44±1.38. The second group was caused by chronic hepatitis C. included 64 patients with liver cirrhosis. 3 patients died of esophageal variceal bleeding and 1 died of hepatocarcinoma and were not included in the follow-up group. Of the remaining 60 patients, 25 were men (41.6%) and 35 were women (58.4%), the average age was 48.82±1.6. 45% of them were patients with genotype 1, 15% with genotype 2, and 13% with genotype 3. Genotypes were not determined in the remaining cases.

Class A according to Child Pew, class B in 46% and class C in 24% were recorded in 30% of the monitored patients.

Based on the goals and tasks set before us, all patients underwent excellent clinical and laboratory-instrumental examinations at the clinic of the Andijan State Medical Institute and were observed in an outpatient setting for 3 months.

Eplerenone, veroshpiron, glutathione and L-ornithine L-aspartate drugs with hepato-nephroprotective effects were prescribed to all patients with clinical and laboratory signs of hepatorenal syndrome. Based on the instructions, albumin preparations in the amount of 1 mg per 1 kg of body weight were administered intravenously several times.

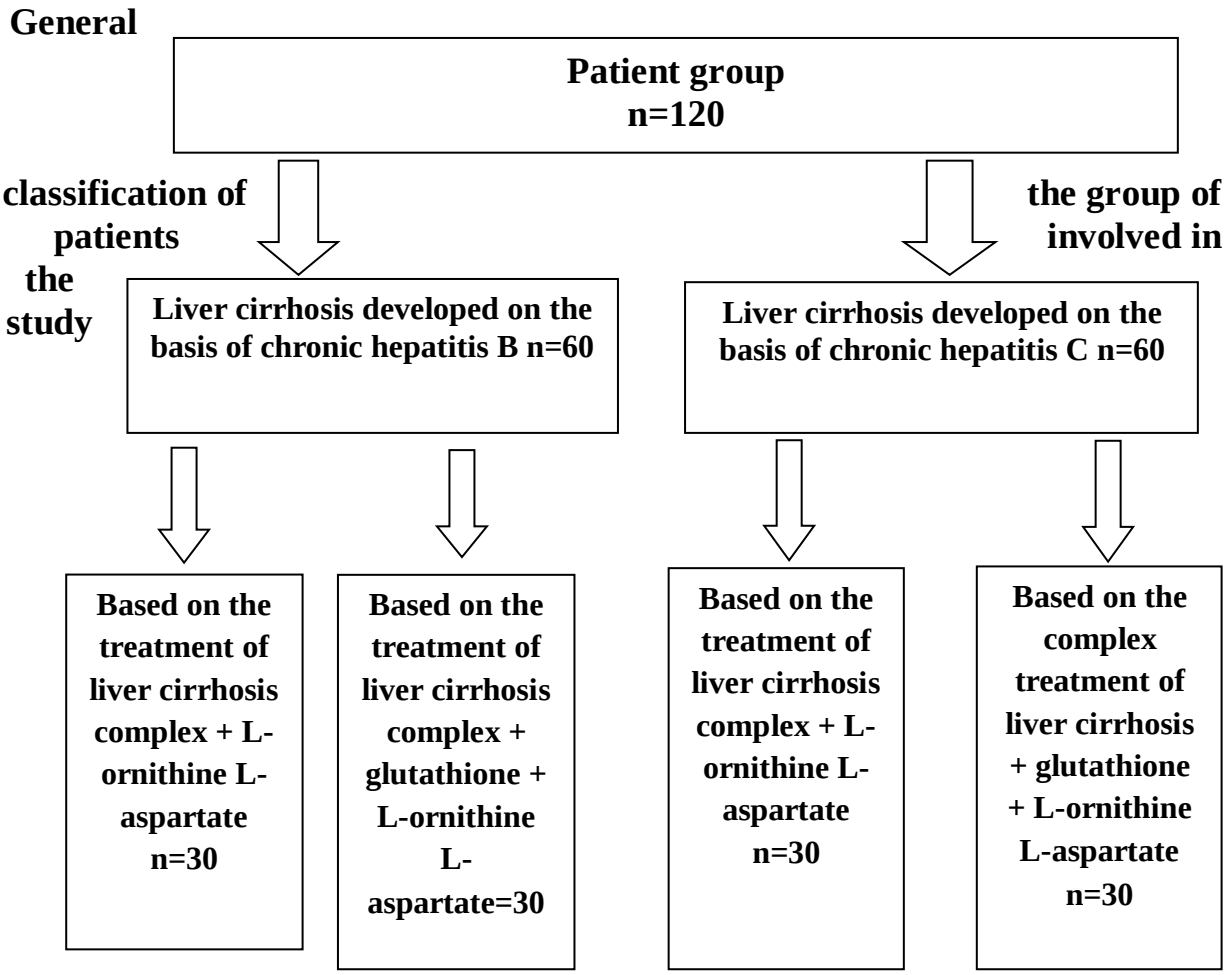
Follow-up criteria: patients diagnosed with advanced liver cirrhosis due to chronic hepatitis B and C.

Criteria for exclusion from the study: liver fibrosis developed as a result of chronic heart failure, all diseases leading to nephropathy (autoimmune and systemic diseases, kidney diseases, amyloidosis and related diseases, etc.).

All scheduled general and special laboratory-instrumental examinations were performed in the patients under observation, in the first three days of hospitalization before the start of treatment and after 3 months. Patients diagnosed with hepatorenal syndrome received glutathione and L-ornithine L-aspartate drugs, which have nephroprotective and antifibrosis effects, along with the standard treatment used in liver cirrhosis and its complications. Glutathione was given to patients 1.2g based on the severity of the disease. in a dose of 0.6 g intravenously for 10 days, then intramuscularly in a dose of 0.6 g for a week. L-ornithine L-aspartate was also given intravenously to patients in a dose of 5 g for 10 days according to the severity of the disease.

Detailed information about the groups of patients included in the study is presented in Figure 1.

Drawing2.1



§ 2.2. Inspection methods

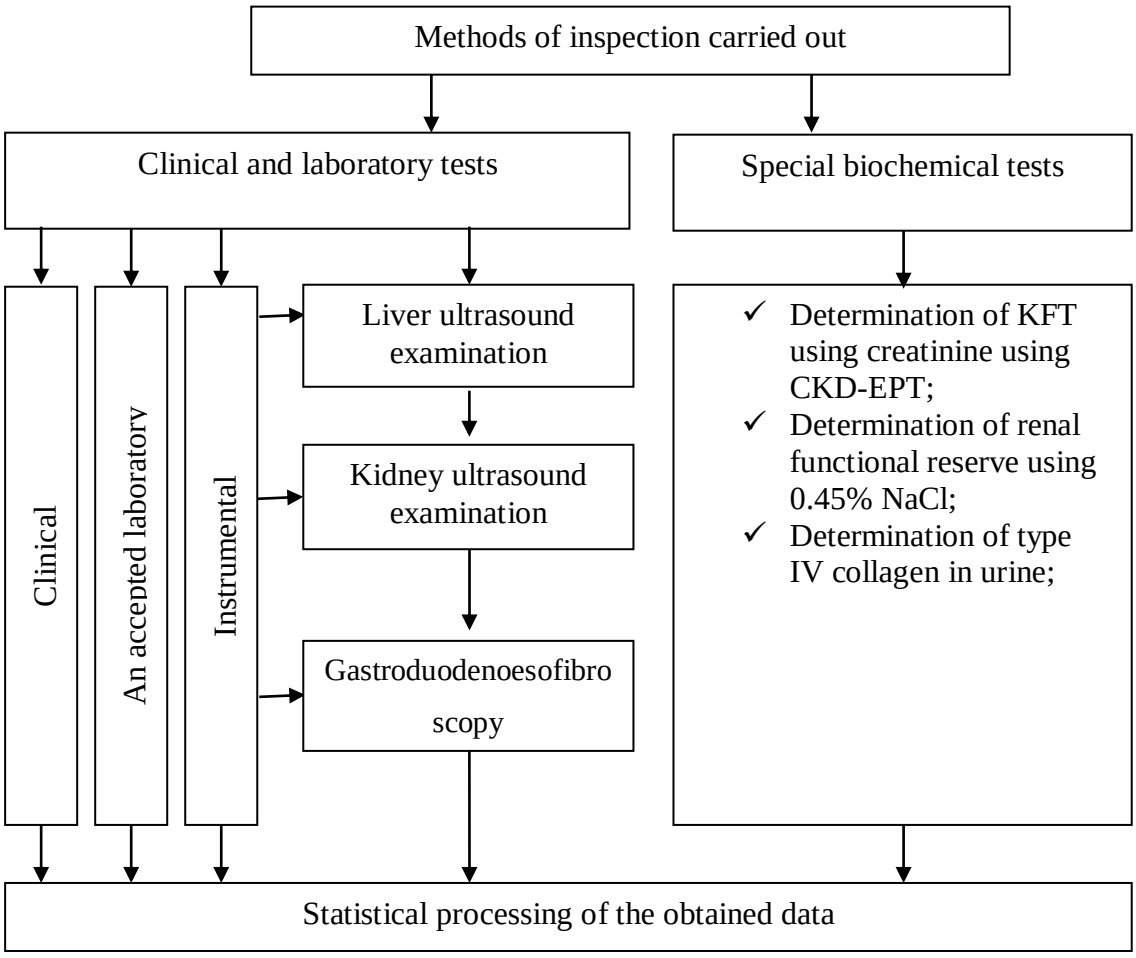
The inspection plan covered the following:

- Patient complaints, anamnesis, objective examination. When collecting anamnesis, special attention should be paid to their profession, if they consumed alcohol, the duration during the week (daily, once a week, once a month in small amounts or 200-300-500 ml or more). given Also, complaints were carefully asked and objectively examined;

- In addition to the generally accepted ones, the special laboratory and instrumental tests presented in Figure 2 were carried out.

Drawing- 2.2

Examinations of patients included in the follow-up



The examinations presented in the drawing, as we described above, were repeated in the first three days of the patients' admission to the clinic and again three months later. After they were discharged from the hospital, their condition was monitored by phone.

Conducted laboratory analyses. Complete blood analysis was performed on Mindray BA-88A (Switzerland) hematological analyzer. Hemoglobin amount, erythrocytes, leukocytes, thrombocytes, hematocrit indicators were determined.

The leukocyte formula was counted by staining the blood smear with the Romanovsky-Giemza method and using a "BAUSCH-LOMB" (Russia) microscope. Erythrocyte sedimentation rate was determined by Panchenko's apparatus when blood was mixed with 5% sodium citrate solution in a 100 mm tube.

Microalbuminuria and overnight proteinuria were determined using the laboratory test method recommended by V. V. Dolgov and co-authors [21].

Analysis of biochemical indicators of blood. For the biochemical analysis of blood, 10 ml of blood was taken from the wrist vein in the morning on an empty stomach before the patients took the drugs. The collected blood was centrifuged for 15 minutes until the serum was separated. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, glucose, urea, creatinine, total protein, potassium, sodium, blood lipid spectrum were determined using the reagents of the company "Human" (Germany). Analyzes were carried out on a "Mindry BA-88" biochemical analyzer.

Type IV collagen in urine was determined as follows. The VESTER-BEST immunoenzyme analysis (IFA) kit, consisting of 96 tests, was used for its determination in urine. This set of reagents (VESTER-BEST, Russia) detects COL4 in human blood, plasma, cell homogenates, enables detection by immunoenzymatic method in cell lysate and other biological fluids in vitro.

Glomerular filtration rate was calculated using the CKD-EPI (2009) formula modified in 2011 based on serum creatinine (with the help of an online calculator at http://nefrosovet.ru/site).

Taking into account that glomerular filtration rate increases with infusions or excessive fluid intake, high protein intake, and decreases with physical exertion and negative emotions, patients should be listed above to correctly assess this indicator. We made it free from the above factors. Stages of chronic kidney disease were determined according to modern recommendations. Stage 1 - markers of kidney damage are present and CFT is within the norm or when it is □90 ml/min/1.73 m2. Stage 2 - when there are markers of kidney damage and GFR is

60-89 ml/min/1.73 m2. Stages 3a and 3b – when CFT decreases proportionally to 45-59 and 30-44 ml/min/1.73 m2. Stages 4 and 5 – when CFT decreases proportionally to 15-29 and <15 ml/min/1.73 m2.

The glomerular filtration rate calculated using creatinine and the functional reserve of the kidneys were determined using the CKD-EPI (Cloronic Kidney Disease Epidemiology Collaboration) formula. In order to determine the amount of creatinine in the blood and CFT using it, venous blood was taken and then 0.5% of the body weight was 0.45 - He was ordered to drink 0.50% sodium chloride solution (average 400 ml). After that, the patient was observed in a quiet sitting position for 1 hour. An hour later, venous blood was taken again to determine the amount of creatinine, and BFZ was determined using the following formula.

BFZ = (KFT2 – KFT1) / KFT1 × 100 %

KFT1 is its initial indicator

KFT2 is the indicator after the transfer

Depending on the results obtained, the BFZ is preserved (if the increase in KFT is more than 10%), decreased (if the KFT is in the range of 5-10%) and there is no reserve (increase is 5% and less lsa) was evaluated as [24: pp. 9–14].

All laboratory immunoenzyme and instrumental tests were carried out in the laboratory of Andijondavlat Medical Institute clinic.

INSTRUMENTAL INSPECTION METHODS

Ultrasound examination of the hepatobiliary system. UTT of patients is performed using a 3.5 MHz oscillating sector mechanical sensor on a real-time "DS-40, China" device. After 8-12 hours of fasting, our subjects were examined by the traditional echographic method, and the following indicators of hepatobiliary arteritis were determined: topography, volume (shape, contours, size, lower costal angles) and exoscape (echogeneity, sound conductivity, capsule, parenchyma, bile ducts, intrahepatic vessels).

In order to clarify the small vessels in the UTT image, using the standard program, the magnification mode of the area to be examined was applied. The inferior vena cava diameter was measured by longitudinal scanning of the caudal lobe of the liver. Liver volume (Liver V) was calculated based on the equation proposed by Zoli et al.

At the same time, the topography, shape, size, wall, exogenity of the liquid inside, v portae and v cava inferior diameters of the gallbladder were studied. In addition, in order to exclude the presence of free fluid in the abdominal cavity and chest, patients were subjected to ultrasound examination in horizontal and vertical positions.

Gastroduodenoesofibroscopy. The test was performed on an empty stomach at lunch on a PENTAX Europe (Japan) device. Special attention was paid to the degree of expansion of the esophagus and stomach veins.

Statistical analysis of numerical indicators. MS Excel (2013) package computer program was used for statistical processing of the data obtained in the study. Arithmetic mean and standard deviation (M±m) of the indicators presented in all tables were calculated. Reliability of differences between groups was determined using Student's criterion for odd and even differences. Correlation analysis was conducted using Pearson's correlation coefficient and determining its significance based on reliability tables.

CHAPTER III. PERSONAL TEST RESULTS

§ 3.1. Comparative analysis of complaints of patients diagnosed with advanced liver cirrhosis based on chronic hepatitis B and C before treatment

In both groups of patients diagnosed with advanced liver cirrhosis based on chronic hepatitis B and C under our observation, a careful anamnesis was collected and the following was identified: in 67% of patients, the disease was transmitted parenterally. 5% of them received blood transfusions, 15% underwent surgery, 25% underwent dental services, 12% underwent endoscopic examinations and other medical interventions, and 10% of patients indicated the possibility of sexually transmitted diseases. In the remaining patients, it was not possible to determine the source of the source of infection.

When investigating concomitant diseases, 30% of patients were diagnosed with chronic gastroduodenitis, 15% with duodenum and gastric ulcer disease. 22% of the subjects during the anamnesis collection did not deny that they had abused alcohol on the basis of cirrhosis of the liver, and as a result, it turned out that it aggravated the course of the main disease. In 5% of patients, the auscultation and dopplerographic examination of the vessels showed that the arteries were clearly damaged by atherosclerosis, and the process was noted more in the branches of the brachiocephalic and aortic arches.

In this case, it was confirmed that in the group with liver cirrhosis developed on the basis of chronic hepatitis V, in a number of cases, some complaints and external symptoms of the disease were reliably higher compared to patients with liver cirrhosis developed on the basis of chronic hepatitis C. Information about them is given in table 3.1.

Table 3.1

Complaints and some external symptoms of patients in groups with developed liver cirrhosis based on chronic hepatitis B and C under observation

№	Indicators	Liver cirrhosis developed on the basis of chronic hepatitis B n=60	Liver cirrhosis developed on the basis of chronic hepatitis C n=60	R
1	Pain and heaviness in the right rib area	12 (20%)	24 (40%)	r<0.001
2	Getting angry	9 (15 %)	12 (20 %)	p>0.05
3	Stuttering	4 (6,6%)	5 (8,3%)	p>0.05
4	Yellowing of the sclera	41 (68%)	29 (49%)	r<0.001
5	Nausea	21 (35 %)	39 (65%)	r<0.001
6	Bloating	50 (83,3%)	46 (76,6%)	r<0.01
7	Constipation	30 (50%)	33 (55 %)	p>0.05
8	Indigestion	6 (10%)	9 (15 %)	p>0.05
9	Decreased appetite	54 (90 %)	57 (95%)	p>0.05
10	Sleep disturbance and memory loss	48 (80%)	39 (65%)	r<0.001
11	Laziness	21 (36%)	11 (18%)	r<0.001
12	Dysphagia	48 (80 %)	51 (85%)	p>0.05
13	Pallor of the skin and mucous membranes	45 (75 %)	51 (85%)	p>0.05
14	Skin itching	51 (85 %)	54 (90 %)	p>0.05
15	The presence of vascular stars on the skin	47 (78%)	48 (80%)	p>0.05

16	Body muscle atrophy	20 (34%)	21 (35%)	p>0.05
17	Varicose veins around the navel	6 (10%)	9 (15 %)	p<0.05
18	Ascites	6 (10%)	3 (5%)	p<0.05
19	Peripheral tumors	23 (38%)	8 (14%)	r<0.001
20	Hepatic encephalopathy	48 (80%)	39 (65%)	p<0.05
21	Bleeding from dilated veins of the esophagus	32 (53%)	40 (67%)	r<0.001
22	Hemorrhagic syndrome	10 (17%)	23 (38%)	r<0.001
23	Obvious weakness	27 (45%)	23 (39%)	r<0.01

20% and 40% of patients in both groups, respectively, complained of pain and heaviness in the right rib area. In this case, in patients with advanced liver cirrhosis due to chronic hepatitis C, these complaints were 2 times more frequent than in the first group, and the differences were reliable (r<0.001). Also, complaints such as burning in urine (15% and 20%, respectively), stuttering (6.6% and 8.3%, respectively) were observed relatively rarely in patients, and the differences were not reliable (p>0.05). Scleral yellowing was observed in 68% and 49% of patients in both groups, respectively, and the differences were highly reliable (r<0.001). In patients with liver cirrhosis developed on the basis of chronic hepatitis C, nausea was detected in 65% of cases and was 1.9 times higher than in the first group. was (r<0.001).

In addition, 83.3% of patients with liver cirrhosis developed on the basis of chronic hepatitis B complained of abdominal discomfort, 50% of constipation, and 10% of abdominal discomfort. In the second group, these complaints were 76.6%, 55% and 15%, respectively. When the differences between the groups were compared, no reliable differences were found in all listed complaints (p>0.05). Sleep disorders and memory loss were observed in 80% and 65% of patients in both groups, respectively, and in liver cirrhosis developed on the basis of chronic hepatitis B, its differences compared to those in group C were highly reliable

(r<0.001). Slowness was observed in 36% of patients of the first group, which was 2 times higher than that of patients of the second group (18%), and a highly reliable difference was detected (r<0.001).

In addition to the above, dysphagia (80% and 85%, respectively), pallor of the skin and mucous membranes (75% and 85%, respectively), skin tightening (85% and 90%, respectively) and vascular stars were observed in both groups of patients. complaints such as presence (78% and 80%, respectively), body muscle atrophy (34% and 35%, respectively) were observed in patients, and the differences between them were not reliable (p>0.05).

According to a number of authors, 67% of patients with HCV cirrhosis and its markers were not identified had bleeding from the esophageal veins and stomach, and this indicator was equal to 53% in patients with its B form. Hepatic encephalopathy and ascites syndrome were developed on the basis of hepatitis B in 80% and 10% of cases, respectively, and in its C form, these symptoms were shown to be more likely to occur in 65% and 5%, respectively. Peripheral tumors were observed in 23% of patients in the first group and 8% in the second group, and high reliable differences were found [46]. Our observations also confirm the above data.

The conducted comparative analysis confirms that in most cases of liver cirrhosis developed on the basis of the studied viral hepatitis B and C, the complaints of patients and some external clinical signs do not reliably differ from each other. In addition, liver encephalopathy and ascitic syndrome were observed more often in liver cirrhosis developed on the basis of hepatitis B, and hemorrhagic syndrome and bleeding from esophageal veins were observed more often in its C form, and the results obtained by us correspond to the data in the literature.

§ 3.2. General and biochemical analysis of blood, coagulogram indicators and collagen IV in urine before treatment in patients diagnosed with advanced liver cirrhosis due to chronic hepatitis B and C

Based on the goal set before us, a general analysis of blood was first performed in patients with liver cirrhosis developed on the basis of chronic hepatitis B and C. Table 3.2 below shows the general blood analysis indicators of the patients involved in the study.

Hemoglobin values in the first group of patients with advanced liver cirrhosis due to chronic hepatitis B were 101.9 ± 0.85 g/l and in the second group of patients were 96.6 ± 0.82 g/l, and the differences between them were highly reliable. was (R<0.01). In addition, mild anemia was confirmed in both cases.

Table 3.2

Indicators of general blood analysis before treatment of patients in groups diagnosed with advanced liver cirrhosis based on chronic hepatitis B and C

Laboratory test results	**Liver cirrhosis developed on the basis of chronic hepatitis B, first group n=60**	**Liver cirrhosis developed on the basis of chronic hepatitis C, second group n=60**	**R**
	Before treatment	Before treatment	
Hemoglobin g/l	101,9 ±0,85	96.6 ± 0,82	<0,01
Leukocyte x103 l	10,62 ±0,15	10,4 ±0,15	>0,05
Hematocrit, %	32,48±0,26	31,88 ±0,35	>0,05
Thrombocytes 103 l	134,1±1,13	132,1± 1,06	>0,05
Lymphocyte % x103 l	17,37±0,54	13,4±0,4	<0,01
Erythrocyte sedimentation rate	27,6± 0,46	31,93±0,4	<0,01

mm/h			

The pathogenesis of anemia in cirrhosis of the liver is complex and diverse, in which the release of incompletely formed erythrocytes into the peripheral blood due to the violation of the proliferation and formation of erythroblasts in the bone marrow is of great importance. In addition, anemia may develop due to the toxic effect of the virus on erythrocytes, impaired absorption of iron, folic acid and vitamin B12, as well as the breakdown of erythrocytes in the spleen.

The number of leukocytes was 10.62 ±0.15x103 l and 10.4 ±0.15x103 in both groups, respectively (R>0.05). The hematocrit index was 32.48±0.26 in the first group and 31.88±0.35 in the second group, and no reliable difference was detected (R>0.05). The number of platelets was 134.1±1.13x103 l and 132.1±1.06x103 l in the first and second groups, respectively (R>0.05). The number of lymphocytes was 17.37±0.54% x103 l in patients with advanced liver cirrhosis based on chronic hepatitis V and 13.4±0.4x103 l in patients with advanced liver cirrhosis based on chronic hepatitis C (r<0, 01). The erythrocyte sedimentation rate was 27.6±0.46mm/h and 31.93±0.4mm/h in both groups, and the differences were reliable (r<0.01).

The coagulogram parameters of the patients under our observation were also compared before the procedures. Table 3.3 below shows its indicators.

Table 3.3

Pre-treatment coagulogram indicators of patients in groups diagnosed with advanced liver cirrhosis based on chronic hepatitis B and C

Indicators	**Liver cirrhosis developed on the basis of chronic hepatitis B n=60**	**Liver cirrhosis developed on the basis of chronic hepatitis C n=60**	**R**
	Before treatment	Before treatment	

Prothrombin index, %	57,2 ±0,56	52,68 ± 0,54	<0,01
Partially activated thromboplastin time, seconds	42,72 ±0,68	46,75 ±0,81	<0,01
Fibrinogen, g/l	2,5±0,06	2,04 ±0,052	<0,01
International normalized relations	1,25±0,07	1,05± 0,15	>0,05
Antithrombin III, %	54,6 ±0,74	48,92±0,83	<0,01

The prothrombin index before treatment was 57.2 ± 0.56% in patients with advanced liver cirrhosis due to chronic hepatitis B, and 52.68 ± 0.54% in patients with advanced liver cirrhosis due to hepatitis C, and the differences were highly reliable. ($r<0.01$). Partially active thromboplastin time was equal to 42.72 ±0.68 seconds in the first group and 46.75 ±0.81 seconds in the second group ($r<0.01$). Fibrinogen indicators were 2.5±0.06 g/l and 2.04±0.052 g/l in both groups ($r<0.01$). The international standardized relationship indicators were 1.25±0.07 and 1.05±0.15 in the first and second groups, respectively, and the differences were not reliable ($r>0.05$). Antithrombin SH was 54.6±0.74% and 48.92±0.83% in the first and second groups, respectively, and a highly reliable difference between the two groups was found ($p<0.01$).

In the observation of changes in hemostasis in cirrhosis of the liver, the imbalance between blood coagulation and anti-coagulation factors has a leading role, and the anticoagulant system - antithrombin III and protein C is among them. Prothrombin index decreased by 73%, partial active thromboplastin time (QFTV) increased by 75%, and fibrinogen decreased by 25% compared to myor. According

to a number of authors, antithrombin III and plasminogen are decreased in liver damage caused by viruses compared to cirrhosis of other etiologies. Due to the deficiency of natural anticoagulants protein S and antithrombin III, the markers of the blood coagulation system and also activation of the vascular-thrombocytic joint are observed due to the higher than normal Willebrant factor. Although procoagulation tests (PTI, QFTV) show a high probability of bleeding, these changes indicate a high probability of formation of blood clots. The direction of these studied samples in different directions is considered a laboratory sign of coagulopathy [14].

During the study, biochemical analysis of blood, functional reserve of kidneys and amount of collagen IV in urine were determined in patients with developed liver cirrhosis due to hepatitis B and C. Information about them is presented in table 3.4.

Table 3.4

Pre-treatment blood biochemical analysis and urine collagen IV indicators of patients with advanced liver cirrhosis due to chronic hepatitis B and C

Indicators	**Liver cirrhosis developed on the basis of chronic hepatitis B n=60**	**Liver cirrhosis developed on the basis of chronic hepatitis C n=60**	**R**
	Before treatment	Before treatment	
Total protein, g/l	59,8 ±0,78	52,72 ± 0,88	<0,01
Albumin, g/l	24,52 ±0,7	27,37 ±0,82	<0,05
Urea, mmol/l	10,3±0,27	13,67 ±0,4	<0,01
Alanine	58,58±0,47	85,77 ±1,26	<0,01

aminotransferase (ALT), Ed/l			
Aspartate aminotransferase (AST), Ed/l	104,1±1,36	117,9 ±1,65	<0,01
Total bilirubin, mmol/l	47,52±1,07	66,25 ±1,7	<0,01
Alkaline phosphatase, Ed/l	112,8±2,68	88,48 ±1,6	<0,01
Total cholesterol, mmol/l	2,48±0,15	2,15 ±0,13	>0,05
Functional reserve of kidneys, %	4,3±0,17	4,1±0,12	>0,05
Collagen IV, μg	242.33 ±3,85	259,48 ± 3,55	<0,001

As shown in the table, the amount of total protein in blood serum in patients with cirrhosis developed on the basis of chronic hepatitis B is 59.8 ± 0.78 g/l, and in patients with cirrhosis developed on the basis of chronic hepatitis C is 52.72 ± 0.88 g/l. The scores were highly reliable when compared between groups ($r<0.01$). The amount of albumin in the blood was equal to 24.52 ± 0.7 g/l and 27.37 ± 0.82 g/l in the first and second groups, respectively ($p<0.01$). Urea values were 10.3±0.27mmol/l and 13.67±0.4mmol/l in both groups, respectively ($r<0.01$). ALT and AST indicators in the first (respectively 58.58±0.47Ed/l and 104.1±1.36Ed/l) and second (85.77±1.26Ed/l and 117.9 ±1.65 Ed/l) when compared between groups, the indicators were highly reliable ($r<0.01$). Total bilirubin was 47.52±1.07mmol/l in the first group, 66.25±1.7mmol/l in the second group, and alkaline phosphatase was 112.8±2.68Ed/l and 88.48±1.6Ed in both groups, respectively. /l and the differences were highly reliable ($r<0.01$). Total cholesterol values did not reliably differ between groups (2.48 ± 0.15 mmol/l and 2.15 ± 0.13 mmol/l, respectively, $R>0.05$).

Kidney functional reserve before treatment was 4.3±0.17% and 4.1±0.12% in the first and second group of patients, respectively (R>0.05).

Also, we determined collagen IV indicators in the urine, which is a marker that indicates the level of fibrosis processes in the kidney. In this case, the values of collagen IV in urine in patients with advanced liver cirrhosis due to chronic hepatitis B before treatment were 242.33 ± 3.85 μg, and in patients with advanced liver cirrhosis due to chronic hepatitis C, it was equal to 259.48 ± 3.55 μg, and more When the indicators were compared between the two groups, the differences were reliable, and it was higher in the latter group (r<0.001).

CHAPTER IV. COMPLAINTS OF PATIENTS WITH DEVELOPED LIVER CIRRHOSIS DUE TO CHRONIC HEPATITIS B and C, COMPARATIVE STUDY OF COMPLAINTS, GENERAL AND BIOCHEMICAL BLOOD ANALYSIS, COAGULOGRAM RESULTS, AND COLLAGEN IV INDICATORS IN URINE BEFORE AND AFTER THE TREATMENT

This chapter presents the results of a comparative analysis of patients involved in the study before and after the treatment. Patients of both groups were divided into two subgroups of 30 patients each in order to evaluate the effectiveness of complex treatment procedures with different contents. The first subgroups were prescribed spironolactone (veroshpiron) + L-ornithine L-aspartate on the basis of the complex treatment of liver cirrhosis, and eplerenone + L-ornithine L-aspartate + glutathione drugs were prescribed to the second subgroups on the basis of the complex treatment of liver cirrhosis. Also, taking into account the indications and contraindications and taking into account their genotypes, the second group of patients was prescribed antiviral drugs in monad doses.

§4.1. Comparative analysis of complaints and some external symptoms of patients diagnosed with advanced liver cirrhosis due to chronic hepatitis B and C before and after treatment

The following table 4.1 shows information about the changes observed in the complaints and some external symptoms of the patients under our observation after the treatment procedures.

Table 4.1

Complaints and changes in some external symptoms of patients with advanced liver cirrhosis due to chronic hepatitis B and C before and after complex medical treatment

№	Indicators	Liver cirrhosis developed on the basis of chronic hepatitis B n=60	Liver cirrhosis developed on the basis of chronic hepatitis C n=60

		Before treatment	After treatment	Before treatment	After treatment
1	Pain and heaviness in the right rib area	12 (20%)	3(5%)***	24 (40%)	6(10%)***
2	Getting angry	9 (15 %)	7(11,6%)	12 (20 %)	10(17%)
3	Stuttering	4 (6,6%)	4(3,5%)	5 (8,3%)	3(5%)
4	Yellowing of the sclera	41 (68%)	39 (65%)	29 (49%)	17(28%)***
5	Nausea	21 (35 %)	12(20%)**	39 (65%)	18(30%)***
6	Bloating	46 (76,6%)	30(50%)***	50 (83,3%)	24(40%)***
7	Constipation	30 (50%)	27(45%)	33 (55 %)	30(50%)
8	Indigestion	6 (10%)	4(7%)	9 (15 %)	9(12%)
9	Decreased appetite	54 (90 %)	27(45%)***	57 (95%)	36(60%)***
10	Sleep disturbance and memory loss	39 (65%)	30(50%)*	48 (80%)	33(55%)***
11	Laziness	40 (66.67%)	15 (25%)***	38 (63,3%)	15 (25%)
12	Dysphagia	48 (80 %)	32(53%)***	51 (85%)	35(58%)***
13	Pallor of the skin and mucous membranes	45 (75 %)	21(45%)***	51 (85%)	17(28%)***
14	Skin itching	51 (85 %)	27(45%)***	54 (90 %)	30(50%)***
15	The presence of vascular stars on the skin	47 (78%)	46(77%)	48 (80%)	47(78%)
16	Body muscle atrophy	20 (34%)	17(28%)	21 (35%)	18(30%)
17	Varicose veins around the navel	6 (10%)	5(9%)	9 (15 %)	8(14%)
18	Ascites	3 (5%)	2(3%)	6 (10%)	4(7%)
19	Peripheral tumors	23 (38%)	17(28%)	8 (14%)	5(9%)
20	Hepatic encephalopathy	48 (80%)	27(45%)***	39 (65%)	17(28%)***
21	Bleeding from dilated veins of	32 (53%)	27(45%)	40 (67%)	15 (25%)***

	the esophagus				
22	Hemorrhagic syndrome	10 (17%)	7(11,67%)	23 (38%)	8(13%)***
23	Obvious weakness	27 (45%)	12(20%)***	23 (38%)	9(12%)***
Note: *-r<0.05; **-p<0.01; ***-p<0.001.					

As shown in the table, positive changes were observed in a number of complaints after the complex treatment of patients with the addition of eplerenone + L-ornithine L-aspartate and glutathione. Pain and heaviness in the right rib area decreased from 20% to 5% and from 40% to 10% before and after the treatments in the first and second group of patients, respectively, and the differences were highly reliable in both cases. (r<0.001). In patients with advanced liver cirrhosis due to chronic hepatitis B, boils and belching were observed in 15% and 6.6% of cases, respectively, before treatment, and after treatment, the indicators were equal to 11.6% and 3.5%, respectively. In patients with advanced cirrhosis due to chronic viral hepatitis C, these complaints decreased from 20% to 17% and from 8.3% to 5% before and after treatments, respectively. But the changes in both groups were not reliable (p>0.05). Yellowness of the sclera in the first group was 68% before treatments and 65% after treatments (p>0.05). In the second group, high reliability changes of this sign before and after the treatment were noted, equal to 49% and 28%, respectively (r<0.001).

Nausea in the first group of patients occurred in 35% of patients before treatments and in 20% of patients after treatments, and the changes were reliable (r<0.01). Nausea in the second group decreased by 2.1 times after treatment (65% and 30%, respectively), and the changes were more reliable than in the first group (r<0.001).

In patients with advanced liver cirrhosis due to chronic hepatitis B and C, abdominal rest was significantly reduced before and after treatment (76.6% to 50% and 83.3% to 40%, respectively) (r<0.001). Constipation and irregular bowel movements were observed in 50% and 10% of patients in the first group,

respectively, before treatment, and in 45% and 7.5% of patients after treatment ($p>0.05$). In the second group, positive changes in these complaints were also found after the treatments (reduced from 55% to 50% and from 15% to 12%, respectively), but the differences were not reliable ($p>0.05$).

In patients with advanced liver cirrhosis due to chronic hepatitis B, appetite reduction was 90% before treatment and 45% after treatment, and highly reliable changes were found ($r<0.001$). A highly reliable change was also noted in those who developed on the basis of chronic hepatitis C (decrease from 95% to 60%, respectively, $r<0.001$).

Sleep disturbances and memory loss were reliably reduced in the first group of patients before and after treatments (from 65% to 50%, respectively, $r<0.05$). In the second group, these complaints were observed in 80% of patients before treatment and 55% after treatment, and the differences were highly reliable ($r<0.001$). Symptoms of lethargy were significantly reduced after treatment in both groups of patients ($r<0.001$). Dysphagia was observed in both groups in 80% and 85% of patients before treatment and in 53% and 58% of patients after treatment, respectively, and the differences were noted to be highly reliable ($r<0.001$).

Pallor of the skin and mucous membranes and skin itching were 75% and 45%, 85 and 45%, respectively, before and after treatment in patients with advanced liver cirrhosis due to chronic hepatitis B ($r<0.001$). In those who developed chronic hepatitis C, the above complaints were significantly reduced before and after treatment (from 85% to 28% and from 90% to 50%, $r<0.001$).

In the first and second groups, 78% and 80% of patients had vascular stars before treatment, respectively, and after treatment, these signs were observed in 77% and 78% of patients, respectively, and the changes were not reliable ($r<0.05$). Varicose veins around the navel increased from 10% to 15% in the first group and decreased from 15% to 13% in the second group ($r>0.05$). Despite the medical procedures, ascites in the first group remained in 5% of patients before procedures and 3% after procedures. In the second group of patients, although it decreased from 10% to 7%, the changes were not reliable ($r>0.05$). Peripheral tumors

improved in both groups of patients after the treatments, but no reliable changes were observed. Hepatic encephalopathy reliably decreased from 80% to 45% and 65% to 28% before and after treatments in both groups, respectively ($r<0.001$). Complications of bleeding from esophageal varices decreased in the first group with low reliability (from 53% to 45%, respectively, $r<0.05$) and in the second group with high reliability (from 67% to 27%, respectively, $r<0.001$). Symptoms of fatigue, which were evident in all patients involved in the study, were highly reliable after the treatments ($r<0.001$).

A highly reliable reduction ($r<0.001$) of symptoms such as liver encephalopathy, lethargy, general weakness, and a positive change in pain syndrome as a result of the reduction of hepatomegaly is associated with the effect of glutathione. Its positive effect has been confirmed by Chinese researchers.

Ong J.P. and co-authors studied the effectiveness of L-ornithine L-aspartate in a multicenter prospective observational study conducted in 191 patients. It shows that the drug has a positive effect on the quality of life of patients, including reducing fatigue, improving sleep quality and helping to concentrate.

The obtained results showed that the addition of L-ornithine L-aspartate and glutathione to the complex treatment of liver cirrhosis developed on the basis of hepatitis B and C led to a reliable positive change in complaints and some external clinical signs of both groups of patients. Here it should be noted that they are more clearly manifested in patients with hepatitis C. This may be related to the high effectiveness of antiviral drugs in the latter group.

§ 4.2. Comparative analysis of general and biochemical analysis of blood, coagulogram indicators and collagen IV in urine in patients diagnosed with advanced liver cirrhosis due to chronic hepatitis B and C before and after treatment

As mentioned in the introduction of this chapter, patients of both groups were divided into two subgroups of 30 patients according to the treatment

procedures. The first subgroup of patients received spironolactone (veroshpiron) + L-ornithine L-aspartate based on the complex treatment of liver cirrhosis, and the second subgroup received eplerenone + L-ornithine L-aspartate + glutathione based on the complex treatment

Table 4.2 shows the results of general blood analysis obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis B.

Table 4.2

Indicators of general blood analysis before and after complex treatment of patients in groups with developed liver cirrhosis on the basis of chronic hepatitis B

№	Indicators	On the basis of the complex treatment of liver cirrhosis + L-ornithine L-aspartate + veraspiron n=30		Based on complex treatment of liver cirrhosis + glutathione + L-ornithine L-aspartate + eplerinone n=30		P
		Before treatment	After treatment	Before treatment	After treatment	
1	Hemoglobin, g/l	96,7 ± 1,19	98,7±1,18	93,1±1,15	97,1±1,15*	<0,05
2	Leukocyte 109Ed/l	10,33±0,2	9,2±0,19	10,9±0,19	6,93±0,2***	>0,05
3	Hematocrit, %	32,53±0,37	35,13±0,38	32,43±0,386	37,03±0,5*	>0,05
4	Platelet, 109Ed/l	133,5±1,5	138,2±1,5*	134,7±1,73	145,7±1,7***	>0,05
5	Lymphocyte, 109 Ed/l	14,7±0,8	15,93±0,73*	15,83±0,74	18,03±0,76*	>0,05

6	Erythrocyte sedimentation rate mm/h	27,83±0,7	24,83±0,69	27,4±0,6	18,4±0,62***	>0,05
Note: difference between R-groups before and after treatment: *-r<0.05; **-p<0.01; ***-p<0.001.						

Hemoglobin indicators were 96.7 ± 1.19 g/l in the first group and 93.1 ± 1.15 g/l in the second group, the differences were reliable (r<0.05). Leukocyte, thrombocyte, lymphocyte count, hematocrit, and erythrocyte sedimentation rate did not reliably differ between groups (r>0.05). Such identified changes indicate that both subgroups of patients were selected monad.

Positive changes in a number of indicators of general blood analysis were observed in patients with advanced liver cirrhosis due to chronic hepatitis B after standard treatments with various components. Hemoglobin indicators were 96.7 ± 1.19 g/l before treatment and 98.7 ± 1.18 g/l after treatment in patients who received veroshpiron + L-ornithine L-aspartate on the basis of complex treatment of liver cirrhosis, and there was a reliable difference not detected (r>0.05). In the second group, that is, on the basis of the complex treatment of liver cirrhosis + elerenone + glutathione + L-ornithine L-aspartate, the hemoglobin values before and after the treatments were 93.1±1.15 g/l and 97.1±1, respectively. 15 g/l, the differences were reliable (r<0.05). In the first group of patients, the number of leukocytes in the general blood analysis was 10.33±0.2×109 Ed/l before treatments and 9.2±0.19×109 Ed/l after treatments (r>0.05). In the second group, their number decreased by 1.57 times after treatment and the indicators were highly reliable (10.9±0.19 ×109 Ed/l and 6.93±0.2 ×109 Ed/l, respectively, r <0.001). Hematocrit values in both groups were 32.53±0.37% and 35.13±0.38% before treatment and 32.43±0.38% and 37.03±0.5% after treatment, and on the basis of complex treatment of liver cirrhosis, reliable changes were observed in patients with +eplerenone+L-ornithine L-aspartate +glutathione (r<0.05). The number of

platelets and lymphocytes in the first group was equal to 133.5±1.5 × 109 Ed/l and 14.7±0.8×109 Ed/l before the treatment, and after the treatment, these indicators were 138.2, respectively. It was ±1.5×109 Ed/l and 15.93±0.73×109 Ed/l. A reliable difference was found between both indicators (r<0.05). In the second group, the number of platelets increased from 134.7±1.73×109 Ed/l to 145.7±1.7×109 Ed/l, highly reliable changes were noted (r<0.001), and the number of lymphocytes was 15.83± It changed from 0.74×109 Ed/l to 18.03±0.76×109 Ed/l (r<0.05). The erythrocyte sedimentation rate was 27.83±0.7 mm/h and 24.83±0.69 mm/h in the first group of patients before and after treatments, and the differences were not reliable (r>0.05). In the second group of patients, the erythrocyte sedimentation rate decreased by 1.5 times from 27.4±0.6 mm/hour to 18.4±0.62 mm/hour (p<0.001).

In the course of medical treatment, a reliable reduction in the number of leukocytes and the rate of erythrocyte sedimentation and a reliable increase in the number of thrombocytes were found in the blood of patients who received standard treatment + eplerenone + L-ornithine L-aspartate and glutathione drugs with developed liver cirrhosis due to chronic hepatitis B. These results showed that combined use of eplerenone + L-ornithine L-aspartate and glutathione drugs with standard treatment + veroshpiron + L-ornithine L-aspartate was more effective in patients with advanced liver cirrhosis due to chronic hepatitis B.

Table 4.3 below shows the results of general blood analysis obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis C.

Table 4.3

Indicators of general blood analysis before and after complex treatment of patients in groups with advanced liver cirrhosis due to chronic hepatitis C

№	Indicators	On the basis of the complex treatment of liver cirrhosis + L-	Based on complex treatment of liver cirrhosis + glutathione + L-	R

		ornithine L-aspartate + veraspiron n=30		**ornithine L-aspartate + eplerinone n=30**		
		Before treatment	After treatment	Before treatment	After treatment	
1	Hemoglobin, g/l	97,03±1,27	100±1,27	96,17±1,05	101,2±1,05***	>0,05
2	Leukocyte 109Ed/l	10,6±0,23	9,1±0,2	10,2±0,2	6,6±0,2***	>0,05
3	Hematocrit, %	32,07±0,5	34,07±0,53*	31,7±0,5	38,7±0,5***	>0,05
4	Platelet, 109Ed/l	131,2±1,5	137,1±1,54*	133,1±1,6	151,1±1,6***	>0,05
5	Lymphocyte, 109 Ed/l	13,13±0,54	15,17±0,51*	13,67±0,69	18,67±0,6***	>0,05
6	Erythrocyte sedimentation rate mm/h	32,03±0,6	24,07±0,61*	31,8±0,53	16,83±0,53***	>0,05

Note: difference between R-groups before and after treatment: *-r<0.05; **-p<0.01; ***-p<0.001.

As shown in the table, before the treatment, the parameters of the general blood analysis in both subgroups of patients were compared. There were no reliable changes before treatments in all studied indicators (r>0.05).

The first, i.e., based on the complex treatment of liver cirrhosis + veroshpiron + L-ornithine L-aspartate, hemoglobin values were 97.03±1.27g/l before treatments and 100±1.27g/l after treatments and no reliable difference was observed (r>0.05). Based on the complex treatment of liver cirrhosis + eplerenone + glutathione + L-ornithine L-aspartate, hemoglobin values before and after

treatment were 96.17±1.05 g/l and 101.2±1.05 g/l, respectively. is equal to, and a highly reliable difference was found (r<0.05). The number of leukocytes in the first group of patients was 10.6±0.23×109 Ed/l before treatment and 9.1±0.2×109 Ed/l after treatment (r>0.05). In the second group, the number of leukocytes decreased by 1.5 times after treatment and the indicators were highly reliable (10.2±0.2×109 Ed/l and 6.6±0.2×109 Ed/l, respectively, r <0.001). In the first group, hematocrit values before and after treatment were 32.07±0.5% and 34.07±0.53%, respectively (r<0.05). In the second group, more reliable changes were observed from 31.7±0.5% to 38.7±0.5% after treatments (p<0.001).

The number of platelets and lymphocytes in the first group was equal to 131.2±1.5×109 Ed/l and 13.13±0.54×109 Ed/l before the treatment, and after the treatments these indicators were 137.1 It was ±1.54×109 Ed/l and 15.17±0.51×109 Ed/l (r<0.05). In the second group, the number of platelets increased from 133.1±1.6×109 Ed/l to 151.1±1.6×109 Ed/l, highly reliable changes were noted (r<0.001), and the number of lymphocytes was 13.67± It changed from 0.69×109 Ed/l to 18.67±0.6×109 Ed/l (r<0.001). The erythrocyte sedimentation rate was 32.03±0.6mm/h and 24.07±0.61mm/h in the first group of patients before and after treatments, and the differences were not reliable (r<0.05). In the second group of patients, the erythrocyte sedimentation rate decreased by 1.89 times from 31.8±0.53mm/hour to 16.83±0.53mm/hour (r<0.001).

After the treatment procedures, developed liver cirrhosis due to chronic hepatitis C was detected, high reliable changes in all parameters of the general blood analysis were detected in patients who took +eplerenone + L-ornithine L-aspartate and glutathione drugs with standard treatment. The obtained results showed that the combined use of eplerenone + L-ornithine L-aspartate and glutathione drugs with standard treatment has more positive effects in patients diagnosed with advanced liver cirrhosis based on chronic hepatitis C than in patients diagnosed with advanced liver cirrhosis based on chronic hepatitis B.

Coagulogram indicators before and after the treatment were also compared in the monitored patients.

The following table 4.4 shows the results of the coagulogram obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis B.

Table 4.4

Coagulogram indicators before and after complex treatment of patients in groups diagnosed with advanced liver cirrhosis due to chronic hepatitis B

№	Indicators	On the basis of the complex treatment of liver cirrhosis + L-ornithine L-aspartate + verashpiron n=30		Based on complex treatment of liver cirrhosis + glutathione + L-ornithine L-aspartate + eplerinone n=30		R
		Before treatment	After treatment	Before treatment	After treatment	
1	Prothrombin index, %	57,9 ± 0,69	60,53±0,85*	57,1±0,75	64,1±0,75***	>0,05
2	Partially activated thromboplastin time, seconds	42,6±0,8	40,6±0,86	42,83±0,19	39,83±1,07***	>0,05
3	Fibrinogen, g/l	2,4±0,09	2,75±0,08*	2,58±0,8	3,16±0,08***	>0,05
4	International normalized relations	1,17±0,09	0,98±0,04	1,33±0,11	1,13±0,11	>0,05
5	Antithrombin III	55,53 ± 1,02	60,5± 0,85*	53,67±1,05	61,83±0,6***	>0,05

Izoh: R-davolashdanoldingivakeyingiko‘rsatkichlarfarqi: *-r<0.05; **-p<0.01; ***-p<0.001.

Coagulogram indicators were compared in both subgroups of patients before the treatment as shown in the table. There were no reliable changes before treatments in all studied indicators (r>0.05).

Prothrombin index increased from 57.9 ± 0.69% to 60.53 ± 0.85% in the first group after complex medical treatment in patients diagnosed with advanced liver cirrhosis due to chronic hepatitis B, and the changes were reliable (r<0 .05). In the second group, the differences increased from 57.1±0.75% to 64.1±0.75% and became highly reliable (r<0.001). There were no reliable changes in partially activated thromboplastin time in the first group before and after treatments (42.6±0.8 seconds and 40.6±0.86 seconds, respectively, r>0.05). In the second group, it was 42.83±0.19 seconds before treatments and 39.83±1.07 seconds after treatments, and highly reliable changes were noted (r<0.001).

As a result of acute inflammatory processes and tissue necrosis in the body, the amount of soluble protein fibrinogen in blood serum increases. This protein is one of the important indicators of the homeostasis of the body. Based on the complex treatment of cirrhosis of the liver under our observation, in patients who received L-ornithine + L-aspartate, fibrinogen was 2.4±0.09 g/l before treatment and 2.75±0.08 g/l after treatment, and the differences were reliable. (r<0.05). In the groups of patients who received L-ornithine L-aspartate + glutathione on the basis of the complex treatment of liver cirrhosis, it was 2.58 ± 0.8 g/l and 3.16 ± 0.08 g/l, respectively, before and after the treatments, a more reliable difference was found (r<0.001). Although there were significant positive changes in the international standardized relationship scores in both groups, there were no reliable changes (1.17±0.09 and 0.98±0.04, respectively, before and after treatment, 1 ,33±0.11 and 1.13±0.11, r>0.05). Antithrombin III increased reliably from 55.53±1.02% to 60.5±0.85% in the first group, and from 53.67±1.05% to 61.83±0.6% in the second group (r<0.001).

The following table 4.5 shows the results of the coagulogram obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis C.

Table 4.5

Coagulogram indicators before and after complex treatment of patients in groups with developed liver cirrhosis on the basis of chronic hepatitis C

№	Indicators	On the basis of the complex treatment of liver cirrhosis + L-ornithine L-aspartate + verashpiron n=30		Based on complex treatment of liver cirrhosis + glutathione + L-ornithine L-aspartate + eplerinone n=30		R
		Before treatment	After treatment	Before treatment	After treatment	
1	Prothrombin index, %	52,67±0,73	55,07±0,69*	52,7±0,8	58,7±0,8***	>0,05
2	Partially activated thromboplastin time, seconds	47,5±1,14	43,5±1,14*	46±1,16	34±1,2***	>0,05
3	Fibrinogen, g/l	1,99±0,069	2,24±0,06*	2,09±0,07	3,69±0,07***	>0,05
4	International normalized relations	1,23±0,1	0,8±1,54	1,33±1,6	0,84±0,032	>0,05
5	Antithrombin III	49,33 ± 1,15	52,93 ± 0,93*	48,5 ± 1,2	62,9 ± 0,7***	>0,05

Note: The difference between R-groups before and after treatment: *-r<0.05; **-p<0.01; ***-p<0.001.

As mentioned above, coagulogram indicators were compared before treatment in both subgroups of patients and no reliable differences were found (r>0.05).

Prothrombin index increased from 52.67±0.73% to 55.07±0.69% in the first group after complex treatment in patients diagnosed with advanced liver cirrhosis due to chronic hepatitis C, and the changes were reliable (r<0 .05). In the second group, the differences increased from 52.7±0.8% to 58.7±0.8% and became highly reliable (r<0.001). There were no reliable changes in partially activated thromboplastin time in the first group before and after treatments (47.5±1.14 seconds and 43.5±1.14 seconds, respectively, r<0.05). In the second group, it was 46±1.16 seconds before treatments and 34±1.2 seconds after treatments, and highly reliable changes were noted (r<0.001).

Based on the complex treatment of cirrhosis of the liver under our observation, in patients receiving L-ornithine L-aspartate, fibrinogen was 1.99±0.069 g/l before treatments and 2.24±0.06g/l after treatments, and the differences were reliable (r<0.05). In the groups of patients who received L-ornithine L-aspartate + glutathione on the basis of the complex treatment of liver cirrhosis, a highly reliable difference of 2.09±0.07g/l and 3.69±0.07g/l was found before and after the treatments, respectively (r<0.001). Although significant positive changes were observed in both groups in international normalized relationship indicators, no reliable changes were observed (r>0.05). Antithrombin III increased from 49.33 ± 1.15% to 52.93 ± 0.93% in the first group, and from 48.5 ± 1.2% to 62.9 ± 0.7% in the second group. (r<0.001).

Also, the results of biochemical analysis of the blood of the patients involved in the study were compared before and after the treatment.

Table 4.6 shows the results of biochemical analysis of blood obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis B.

Table 4.6

Results of blood biochemical analysis before and after complex treatment of patients in groups diagnosed with advanced liver cirrhosis due to chronic hepatitis B

№	Indicators	On the basis of complex treatment of liver cirrhosis + hepamer + verashpiron n=30		On the basis of complex treatment of liver cirrhosis + hepamer + verashpiron n=30		R
		Before treatment	After treatment	Before treatment	After treatment	
1	Total protein, g/l	60,43±1,06	62,4±1,17	59,17±1,05	68,16±1,15***	>0,05
2	Albumin, g/l	24,8±1,59	28,6±1,14*	24,23±0,93	32,67±0,9***	>0,05
3	Urea, mmol/l	9,96±0,4	8,6±0,3*	10,3±0,4	8,17±0,3***	>0,05
4	Glucose, mmol/l	6,13±0,28	6,0±0,3	5,9±0,23	5,8±0,2	>0,05
5	Alanine-aminotransferase, Ed/l	58,23±0,7	55,4±0,6*	58,93±0,63	42,17±0,8***	>0,05
6	Aspartate-aminotransferase, Ed/l	106,1±1,93	99,17±1,83*	102,0±1,87	82,13±2,04***	>0,05
7	General Bilirubin, mmol/l	46,13±1,4	42,9±1,4	48,9±1,59	31,0±1,64***	>0,05
8	Alkaline phosphotase, Ed/l	113,2±0,54	110,3±3,34	112,3±3,44	99,63±3,3*	>0,05
9	Total cholesterol, mmol/l	2,26±0,2	2,1±0,19	2,7±0,21	2,23±0,2	>0,05

Note: The difference between R-groups before and after treatment: *-r<0.05; **-p<0.01; ***-p<0.001.

As shown in the table, patients with liver cirrhosis developed as a result of chronic hepatitis B were divided into two subgroups according to the composition of the complex treatment procedures. The first group of patients received L-ornithine L-aspartate on the basis of the complex treatment of liver cirrhosis, and the second group of patients received L-ornithine L-aspartate + glutathione on the basis of its complex treatment.

In the first group, total protein values in blood serum were 60.43±1.06 g/l before treatment and 62.4±1.17 g/l after treatment (r>0.05). In the second group, this indicator was equal to 59.17±1.05 g/l and 68.16±1.15 g/l, respectively, before and after treatments, and highly reliable differences were observed (r<0.001). The albumin values in the first group were 24.8±1.59 g/l and 28.6±1.14 g/l before and after treatments, and the differences were reliable (r<0.05). In the second group, the albumin values increased by 1.33 times from 24.23±0.93 g/l to 32.67±0.9 g/l after the treatments, and highly reliable changes were detected (r<0.001). Urea indicators in the first group from 9.96±0.4 mmol/l to 8.6±0.3 mmol/l (p<0.05), from 10.3±0.4 mmol/l to 8.17± in the second group A highly reliable change was noted down to 0.3 mmol/l (r<0.001). There were no reliable changes in glucose values in both groups (r>0.05).

Alanine aminotransferase and aspartate aminotransferase values were 58.23±0.7Ed/l and 106.1±1.93Ed/l in the first group, respectively, and 55.4±0.6Ed/l and 99.17±1.83Ed after treatments. /l was (p<0.05). In the second group, highly reliable changes were observed after treatments (from 58.93±0.63 Ed/l to 42.17±0.8 Ed/l, from 102.0±1.87 Ed/l to 82, decreased by 13±2.04 Ed/l, r<0.001).

As mentioned above, clear positive changes were noted in the biochemical parameters of the group receiving L-ornithine L-aspartate + glutathione + eplerenone.

Our results are consistent with the conclusions of Italian researchers. They also showed reliable reductions in liver function tests of ALT, AST, and alkaline phosphatase in patients receiving glutathione several months after treatment. Another Chinese scientists noted positive changes in the cytolytic syndrome in cirrhosis of the liver in the group receiving this drug.

K. Grüngreiff and Y. Lambert Baumann in 2001 published the results of a large follow-up of 1167 patients in 250 treatment facilities dedicated to the effectiveness of L-ornithine, which also revealed an average reduction of transaminases by 35%.

No reliable changes were detected in bilirubin indicators in patients who received L-ornithine L-aspartate + L-ornithine on the basis of complex treatment of liver cirrhosis ($r>0.05$). In the second group, it decreased by 1.57 times from 48.9±1.59 mmol/l to 31.0±1.64 mmol/l before and after treatments, and highly reliable changes were noted ($r<0.001$). In the first group, alkaline phosphatase decreased from 113.2±0.54 Ed/l to 110.3±3.34 Ed/l before and after the treatments ($r>0.05$). In the second group, these indicators were 112, It was 99.63±3.3 Ed/l in 3±3.44 Ed/l and reliable changes were detected ($p<0.05$). There were no reliable changes in total cholesterol values in both groups ($r>0.05$).

The results of blood biochemical analysis of patients in the groups with developed liver cirrhosis based on chronic hepatitis C are presented in table 4.7.

Table 4.7

Results of blood biochemical analysis before and after complex treatment of patients in groups diagnosed with advanced liver cirrhosis on the basis of chronic hepatitis C

№	Indicators	On the basis of complex treatment of liver cirrhosis + hepamer + verashpiron n=30	Based on complex treatment of liver cirrhosis + glutathione + L-ornithine L-	R

				aspartate + eplerenone n=30		
		Before treatment	After treatment	Before treatment	After treatment	
1	Total protein, g/l	52,43±1,19	57,4±1,23	53±1,32	66,16±1,4***	>0,05
2	Albumin, g/l	28,27±1,15	31,4±1,19	27,77±1,03	36,7±1,07***	>0,05
3	Urea, mmol/l	13,8±0,53	11,7±0,54*	13,5±0,6	8,7±0,4***	>0,05
4	Glucose, mmol/l	4,26±0,2	4,1±0,17*	4,1±0,17	4,0±0,17	>0,05
5	Alanine-aminotransferase, Ed/l	83,87±1,6	66,4±1,5***	87,67±1,94	40,67±1,87***	>0,05
6	Aspartate-aminotransferase, Ed/l	115,8±2,2	92,63±2,17***	119,9±2,43	61,07±2,7***	>0,05
7	General Bilirubin, mmol/l	67,2±2,7	56,37±2,8***	65,3±1,99	21,0±1,54***	>0,05
8	Alkaline phosphotase, Ed/l	90,73±2,12	86,7±2,15	86,23±2,34	74,5±2,35***	>0,05
9	Total cholesterol, mmol/l	2,13±0,2	2,0±0,16	2,17±0,2	1,8±0,16	>0,05

Note: The difference between R-values before and after treatment: *-r<0.05; **-p<0.01; ***-p<0.001.

As mentioned above, in the group receiving veroshpiron + L-ornithine L-aspartate on the basis of the complex treatment of liver cirrhosis, the total protein in the blood serum and the albumin, which is its main part, were 52.43 ± 1.19 g/l

and 28.27 ± 2, respectively. It was 1.15 g/l. Differences were not reliable (r>0.05) despite the fact that these parameters increased by 57.4±1.23 g/l and 31.4±1.19 g/l after the treatments. In the group receiving eplerenone + L-ornithine L-aspartate + glutathione on the basis of the second, i.e. complex treatment of liver cirrhosis, total protein and albumin were 53±1.32 g/l and 27.77±1.03 g/l, respectively, before treatment. and after treatments were 66.16±1.4 g/l and 36.7±1.07 g/l, respectively, and highly reliable changes were found in both parameters (r<0.001). Urea indicators in the first group from 13.8±0.53mmol/l to 11.7±0.54mmol/l (p<0.05), in the second group from 13.5±0.6mmol/l to 8.7±0 High reliable changes were noted down to .4 mmol/l (r<0.001). There were no reliable changes in glucose indicators in both groups (r>0.05).

The values of alanine aminotransferase and aspartate aminotransferase in the first group were 83.87±1.6Ed/l and 115.8±2.2Ed/l before treatments, and 66.4±1.5Ed/l and 92.63±2, 66.4±1.5Ed/l after treatments. It was 17 Ed/l. In the second group, 2.16 times from 87.67±1.94 Ed/l to 40.67±1.87 Ed/l and from 119.9±2.43 Ed/l to 61.07± It decreased by 1.96 times to 2.7Ed/l, and highly reliable changes were observed in both groups (r<0.001). Total bilirubin levels decreased by 1.2 times in the first group (r>0.05) and by 3.1 times in the second group (r<0.001). In the first group, alkaline phosphatase decreased from 90.73±2.12 Ed/l to 86.7±2.15 Ed/l before and after treatments (r>0.05). In the second group, these indicators were 86.23±2.34 Ed/l and 74.5±2.35 Ed/l, respectively, and highly reliable changes were detected (p<0.001). No significant changes in total cholesterol were observed in both groups (r>0.05).

Figure 4.1 shows collagen IV values in urinalysis obtained after complex medical procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis B.

After the treatment, collagen IV values in the group of patients who received eplerenone + L-ornithine L-aspartate and glutathione with the standard treatment of liver cirrhosis were 245.37 ± 5.2 μg before the treatment and 224.6 ± 6.4 μg after the treatment. differences were reliable (p<0.05). In patients receiving

veroshpiron + L-ornithine L-aspartate with the standard treatment of liver cirrhosis, it was 239.3 ± 5.7 μg and 231.8 ± 6.1 μg before and after the treatments, respectively ($p>0.05$).

The results of collagen IV in patients with advanced cirrhosis of the liver due to chronic hepatitis C were more reliable than in patients with advanced cirrhosis of the liver due to chronic hepatitis B after complex treatment of various components (Fig. 4.2).

In the group of patients who received eplerenone + L-ornithine L-aspartate and glutathione with the standard treatment of liver cirrhosis, collagen IV values decreased from 256 ± 4.2 μg to 224 ± 4.25 μg before and after the treatments, and the differences were highly reliable ($p<0.001$). In the second group of patients, the indicators before and after treatment were 263 ± 5.7 μg and 244.2 ± 5.13 μg, respectively, and reliable differences were noted ($p<0.05$).

In patients with developed hepatorenal syndrome, BFZ is the main indicator of deterioration of kidney function and its severity. BFZ was determined before and after procedures in all patients in our follow-up.

In this figure, we can see that the BFZ values in the patients were significantly reduced regardless of the treatment received. In the first group of patients, BFZ decreased from 4.34 ± 0.13 % to 3.7 ± 0.2 % before and after treatments, respectively. In the second group, it was 4.23±0.3% and 4.0±0.2% ($p<0.05$). The fact that BFZ did not appear in patients can be explained by the fact that the hepatitis B virus has an aggressive effect on the liver and kidneys, causing irreversible changes in them.

Positive changes were noted in both groups after the treatment of patients with developed liver cirrhosis due to chronic hepatitis C.

In the first group of patients, the indicators before and after treatments increased from 4.09 ± 0.15% to 4.54 ± 0.13%, but they did not develop BFZ. In the second group of patients, this indicator was 4.1 ± 0.2% and 5.09 ± 0.14%, respectively, before and after treatment, and high reliable changes were noted ($p<0.001$).

Siydikda kollagen IV ning kamayishi va BFZ da muolajalardan keyin kuzatilgan ijobiy o‘zgarishlarni glutation va eplerenonning fibrozga qarshi samarali ta’sir qilishi bilan bog‘lash mumkin. Shuningdek, surunkali gepatit C negizida rivojlangan jigar sirrozida uning gepatit B negizida rivojlanganlarga qaraganda fibroz jarayonlarini ishonchli kamayganligi kompleks davoga virusga qarshi preparatlarni buyurilishi bilan bog‘liq.

Consummation

Cirrhosis of the liver is a diffuse disease with a chronic exacerbation, manifested by necrosis of hepatocytes, disruption of its normal architecture due to the growth of connective tissue and the formation of regeneration nodes, as well as developing fibrosis. As a result, serious complications leading to death are observed with the development of chronic liver failure, signs of portal hypertension.

The disease is one of the six main causes of death of patients aged 35 to 60 years in economically developed countries. It is recorded in 14-30 people out of every 100,000 inhabitants. Every year, about 1.4 million people in the world die from cirrhosis of the liver and its complications. Scientific observations confirm that cirrhosis of the liver is more common in men [8; pp. 59-67, 13; p. 76-80, 79; pp. 545–59. 130; pp. 117–71, 96; 109; pp. 125-133].

Cirrhosis of the liver is a polyetiological disease, in most cases it is caused by hepatitis B, C, D viruses (mostly type C), alcohol abuse. Alimentary - allergic, toxic and other factors also cause the disease [8; p. 59-67, 170; 805-811-b].

The mechanism of development of liver cirrhosis is closely related to its morphological changes. In this case, blood circulation disturbance as a result of necrosis of liver cells and the growth of connective tissue in their place takes the leading place [107; pp. 221-234, 125; 31; 70;].

Liver cirrhosis is characterized by the transformation of its normal structure into fibrous tissue and the formation of regeneration nodes. It is the final stage of a number of chronic liver diseases. It is the final stage of a number of chronic liver diseases [8; pp. 59-67, 79: pp. 545–59, 130: pp. 117–71. 26; pp. 71-102].

The decompensation stage of liver cirrhosis is manifested by obvious clinical signs of the disease, and the average life expectancy of patients does not exceed two years. The manifest state of this stage is manifested by a number of complications, and the prognosis of the disease is inextricably linked with them [8; p. 59-67, 87; 241-242-b]. These include hepatic encephalopathy, bleeding from esophageal and gastric varices, ascites (abdominal fluid with or without infection),

hepatorenal syndrome, hyponatremia, and infection-related complications [9; p. 152, 66; 24-31., 42;. pp. 25-38].

In most cases, cirrhosis of the liver develops as a result of viral hepatitis (mostly hepatitis B and C). According to information from various sources, hepatitis causes liver cirrhosis from 40-50% to 70-80% [22; pp. 24-31, 41; pp. 5-8, 44; pp. 75-82].

The clinical manifestation of the disease is different - it can be asymptomatic for many years or in the form of acute hepatitis and chronic inflammatory diseases of the liver. About 20% of patients are diagnosed with liver cirrhosis at autopsy after their death [42;. pp. 25-38, 9; p. 152].

According to the results of observations of Scandinavian scientists, less than 20% of women and 40% more men with cirrhosis of the liver retained their work. The above-mentioned varnished tongue, vascular asterisks, palmar erythema, gynecomastia occur in up to 75% of patients during the manifest period of liver cirrhosis. One of the most common symptoms in patients is the expansion of the veins of the esophagus, stomach, and intestines, and bleeding from them in most cases ends with the death of the patient. As a result of reflux esophagitis caused by increased intra-abdominal pressure, patients experience gasping for air, sometimes belching. In addition to the above symptoms, mental disorders occur as a result of central nervous system intoxication and toxic encephalopathy [42;. 25-38., 9;].

In the initial stages of cirrhosis of the liver, the enlargement of both lobes is determined. Later, its left lobe becomes more enlarged. In one third of patients, the surface of the liver may be uneven. In the last stages, the size of the liver decreases, the hepatolienal syndrome is accompanied by hypersplenism [52; p. 87-88, 30;].

In the biochemical analysis of blood, approximately 40% of patients have a normal level of bilirubin, transaminases are slightly elevated. Elevated gamma transferases and presence of hypoalbuminuria are characteristic features of liver cirrhosis. In the general analysis of blood, thrombocytopenia, sometimes post-

bleeding anemia, increased erythrocyte sedimentation rate and leukocytosis are detected when infection is added [42;. 25-38., 67; pp. 13-17].

In the biochemical analysis of blood, approximately 40% of patients have a normal level of bilirubin, transaminases are slightly elevated. Elevated gamma transferases and presence of hypoalbuminuria are characteristic signs of liver cirrhosis. In the general analysis of blood, thrombocytopenia, sometimes post-bleeding anemia, increased erythrocyte sedimentation rate and leukocytosis are detected when infection is added [42;. 25-38., 67; pp. 13-17].

A number of complications observed in cirrhosis of the liver play a decisive role in the quality and duration of the patient's life. Therefore, early identification of these complications and appropriate treatment are of great importance for scientific and practical medicine.

Among the many complications of liver cirrhosis, hepatorenal syndrome is one of the least studied. Full-fledged scientific observations dedicated to it have not been conducted in our republic.

Hepatorenal syndrome occurs as a result of kidney damage based on obvious clinical signs of liver disease, including cirrhosis, in the absence of other causes leading to kidney failure. In 1994, the international ascites club formulated the major criteria for hepatorenal syndrome, and in 2007 they were revised and partially changed. According to some information from scientific sources, approximately 15% of patients with cirrhosis of the liver develop hepatorenal syndrome within 6 months after the first hospitalization due to ascites, and 40% within 5 years [62; 72; 92; p. 397-417, 89; 90; 156; p. 364-375, 157; 1246-1255-b].

There are two types of hepatorenal syndrome. Its first type is associated with rapid deterioration of kidney function in response to increasing deterioration of liver function. This type is often observed in severe alcoholic hepatitis and in the terminal stages of liver cirrhosis with spontaneous bacterial peritonitis. A 100% increase (at least 221mmol/l) of creatinine in the blood compared to the initial level is typical for this type of patients [47; 75; 600-610-p, 78:1505-13-p, 153; 1735-1744-b, 155; 578-581-b].

The second type of hepatorenal syndrome is observed in liver cirrhosis with ascites and resistant to diuretics, it is stable and slowly increases [26: pp. 71-102, 161; 352-9-b, 162; 43-8-b].

There are no specific clinical signs characteristic of hepatorenal syndrome. Patients are disturbed by symptoms such as thirst, apathy, lethargy. In the objective examination, the abdomen is enlarged, blood pressure is reduced, and in some cases, jaundice is increasing. Oliguria, reduced glomerular filtration rate and a slight increase in serum creatinine are detected. In rare cases, obvious proteinuria and minor changes in urine sediment are found [105:1819-27-b, 91; 93; 101].

If positive results are not observed in patients with obvious ascites, arterial hypotension and hyponatremia are detected, it indicates the development of hepatorenal syndrome. Here, this syndrome, which develops in liver cirrhosis, should be distinguished from acute tubular necrosis, glomerulonephritis, toxic nephropathy, and nephropathies developed in chronic heart failure [124; 69: pp. 659-682, 121; 83-100 p. 139; p. 61-68].

30 years ago, creatinine levels of 150 mmol/l and higher were accepted as criteria for kidney failure in hepatorenal syndrome. This corresponds to an indicator of KFT of 40 ml per minute and below [17; pp. 36-38, 76; pp. 164–176, 122; 2017-26-p, 103; 593-603-b, 138; pp. 116–122].

According to the new concept of the International Ascites Club (International Ascites Club), the amount of urine excreted in the diagnosis of acute kidney injury in patients diagnosed with liver cirrhosis is not taken into account. Oliguria is often caused by sodium retention in cirrhosis with ascites syndrome. They may have increased diuresis on the basis of diuretic drugs, even if the KFT is relatively normal [108; 317-24-p, 74; 968–974., 150; 1310-1318-b, 151; 715-32-b].

Classification of acute kidney injury in cirrhosis of the liver is based on the new system of increasing creatinine compared to the basal (primary) indicator or high (peak/peak) increase during hospitalization [123; 505-20-p, 146; 2087-107-p, 147; 1651-3].

According to the criteria of KDIGO, its I stage is 1.5-2.0 times the basal/primary indicator or 265 mmol/l and higher. Acute kidney injury in the 2nd stage is defined as cases where creatinine is 2 times more than the norm but less than 3 times. In stage 3, creatinine increases more than 3 times [118; 179–184 p].

Recent studies have shown that the efficiency of treatment in stage 1 of acute kidney injury developed on the basis of cirrhosis of the liver is inextricably linked with creatinine values. If it exceeds 132.6 μmol/l, it is not good because of the disease [95; pp. 474–481, 111;].

When hepatorenal syndrome is accompanied by ascites, it is necessary to inject albumin in order to prevent it. Therefore, if symptoms of bacterial peritonitis are observed in them, 1 mg of albumin per 1 kg of body weight is injected into the patient, this dose is reduced by 1 mg from the third day [134:529-537-p., 132: 360-367-p., 144; pp. 955–961, 148; 424-9-b]. Also, 400 mg of norfloxacin per day is prescribed to prevent bacterial peritonitis in hepatorenal syndrome.

In a number of scientific works, the changes in the kidneys observed in cirrhosis of the liver were considered as a functional state (p. 26:71-102), but at the same time, modern tests used to detect nephropathy in the early stages were not used. In particular, as one of the diagnostic criteria of hepatorenal syndrome, the indicator of protein excreted in urine overnight is defined as 0.5 g or less. But according to the latest recommendation, if less than 10 mg of protein is excreted in the urine in one night, optimal albuminuria, if 10-29 mg is excreted, it is more than normal albuminuria (in the previous high norm), if 30-299 mg is excreted in the high norm (in the previous microalbuminuria), 300-1999 mg of excretion is very high (former macroalbuminuria/proteinuria), in cases of excretion of 2000 mg and more, nephrotic albuminuria was considered [117; 1-150-b].

It is known that KFT can be determined using special formulas based on the level of endogenous creatinine in blood serum. One of the currently used formulas is the Cockroft-Gault formula, according to some data, the indicator is 23% higher than the original level when it is used to determine the KFT [57;62-66-b]. Also, MDRD (Modification of Diet in Renal Disease [58; 82-85-p.] CKD - EPI

(Cloronic Kidney Disease Epidemiology Collaboration) formulas are used in practice to determine it [59; 259-298-p, 60; 77-80 -b].

Using the MDRD formula, KFT is calculated based on gender, age, nationality and the patient's body surface area of 1.73 m2. This will help him identify the stages of SBK. However, the formula increases the number of patients with SBK in screening examinations in people under 18 years old, pregnant women, people over 70 years old, in cases where kidney function is normal or slightly weakened [61; 425-428-b, 60; 77-80 p].

Based on the mentioned data, the renal functional reserve (RBF) consensus and its evaluation tests were created. BFZ is understood as its ability to raise KFT from the basal, i.e., primary state to a maximum high level. To achieve it, all nephrons, not only deep, but also superficial, take part in the process. The method of determining BFZ was first developed by J.P. Recommended by Bosch. Usually, the expression of the difference in the percentage of the filtration of the balls determined after the loading with the basal, that is, the initial KFT, is called BFZ. If this indicator is more than 10%, BFZ is preserved, between 5-10% it is reduced, and if it is less than 5% or negative, it is considered that there is no reserve [36; 112-118-b, 115; 260-272-b]. The absence of BFZ indicates that the glomeruli are in a state of hyperfiltration [49; pp. 48-53, 131; pp. 1138-1139, 133; pp. 11-17, 151; 5-10 p].

One of the simplest and most physiological methods for testing renal functional reserve is the use of a semi-diluted (0.45%) solution of NaCl. Initially, KFT is calculated based on the amount of creatinine in the blood. Then the patients drink 0.45% aqueous NaCl solution in the amount of 0.5% of body weight for 3-5 minutes. This volume and concentration of the solution is considered sufficient to remove excess sodium ions. After one hour, the concentration of keatinine in the blood is determined and the KFT is calculated. Its percentage increase indicates the presence of BFZ.

An increase in KFT after screening indicates that there is a reserve in the filtration fraction. According to the change in KFT, BFZ is evaluated as preserved

(increased by more than 10%), decreased (if increased by 5 - 10%) or no reserve (in cases where it is less than 5%). BFZ may not be present even with preserved KFT, which indicates that the organ is undergoing a hyperfiltration process and the non-immune process is increasing. It confirms that the kidney is working in a state of hyperfiltration with high power in cases of reduced or absent scores.

In most of the literature, in the presented data, BFZ was studied in patients with diabetes in most cases. However, there is almost no information on the use of this test in a number of other diseases, including hepatorenal syndrome. However, the study of BFZ in hepatorenal syndrome developed on the basis of liver cirrhosis provides an opportunity for early diagnosis of nephropathy.

In addition to the above, one of the markers of kidney damage is the excretion of type IV collagen in the urine. It forms the basis of the basal membrane of balls and tubules. According to some authors, the appearance of this protein in urine is one of the early morphological signs of nephropathy [31; 32; 33; p. 87-93, 120; pp. 885-893, 143; 1473-80-b]. Compared to healthy people, patients with normoalbuminuria have a higher urinary excretion rate. It was noted that there is a high accumulation of IV collagen in the tissue of patients who underwent a kidney biopsy, and it is directly related to the protein level in the urine of patients diagnosed with normoalbuminuria. In this study, urinary excretion of type IV collagen was detected even in individuals with normal albumin levels. The authors showed that type IV collagen was present in 26% to 45% of patients with a confirmed diagnosis of diabetes and normoalbuminuria in their urine based on another examination. In most cases, this condition can be noted more often when hypertension and diabetes occur together [142; pp. 3337-3344, 65; 552-560-b]. The given data confirm that urinary excretion of type IV collagen can be observed before the clinical symptoms of nephropathy appear, and that it is appropriate to use it in the diagnosis of fibrotic processes in the kidney even in hepatorenal syndrome.

It is known that the development of the fibrosis process in the kidneys greatly aggravates the course of the main disease, including cirrhosis of the liver.

In this case, the use of effective anti-fibrosis drugs and the control of the process with the help of collagen IV are of great practical importance in liver cirrhosis.

In an experimental study conducted by Chinese scientists, a model of interstitial fibrosis in the kidney was called in rats. The effect of eplerenone on kidney damage was studied. According to the obtained results, eplerenone reduced the processes of interstitial fibrosis. Histological examination of eplerenone-treated rats on days 7 and later showed significantly higher amounts of fibrotic tissue in the kidneys of the latter group compared with those in the control group. Immunohistological tests conducted by the authors showed that eplerenone reduces inflammatory processes in the kidney, proliferation in interstitial tissues, and oxidative stress. Based on the obtained results, the researchers concluded that eplerenone reduces renal interstitial fibrosis by having an anti-inflammatory effect [p. 84:557-66].

In numerous studies, it has been confirmed that the deficiency of endogenous glutathione in liver diseases, including liver cirrhosis developed on the basis of viral hepatitis, by supplementing the body, gives positive results [3].

Liver cirrhosis developed as a result of viral hepatitis B and C has not been compared in our republic. Also, type IV collagen, a marker of fibrosis, was not used in the early diagnosis of hepatorenal syndrome, one of the serious complications of liver cirrhosis. In addition, a reliable and early sign of kidney dysfunction is the calculation of its functional reserve, scientifically proven. But until now, this test has not been used to evaluate the functional changes in the kidneys observed in liver cirrhosis. However, its detection allows early detection of kidney dysfunction observed in liver cirrhosis.

From this point of view, early detection of hepatorenal syndrome in patients with advanced liver cirrhosis due to chronic viral hepatitis B and C, studying the condition of BFZ opens new perspectives in the treatment of this severe syndrome.

Taking into account the above, in our study, among 350 patients treated in the clinic of Andijan State Medical Institute, who were diagnosed with advanced liver cirrhosis based on hepatitis B and C, 124 patients with clinical signs of type II

hepatorenal syndrome were observed. The following criteria of hepatorenal syndrome, recommended by the International Ascites Club in 1994 and revised and partially amended in 2007, were used to separate them into a separate group.

Patients with hepatorenal syndrome and included in the study were divided into two groups. The first group consisted of 60 patients with liver cirrhosis caused by viral hepatitis B, 28 men (46.7%) and 32 women (53.3%), their average age was 46.44±1.38. The second group was caused by chronic hepatitis C. included 64 patients with liver cirrhosis. 4 patients died of esophageal variceal bleeding and 1 died of hepatocarcinoma and were not included in the follow-up group. Of the remaining 60 patients, 25 were men (41.6%) and 35 were women (58.4%), the average age was 48.82±1.6. 45% of them were patients with genotype 1, 15% with genotype 2, and 13% with genotype 3. Genotypes were not determined in the remaining cases.

Class A according to Child Pew, class B in 46% and class C in 24% were recorded in 30% of the monitored patients.

Based on the goals and tasks set before us, all patients underwent excellent clinical and laboratory-instrumental examinations at the clinic of the Andijan State Medical Institute and were observed in an outpatient setting for 3 months.

Eplerenone + glutathione and L-ornithine L-aspartate additional drugs with hepato-nephroprotective and antifibrosis effects were prescribed to all patients with clinical and laboratory signs of hepatorenal syndrome.

Depending on the severity of the disease, Glutathione was administered intravenously in a dose of 1.2-2.4 g for 10 days, and then in a dose of 0.6 g intramuscularly for a week. L-ornithine L-aspartate was also administered intravenously to patients in a dose of 5-20 g for 10 days depending on the severity of the disease.

The results obtained in the study were statistically processed, the mutual unity and dependence and difference in the groups were determined, and summary information and practical recommendations were developed.

In both groups of patients diagnosed with advanced liver cirrhosis based on chronic hepatitis B and C under our observation, a careful anamnesis was collected and the following were identified: in 67% of patients, the disease was transmitted parenterally. 5% of them had blood transfusions, 15% had surgery, 25% had dental services, 12% had endoscopic examinations and other medical interventions, and 10% of patients had sexually transmitted diseases. In the rest of the patients, there was no possibility of the source of infection.

When investigating concomitant diseases, 30% of patients were diagnosed with chronic gastroduodenitis, 15% with duodenum and gastric ulcer disease. During the anamnesis collection, 22% of the subjects did not deny that they had abused alcohol on the basis of liver cirrhosis, and it was found that this aggravated the course of the main disease. In 5% of patients, the auscultation and dopplerographic examination of the vessels showed that the arteries were clearly damaged by atherosclerosis, and the process was noted more in the branches of the brachiocephalic and aortic arches.

In this case, it was confirmed that in the group with developed liver cirrhosis based on chronic hepatitis B, in a number of cases, some complaints and external symptoms of the disease were reliably higher compared to patients with developed liver cirrhosis based on chronic hepatitis C.

20% and 40% of patients in both groups, respectively, complained of pain and heaviness in the right rib area. In this case, in patients with advanced liver cirrhosis due to chronic hepatitis C, these complaints were 2 times more frequent than in the first group, and the differences were reliable ($r<0.001$). Also, complaints such as burning in urine (15% and 20%, respectively), stuttering (6.6% and 8.3%, respectively) were observed relatively rarely in patients, and the differences were not reliable ($p>0.05$). Scleral yellowing was observed in 68% and 49% of patients in both groups, respectively, and the differences were highly reliable ($r<0.001$). In patients with liver cirrhosis developed on the basis of chronic hepatitis C, nausea was detected in 65% of cases and was 1.9 times higher than in the first group ($r<0.001$).

In addition, 83.3% of patients with liver cirrhosis developed on the basis of chronic hepatitis B complained of abdominal discomfort, 50% of constipation, and 10% of abdominal discomfort. In the second group, these complaints were 76.6%, 55% and 15%, respectively. When the differences between the groups were compared, no reliable differences were found in all listed complaints ($p>0.05$). Sleep disorders and memory loss were observed in 80% and 65% of patients in both groups, respectively, and in liver cirrhosis developed on the basis of chronic hepatitis B, its differences compared to those in group C were highly reliable ($r<0.001$). Slowness was observed in 36% of patients of the first group, which was 2 times higher than that of patients of the second group (18%), and a highly reliable difference was detected ($r<0.001$).

In addition to the above, dysphagia (80% and 85%, respectively), pallor of the skin and mucous membranes (75% and 85%, respectively), skin tightening (85% and 90%, respectively) and vascular stars were observed in both groups of patients. complaints such as presence (78% and 80%, respectively), body muscle atrophy (34% and 35%, respectively) were observed in patients, and the differences between them were not reliable ($p>0.05$).

According to a number of authors, 67% of patients with HCV cirrhosis and its markers were not identified had bleeding from esophageal veins and stomach, this indicator was equal to 53% in patients with its B form. Hepatic encephalopathy and ascites syndrome were developed on the basis of hepatitis B in 80% and 10% of cases, respectively, and in its C form, these symptoms were shown to be more likely to occur in 65% and 5%, respectively. Peripheral tumors were observed in 23% of patients in the first group and 8% in the second group, high reliability differences were found[46]. Our observations also confirm the above information.

The conducted comparative analysis confirms that in most cases of liver cirrhosis developed on the basis of the studied viral hepatitis B and C, the complaints of patients and some external clinical signs do not reliably differ from each other. In addition, liver encephalopathy and ascitic syndrome were observed

more often in liver cirrhosis developed on the basis of hepatitis B, and hemorrhagic syndrome and bleeding from esophageal veins were observed more often in its C form, and the results obtained by us correspond to the data in the literature.

Based on the goal set before us, a general analysis of blood was first performed in patients diagnosed with liver cirrhosis developed on the basis of chronic hepatitis B and C.

Hemoglobin levels in the first group of patients with advanced liver cirrhosis due to chronic hepatitis B were 101.9 ± 0.85 g/l and in the second group of patients were 96.6 ± 0.82 g/l, and the differences between them were highly reliable. was (R<0.001). In addition, mild anemia was confirmed in both cases. The pathogenesis of anemia in cirrhosis of the liver is complex and unclear, in which the release of incompletely formed erythrocytes into the peripheral blood due to the violation of the proliferation and formation of erythroblasts in the bone marrow is of great importance. In addition, anemia may develop due to the toxic effect of the virus on erythrocytes, impaired absorption of iron, folic acid and vitamin B12, as well as the breakdown of erythrocytes in the spleen.

The number of leukocytes was 10.62 ±0.15x103 l and 10.4 ±0.15x103 in both groups, respectively (R>0.05). The hematocrit index was 32.48±0.26 in the first group and 31.88±0.35 in the second group, and no reliable difference was detected (R>0.05). The number of platelets was 134.1±1.13x103 l and 132.1±1.06x103 l in the first and second groups, respectively (R>0.05). The number of lymphocytes was found to be 17.37±0.54% x103 l in patients with advanced liver cirrhosis based on chronic hepatitis B and 13.4±0.4x103 l in patients with advanced liver cirrhosis based on chronic hepatitis C (r<0.001). . Erythrocyte sedimentation rate was 27.6±0.46mm/h and 31.93±0.4mm/h in both groups, respectively, and the differences were reliable (r<0.001).

The coagulogram parameters of the patients under our observation were also compared before the procedures. Prothrombin index was 57.2 ± 0.56% before treatment in patients with advanced liver cirrhosis due to chronic hepatitis B, and 52.68 ± 0.54% in patients with advanced liver cirrhosis due to hepatitis C, and the

differences were highly reliable. (r<0.001). Partially active thromboplastin time was equal to 42.72 ±0.68 seconds in the first group and 46.75 ±0.81 seconds in the second group (r<0.001). Fibrinogen indicators were 2.5±0.06 g/l and 2.04±0.052 g/l in both groups (r<0.001). International normalized relationship indicators were 1.25±0.07 and 1.05±0.15 in the first and second groups, respectively, and the differences were not reliable (r>0.05). Antithrombin SH was 54.6±0.74% and 48.92±0.83% in the first and second groups, respectively, and a highly reliable difference between the two groups was noted (r<0.001).

In the observation of changes in hemostasis in liver cirrhosis, the imbalance between blood coagulation and anti-coagulation factors has a leading role, in particular, the anticoagulant system - antithrombin III and protein S. Prothrombin index decreases up to 73%, partially active thromboplastin time (QFTV) increases up to 75%. , a 25% decrease in fibrinogen compared to myor was noted. According to a number of authors, antithrombin III and plasminogen are decreased in liver damage caused by viruses compared to cirrhosis of other etiologies. As a result of deficiency of natural anticoagulants protein S, antithrombin III, markers of the blood coagulation system, as well as activation of the vascular-thrombocytic joint, are observed due to an increase in Willebrant factor. Although procoagulation tests (PTI, QFTV) show a high probability of bleeding, these changes indicate a high probability of formation of blood clots. The direction of these studied samples in different directions is considered a laboratory sign of coagulopathy [14].

During the study, biochemical analysis of blood, functional reserve of kidneys and amount of collagen IV in urine were determined in patients with developed liver cirrhosis due to hepatitis B and C. The total protein content in blood serum was 59.8 ± 0.78 g/l in patients with advanced liver cirrhosis due to chronic hepatitis B and 52.72 ± 0.88 g/l in patients with advanced liver cirrhosis due to chronic hepatitis B. scores were highly reliable when compared between groups (r<0.001). The amount of albumin in the blood was equal to 24.52 ± 0.7 g/l and 27.37 ± 0.82 g/l in the first and second groups, respectively (r<0.001). Urea values were 10.3±0.27mmol/l and 13.67±0.4mmol/l in both groups, respectively

(r<0.001). ALT and AST indicators in the first (respectively 58.58±0.47Ed/l and 104.1±1.36Ed/l) and second (85.77±1.26Ed/l and 117.9 ±1.65 Ed/l) when compared between groups, the values were highly reliable (r<0.001). Total bilirubin was 47.52±1.07mmol/l in the first group, 66.25±1.7mmol/l in the second group, and alkaline phosphatase was 112.8±2.68Ed/l and 88.48±1.6Ed in both groups, respectively. /l and the differences were highly reliable (r<0.001). Total cholesterol values did not reliably differ between groups (2.48 ± 0.15 mmol/l and 2.15 ± 0.13 mmol/l, respectively, R>0.05).

Kidney functional reserve before treatment was 4.3±0.17% and 4.1±0.12% in the first and second group of patients, respectively (R>0.05).

We also determined collagen IV indicators in the urine, which is a marker that indicates the level of fibrosis processes in the kidney. In this case, in patients with advanced liver cirrhosis based on chronic hepatitis B, the values of collagen IV in urine before treatment were 242.33 ± 3.85, and in patients with advanced liver cirrhosis based on chronic hepatitis B, it was equal to 259.48 ± 3.55, and the indicators of both differences were reliable when compared between groups (r<0.001).

At the next stage of our research, the results of the patients before and after the treatment were compared. Patients of both groups were divided into two subgroups of 30 patients each in order to evaluate the effectiveness of complex treatment procedures with different contents. The first subgroups were prescribed spironolactone (veroshpiron) + L-ornithine L-aspartate on the basis of the complex treatment of liver cirrhosis, and eplerenone + L-ornithine L-aspartate + glutathione drugs were prescribed to the second subgroups on the basis of the complex treatment of liver cirrhosis.

Initially, the changes observed in the complaints and some external symptoms of the patients under our observation after the treatment procedures were evaluated.

As shown in the table, positive changes were observed in a number of complaints after the complex treatment of patients with the addition of eplerenone

+ L-ornithine L-aspartate and glutathione. Pain and heaviness in the right rib area decreased from 20% to 5% and from 40% to 10% before and after the treatments in the first and second group of patients, respectively, and the differences were highly reliable in both cases. ($r<0.001$). In patients with advanced liver cirrhosis due to chronic hepatitis B, boils and belching were observed in 15% and 6.6% of cases, respectively, before treatment, and after treatment, the indicators were equal to 11.6% and 3.5%, respectively. In patients with advanced cirrhosis due to chronic viral hepatitis C, these complaints decreased from 20% to 17% and from 8.3% to 5% before and after treatments, respectively. But the changes in both groups were not reliable ($p>0.05$). Yellowness of the sclera in the first group was 68% before treatments and 65% after treatments ($p>0.05$). In the second group, high reliability changes of this sign before and after the treatment were noted, equal to 49% and 28%, respectively ($r<0.001$).

Nausea in the first group of patients occurred in 35% of patients before treatments and in 20% of patients after treatments, and the changes were reliable ($r<0.01$). Nausea in the second group decreased by 2.1 times after treatment (65% and 30%, respectively), and the changes were more reliable than in the first group ($r<0.001$).

In patients with advanced liver cirrhosis due to chronic hepatitis B and C, abdominal rest was significantly reduced before and after treatment (76.6% to 50% and 83.3% to 40%, respectively) ($r<0.001$). Constipation and irregular bowel movements were observed in 50% and 10% of patients in the first group, respectively, before treatment, and in 45% and 7.5% of patients after treatment ($p>0.05$). In the second group, positive changes in these complaints were also found after the treatments (reduced from 55% to 50% and from 15% to 12%, respectively), but the differences were not reliable ($p>0.05$).

In patients with advanced liver cirrhosis due to chronic hepatitis B, appetite reduction was 90% before treatment and 45% after treatment, and highly reliable changes were found ($r<0.001$). A highly reliable change was also noted in those

who developed on the basis of chronic hepatitis C (decrease from 95% to 60%, respectively, $r<0.001$).

Sleep disturbances and memory loss were reliably reduced in the first group of patients before and after treatments (from 65% to 50%, respectively, $r<0.05$). In the second group, these complaints were observed in 80% of patients before treatment and 55% after treatment, and the differences were highly reliable ($r<0.001$). Symptoms of lethargy were significantly reduced after treatment in both groups of patients ($r<0.001$). Dysphagia was observed in both groups in 80% and 85% of patients before treatment and in 53% and 58% of patients after treatment, respectively, and the differences were noted to be highly reliable ($r<0.001$).

Pallor of the skin and mucous membranes and skin itching were 75% and 45%, 85 and 45%, respectively, before and after treatment in patients with advanced liver cirrhosis due to chronic hepatitis B ($r<0.001$). In those who developed chronic hepatitis C, the above complaints were significantly reduced before and after treatment (from 85% to 28% and from 90% to 50%, $r<0.001$).

In the first and second groups, 78% and 80% of patients had vascular stars before treatment, respectively, and after treatment, these signs were observed in 77% and 78% of patients, respectively, and the changes were not reliable ($r<0.05$). Varicose veins around the navel increased from 10% to 15% in the first group and decreased from 15% to 13% in the second group ($r>0.05$). Despite the medical procedures, ascites in the first group remained in 5% of patients before procedures and 3% after procedures. In the second group of patients, although it decreased from 10% to 7%, the changes were not reliable ($r>0.05$). Peripheral tumors improved in both groups of patients after the treatments, but no reliable changes were observed. Hepatic encephalopathy reliably decreased from 80% to 45% and 65% to 28% before and after treatments in both groups, respectively ($r<0.001$). Complications of bleeding from esophageal varices decreased in the first group with low reliability (from 53% to 45%, respectively, $r<0.05$) and in the second group with high reliability (from 67% to 27%, respectively, $r<0.001$). Symptoms

of fatigue, which were evident in all patients involved in the study, were highly reliable after the treatments ($r<0.001$).

A highly reliable reduction ($r<0.001$) of symptoms such as hepatic encephalopathy, lethargy, general weakness, and a positive change in pain syndrome as a result of the reduction of hepatomegaly is associated with the effect of glutathione. Its positive effect was also confirmed by Chinese researchers (M.Yimin et al., 2000).

Ong J.P. and co-authors studied the effectiveness of L-ornithine L-aspartate in a multicenter prospective observational study conducted in 191 patients. It shows that the drug has a positive effect on the quality of life of patients, including reducing fatigue, improving sleep quality and helping to concentrate.

The obtained results showed that the addition of eplerenone + L-ornithine L-aspartate and glutathione to the complex treatment of liver cirrhosis developed on the basis of hepatitis B and C led to a reliable positive change in complaints and some external clinical signs of both groups of patients. Here it should be noted that they are more clearly manifested in patients with hepatitis C. This may be related to the high effectiveness of antiviral drugs in the latter group.

When comparing the results of general blood analysis obtained after the complex treatment of various components in patients with developed liver cirrhosis on the basis of chronic hepatitis B, hemoglobin values were 96.7 ± 1.19 g/l in the first group, 93 ± 1.19 g/l in the second group. 1±1.15 g/l, the differences were reliable ($r<0.05$). Leukocyte, thrombocyte, lymphocyte count, hematocrit, and erythrocyte sedimentation rate did not reliably differ between groups ($r>0.05$). Such identified changes indicate that both subgroups of patients were selected monad.

Positive changes in a number of indicators of general blood analysis were observed in patients with advanced liver cirrhosis due to chronic hepatitis B after standard treatments with various components. Hemoglobin indicators were 96.7 ± 1.19 g/l before treatment and 98.7 ± 1.18 g/l after treatment in patients who received veroshpiron + L-ornithine L-aspartate on the basis of complex treatment

of liver cirrhosis, and there was a reliable difference not detected (r>0.05). In the group receiving eplerenone + glutathione + L-ornithine L-aspartate on the basis of the second, i.e. complex treatment of liver cirrhosis, the hemoglobin values before and after the treatments were 93.1±1.15 g/l and 97.1±1, respectively. 15 g/l, the differences were reliable (r<0.05). In the first group of patients, the number of leukocytes in the general blood analysis was 10.33±0.2×109 Ed/l before treatment and 9.2±0.19×109 Ed/l after treatment (r>0.05). In the second group, their number decreased by 1.57 times after treatment and the indicators were highly reliable (10.9±0.19 ×109 Ed/l and 6.93±0.2 ×109 Ed/l, respectively, r <0.001). Hematocrit values in both groups were 32.53±0.37% and 35.13±0.38% before treatment and 32.43±0.38% and 37.03±0.5% after treatment, and reliable changes were observed in patients with eplerenone + L-ornithine L-aspartate + glutathione on the basis of complex treatment of liver cirrhosis (r<0.05). The number of platelets and lymphocytes in the first group was equal to 133.5±1.5 × 109 Ed/l and 14.7±0.8×109 Ed/l before the treatment, and after the treatment, these indicators were 138.2, respectively. It was ±1.5×109 Ed/l and 15.93±0.73×109 Ed/l. A reliable difference was found between both indicators (r<0.05). In the second group, the number of platelets increased from 134.7±1.73×109 Ed/l to 145.7±1.7×109 Ed/l, highly reliable changes were noted (r<0.001), and the number of lymphocytes was 15.83± It changed from 0.74×109 Ed/l to 18.03±0.76×109 Ed/l (r<0.05). The erythrocyte sedimentation rate was 27.83±0.7 mm/h and 24.83±0.69 mm/h in the first group of patients before and after treatments, and the differences were not reliable (r>0.05). In the second group of patients, the erythrocyte sedimentation rate decreased by 1.5 times from 27.4±0.6 mm/hour to 18.4±0.62 mm/hour (p<0.001).

During the medical treatment, it was found that the number of leukocytes and the rate of erythrocyte sedimentation in the blood of patients who received eplerenone + L-ornithine L-aspartate and glutathione drugs with the standard treatment, which developed liver cirrhosis due to chronic hepatitis B, and the number of platelets increased reliably. These results showed that the combined use

of L-ornithine L-aspartate and glutathione drugs with standard treatment is more effective than the use of L-ornithine L-aspartate alone in patients with advanced liver cirrhosis due to chronic hepatitis B.

The indicators of general blood analysis were compared in both subgroups of patients before and after complex treatment procedures with different components in patients with advanced liver cirrhosis due to chronic hepatitis C. There were no reliable changes before treatments in all studied indicators ($r>0.05$).

The first, i.e., based on the complex treatment of liver cirrhosis, in the group receiving veroshpiron + L-ornithine L-aspartate, the hemoglobin values before treatment were 97.03±1.27 g/l and after treatment were 100±1.27 g/l and no reliable difference was observed ($r>0.05$). In the group receiving eplerenone + glutathione + L-ornithine L-aspartate based on the complex treatment of liver cirrhosis, the hemoglobin values before and after the treatments were 96.17±1.05 g/l and 101.2±1.05 g/l, respectively. being equal, a highly reliable difference was determined ($r<0.05$). The number of leukocytes in the first group of patients was 10.6±0.23×109 Ed/l before treatment and 9.1±0.2×109 Ed/l after treatment ($r>0.05$). In the second group, the number of leukocytes decreased by 1.5 times after treatment and the indicators were highly reliable (10.2±0.2×109 Ed/l and 6.6±0.2×109 Ed/l, respectively, $r <0.001$). In the first group, hematocrit values before and after treatment were 32.07±0.5% and 34.07±0.53%, respectively ($r<0.05$). In the second group, more reliable changes were observed from 31.7±0.5% to 38.7±0.5% after treatments ($p<0.001$).

Based on the complex treatment of liver cirrhosis developed due to chronic hepatitis C, in the group receiving veroshpiron + L-ornithine L-aspartate, the total protein in the blood serum and albumin, which is the main part of it, were 52.43±1.19 g/l and 28, respectively. It was 27±1.15 g/l. Differences were not reliable ($r>0.05$) despite the fact that these parameters increased by 57.4±1.23 g/l and 31.4±1.19 g/l after the treatments. In the group receiving eplerenone + L-ornithine L-aspartate + glutathione on the basis of the second, i.e. complex treatment of liver cirrhosis, total protein and albumin were 53±1.32 g/l and

27.77±1.03 g/l, respectively, before treatment. and after treatments were 66.16±1.4 g/l and 36.7±1.07 g/l, respectively, and highly reliable changes were found in both parameters (r<0.001). Urea indicators in the first group from 13.8±0.53mmol/l to 11.7±0.54mmol/l (p<0.05), in the second group from 13.5±0.6mmol/l to 8.7±0 High reliable changes were noted with a decrease of 0.4 mmol/l (r<0.001). There were no reliable changes in glucose values in both groups (r>0.05).

The values of alanine aminotransferase and aspartate aminotransferase in the first group were 83.87±1.6Ed/l and 115.8±2.2Ed/l before treatments, and 66.4±1.5Ed/l and 92.63±2, 66.4±1.5Ed/l after treatments. It was 17 Ed/l. In the second group, 2.16 times from 87.67±1.94 Ed/l to 40.67±1.87 Ed/l and from 119.9±2.43 Ed/l to 61.07± It decreased by 1.96 times to 2.7Ed/l, and highly reliable changes were observed in both groups (r<0.001). Total bilirubin decreased by 1.2 times in the first group (r>0.05) and 3.1 times in the second group (r<0.001). Alkaline phosphatase in the first group was 90.73±2.12 Ed/l before and after treatment. decreased to 86.7±2.15 Ed/l (r>0.05). In the second group, these indicators were 86.23±2.34 Ed/l and 74.5±2.35 Ed/l, respectively, and highly reliable changes were detected (p<0.001). There were no significant changes in total cholesterol in both groups (r>0.05).

The indicators of collagen IV in urinalysis obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis B were also studied.

The number of platelets and lymphocytes in the first group was equal to 131.2±1.5×109 Ed/l and 13.13±0.54×109 Ed/l before the treatment, and after the treatments these indicators were 137.1 It was ±1.54×109 Ed/l and 15.17±0.51×109 Ed/l (r<0.05). In the second group, the number of platelets increased from 133.1±1.6×109 Ed/l to 151.1±1.6×109 Ed/l, highly reliable changes were noted (r<0.001), and the number of lymphocytes was 13.67± It changed from 0.69×109 Ed/l to 18.67±0.6×109 Ed/l (r<0.001). The erythrocyte sedimentation rate was 32.03±0.6mm/h and 24.07±0.61mm/h in the first group of patients before and after treatments, and the differences were not reliable (r<0.05). In the second group of

patients, the erythrocyte sedimentation rate decreased by 1.89 times from 31.8±0.53mm/hour to 16.83±0.53mm/hour (r<0.001).

After the treatment, developed cirrhosis of the liver due to chronic hepatitis C was detected, high reliable changes in all indicators of general blood analysis were found in patients who received eplerenone + L-ornithine L-aspartate and glutathione drugs with standard treatment. The obtained results showed that the combined use of eplerenone L-ornithine L-aspartate and glutathione drugs with standard treatment has a more positive effect in patients diagnosed with liver cirrhosis developed on the basis of chronic hepatitis C compared to patients diagnosed with liver cirrhosis developed on the basis of chronic hepatitis B.

Coagulogram indicators before and after the treatment were also compared in the monitored patients.

Prothrombin index increased from 57.9 ± 0.69% to 60.53 ± 0.85% in the first group after complex medical treatment in patients diagnosed with advanced liver cirrhosis due to chronic hepatitis B, and the changes were reliable (r<0 .05). In the second group, the differences increased from 57.1±0.75% to 64.1±0.75% and became highly reliable (r<0.001). There were no reliable changes in partially activated thromboplastin time in the first group before and after treatments (42.6±0.8 seconds and 40.6±0.86 seconds, respectively, r>0.05). In the second group, it was 42.83±0.19 seconds before treatments and 39.83±1.07 seconds after treatments, and highly reliable changes were noted (r<0.001).

As a result of acute inflammatory processes and tissue necrosis in the body, the amount of soluble protein fibrinogen in blood serum increases. This protein is one of the important indicators of the homeostasis of the body. Based on the complex treatment of cirrhosis of the liver under our observation, in patients receiving veroshpiron + L-ornithine L-aspartate, fibrinogen was equal to 2.4±0.09 g/l before treatment and 2.75±0.08 g/l after treatment, and the differences were reliable. was (r<0.05). On the basis of the complex treatment of liver cirrhosis, in the groups of patients who received eplerenone + L-ornithine L-aspartate + glutathione, it was 2.58±0.8 g/l and 3.16±0.08 g/l, respectively, before and after the

treatments. difference was found (r<0.001). Although there were significant positive changes in the international standardized relationship scores in both groups, there were no reliable changes (1.17±0.09 and 0.98±0.04, respectively, before and after treatment, 1 ,33±0.11 and 1.13±0.11, r>0.05). Antithrombin III increased reliably from 55.53±1.02% to 60.5±0.85% in the first group, from 53.67±1.05% to 61.83±0.6% in the second group (p<0.001) .

Prothrombin index increased from 52.67±0.73% to 55.07±0.69% in the first group after complex treatment in patients diagnosed with advanced liver cirrhosis due to chronic hepatitis C, and the changes were reliable (r<0 .05). In the second group, the differences increased from 52.7±0.8% to 58.7±0.8% and became highly reliable (r<0.001). There were no reliable changes in partially activated thromboplastin time in the first group before and after treatments (47.5±1.14 seconds and 43.5±1.14 seconds, respectively, r<0.05). In the second group, it was 46±1.16 seconds before treatments and 34±1.2 seconds after treatments, and highly reliable changes were noted (r<0.001).

Based on the complex treatment of liver cirrhosis in our observation, fibrinogen was 1.99±0.069 g/l before treatment and 2.24±0.06 g/l after treatment in patients receiving veroshpion + L-ornithine L-aspartate, and the differences were reliable. (r<0.05). In the groups of patients receiving eplerenone + L-ornithine L-aspartate + glutathione on the basis of the complex treatment of liver cirrhosis, it was 2.09±0.07 g/l and 3.69±0.07 g/l, respectively, before and after the treatment. a reliable difference was found (r<0.001). Although significant positive changes were observed in both groups in international normalized relationship indicators, no reliable changes were observed (r>0.05). Antithrombin III increased from 49.33 ± 1.15% to 52.93 ± 0.93% in the first group, and from 48.5 ± 1.2% to 62.9 ± 0.7% in the second group. (r<0.001).

Also, the results of biochemical analysis of the blood of the patients involved in the study were compared before and after the treatment.

Patients with liver cirrhosis developed as a result of chronic hepatitis B were divided into two subgroups according to the composition of complex treatment

procedures. The first group of patients received L-ornithine L-aspartate on the basis of the complex treatment of liver cirrhosis, and the second group of patients received eplerenone + L-ornithine L-aspartate + glutathione on the basis of its complex treatment.

In the first group, total protein values in blood serum were 60.43±1.06 g/l before treatment and 62.4±1.17 g/l after treatment ($r>0.05$). In the second group, this indicator was equal to 59.17±1.05 g/l and 68.16±1.15 g/l, respectively, before and after treatments, and highly reliable differences were observed ($r<0.001$). The albumin values in the first group were 24.8±1.59 g/l and 28.6±1.14 g/l before and after treatments, and the differences were reliable ($r<0.05$). In the second group, the albumin values increased by 1.33 times from 24.23±0.93 g/l to 32.67±0.9 g/l after the treatments, and highly reliable changes were detected ($r<0.001$). Urea indicators in the first group from 9.96±0.4 mmol/l to 8.6±0.3 mmol/l ($p<0.05$), from 10.3±0.4 mmol/l to 8.17± in the second group A highly reliable change was noted down to 0.3 mmol/l ($r<0.001$). There were no reliable changes in glucose values in both groups ($r>0.05$).

The definition of HRS has significantly evolved over the past several decades. In 1996, the International Club of Ascites (ICA) defined acute kidney injury (AKI) in cirrhosis as an increase in serum creatinine of ≥50% from baseline to ≥1.5 mg/dL. Other important components of AKI in cirrhosis included oliguria, as well as proteinuria <500 mg/dL. In 2007, HRS was further classified into two types: type 1, characterized by a rapid deterioration of kidney function by doubling of initial serum creatinine to ≥2.5 mg/dL or a 50% reduction in less than 2 weeks in the initial 24-hour creatinine clearance to below 20 mL/min that often occurs due to a precipitating event; and type 2, in which kidney failure progression did not meet the criteria for type 1. Importantly, urinary sodium and oliguria were removed from the new diagnostic criteria. Several studies indicating that the diagnosis of AKI in patients with cirrhosis, based on an absolute increase in serum creatinine by ≥0.3 mg/dL or 50% from baseline, leads to earlier identification of patients with poorer outcomes led to the ICA to revise the definition of HRS in

2015, incorporating a new definition and classification of AKI with modifications. Serum creatinine obtained in the previous 3 months can be used as baseline when a baseline level obtained during the previous 7 days is not available. Although oliguria was not included in the definition of AKI in patients with cirrhosis, a study indicating that urine output was found to be significantly associated with adverse outcomes in patients with AKI and cirrhosis led to calls for a new definition and overall a new classification for HRS that expands on the 2015 ICA consensus document. Most recently, the ICA completely revised the nomenclature and diagnostic criteria for HRS type 1, which is now called HRS-AKI. Results of several studies showed that the higher the initial serum creatinine level at the start of treatment, the lower the probability of HRS reversal. This led to the ICA removing the minimum creatinine value for diagnosis, and therefore HRS-AKI can be diagnosed even when the serum creatinine level is below 2.5 mg/dL. Functional kidney injury that does not meet the criteria of HRS-AKI is termed HRS-NAKI (i.e., non-AKI), of which NAKI is further divided into HRS-acute kidney disease (HRS-AKD) if the estimated glomerular filtration rate (eGFR) is below 60 mL/min/1.73m^2 for less than 3 months and HRS-chronic kidney disease (HRS-CKD) if eGFR is below 60 mL/min/1.73m^2 for more than 3 months.

End-stage liver disease resulting in cirrhosis leads to increased intrahepatic vascular resistance, which subsequently causes splanchnic vasodilation triggered by increased production of vasodilators including nitric oxide, prostacyclins, carbon monoxide, and endocannabinoids. Splanchnic vasodilation subsequently leads to decreased vascular resistance and reduced effective arterial blood volume (EABV). Although the heart is able to compensate for this decrease in EABV in the early stages of cirrhosis by increasing cardiac output, but subsequent development of cirrhotic cardiomyopathy, aggravation of portal hypertension and splanchnic vasodilation results in effective arterial hypovolemia and arterial hypotension. This decrease in EABV subsequently activates various vasoconstriction factors that include the renin-angiotensin-aldosterone system (RAAS), the sympathetic nervous system (SNS), and the non-osmotic secretion of

arginine vasopressin. Although these vasoconstriction factors assist in maintaining arterial pressure near normal limits, their activation has detrimental effects on kidney function, resulting in renal vasoconstriction, impaired solute-free water excretion, and subsequent decline in kidney function. The kidneys are also able to compensate for such changes during earlier stages, owing to the vasodilatory effects of renal prostaglandins (prostaglandins E2 and I2) on afferent renal arterioles. This maintains glomerular pressure despite reduced renal blood flow (RBF). Progression of liver disease and the use of concomitant non-steroidal anti-inflammatory drugs that inhibit prostaglandin synthesis disrupts this balance and, therefore, causes AKI.

Diastolic dysfunction may be present in up to 60% of patients with cirrhosis; however, the relationship between diastolic and circulatory dysfunction or development of HRS has not been demonstrated. Nevertheless, decreased cardiac output in patients with cirrhotic cardiomyopathy is associated with the development of kidney hypoperfusion and HRS. For example, in a study of 66 patients who had cirrhosis with ascites and normal serum creatinine levels, baseline mean arterial pressure and cardiac output were significantly higher in patients who did not develop HRS than in those who developed HRS. Plasma renin activity and cardiac output were independent predictors of HRS. Complications occurred in the setting of a significant reduction in mean arterial pressure, cardiac output, and wedged pulmonary pressure, as well as an increase in plasma renin activity, norepinephrine concentration, and hepatic venous pressure gradient. In another study of 23 patients with spontaneous bacterial peritonitis (SBP) at diagnosis and after resolution of infection, those who developed HRS had a significantly lower cardiac output at the time of diagnosis of SBP, compared with those who did not develop HRS, indicating a relationship between HRS and diminished cardiac output.

The pathophysiological hallmark of HRS is vasoconstriction of the renal circulation. Marked renal vasoconstriction in patients with HRS has been demonstrated in a number of studies. This phenomenon may most likely be due to

several factors and may involve alterations in systemic hemodynamics, activation of multiple vasoconstrictor factors, and suppression of vasodilatory factors that act on renal circulation. Two major vasoconstrictor systems that are important in this pathophysiological process is the RAAS and the SNS. In several studies of patients with cirrhosis, activity of the RAAS, as estimated by plasma renin activity, was shown to increase from compensated to decompensated cirrhosis. Peak activity was seen in patients with HRS and it was shown to correlate inversely with kidney function. Moreover, in patients with infection associated HRS, patients with higher RAAS activity had a significantly lower probability of HRS reversal than those with lower RAAS activity. Plasma levels of norepinephrine, which reflects SNS activity, are increased in patients with HRS than in those with ascites and intact kidney function, and were shown to be inversely correlated with GFR. However, considering that both RAAS and SNS are two vasoconstrictor systems that act to increase arterial blood pressure and counteract splanchnic vasodilation, studies have been unable to assess whether the blockade of these RAAS and SNS lead to improved outcomes in patients with cirrhosis. Other than the aforementioned vasoconstrictor systems, other factors with a potential role in kidney vasoconstriction in HRS include endothelin, cysteinyl leukotrienes, and prostaglandins.

Hepatorenal syndrome (HRS) is the development of functional renal failure in patients with advanced chronic liver disease, liver failure, and portal hypertension in the absence of any identifiable renal pathology. Patients with HRS show a severe disturbance in their systemic hemodynamics with low arterial pressure and high cardiac output. The splanchnic circulation in patients with HRS is subjected to the effects of circulating vasodilators arising from the endothelium that cause significant arterial vasodilation in this vascular bed with resulting activation of endogenous vasoconstrictor systems. In several nonsplanchnic vascular beds there is marked vasoconstriction, which in the kidney results in low glomerular filtration rate (GFR). Although HRS occurs predominantly in advanced cirrhosis, it may also develop in other chronic liver diseases associated

with severe liver failure and portal hypertension, such as alcoholic hepatitis, or in acute liver failure.

With the advent of liver transplantation, HRS is now relatively uncommon with a reported incidence of about 7-10% among hospitalized patients with cirrhosis and ascites.Nonetheless the probability of developing HRS in patients with cirrhosis and ascites is near 20% at one year and increases to 40% at 5 years. Patients with ascites and marked sodium and water retention as well as those with marked arterial hypotension have the highest risk of developing HRS. Two types of HRS are observed in clinical practice. Type 1 HRS is an acute form with a very poor prognosis. Type 2 HRS develops slowly over weeks; these patients usually have diuretic-resistant ascites and have a slightly better prognosis compared with those with type 1 HRS.

There are several mechanisms that play a contributory role in pathogenesis of HRS, including extrarenal and intrarenal factors, abnormalities in systemic hemodynamics, and the diseased liver causing portal hypertension and hepatic failure. This review will describe the pathogenesis, clinical features, diagnostic approach and treatment of HRS in cirrhosis.

There are no specific clinical findings in HRS. The majority of patients have features of advanced liver disease with hyperbilirubinemia, elevated prothrombin time, low platelets, hepatic encephalopathy, low albumin, and large ascites. Low arterial blood pressure and elevated heart rate and cardiac output are present in most patients. Renal failure in HRS is often associated with oliguria, urinary sodium retention, and spontaneous dilutional hyponatremia. Two types of HRS have been described. Type 1 HRS is characterized by a rapid and progressive impairment of renal function as defined by a doubling of the initial serum creatinine to a level higher than 2.5 mg/dL or a 50% reduction of the initial 24-hr creatinine clearance to a level lower than 20 mL/min in less than 2 weeks. Serum creatinine levels in patients with HRS are usually lower than values observed in patients with acute renal failure without liver disease due to a reduced muscle mass and low endogenous production of creatinine in cirrhosis. In some

patients, this type of HRS develops spontaneously without any identifiable precipitating factor, whereas in others it can occur in close association with systemic bacterial infections, in particular SBP or acute alcoholic hepatitis. SBP is a common precipitating cause of type 1 HRS. It occurs in approximately one-third of cases with SBP despite a rapid resolution of the infection with intravenous antibiotics. In addition, large-volume paracentesis without plasma expansion may precipitate type 1 HRS.

Although gastrointestinal bleeding is considered to be a major precipitating factor of HRS, the development of renal failure after this complication is uncommon in patients with cirrhosis and occurs almost exclusively in patients who develop hypovolemic shock, and in most cases is associated with ischemic hepatitis, which suggests that renal failure in patients with gastrointestinal bleeding is probably related to the development of acute tubular necrosis. Without treatment, the median survival time of patients with type 1 HRS is less than 2 weeks and practically all patients die within 8-10 weeks after the onset of renal failure.

Alanine aminotransferase and aspartate aminotransferase values were 58.23±0.7Ed/l and 106.1±1.93Ed/l in the first group, respectively, and 55.4±0.6Ed/l and 99.17±1.83Ed after treatments. /l was ($p<0.05$). In the second group, highly reliable changes were observed after treatments (from 58.93±0.63 Ed/l to 42.17±0.8 Ed/l, from 102.0±1.87 Ed/l to 82, decreased by 13±2.04 Ed/l, $r<0.001$).

As mentioned above, clear positive changes were noted in the biochemical indicators of the group receiving L-ornithine L-aspartate + glutathione + eplerenone.

Our results are consistent with the results obtained by Italian researchers (R.Dentico et al, M.Yimin et al., 2000). They also showed reliable reductions in liver function tests of ALT, AST, and alkaline phosphatase in patients receiving glutathione several months after treatment. Another Chinese scientists (J. Nuyun et

al., 2005) noted that positive changes were observed in the cytolytic syndrome in cirrhosis of the liver in the group receiving this drug.

K. Grüngreiff and Y. Lambert Baumann in 2001 published the results of a large follow-up of 1167 patients in 250 treatment facilities dedicated to the effectiveness of L-ornithine, which also revealed an average reduction of transaminases by 35%.

No reliable changes were detected in bilirubin indicators in patients receiving veroshpiron + L-ornithine L-aspartate on the basis of complex treatment of liver cirrhosis ($r>0.05$). In the second group, it decreased by 1.57 times from 48.9±1.59 mmol/l to 31.0±1.64 mmol/l before and after treatments, and highly reliable changes were noted ($r<0.001$). In the first group, alkaline phosphatase decreased from 113.2±0.54 Ed/l to 110.3±3.34 Ed/l before and after the treatments ($r>0.05$). In the second group, these indicators were 112, 3±3.44 Ed/l was 99.63±3.3 Ed/l and reliable changes were detected ($p<0.05$). No reliable changes were observed in total cholesterol indicators in both groups ($r>0.05$).

Based on the complex treatment of liver cirrhosis developed due to chronic hepatitis C, in the group receiving veroshpiron + L-ornithine L-aspartate, the total protein in the blood serum and albumin, which is the main part of it, were 52.43±1.19 g/l and 28, respectively. It was 27±1.15 g/l. Differences were not reliable ($r>0.05$) despite the fact that these parameters increased by 57.4±1.23 g/l and 31.4±1.19 g/l after the treatments. In the group receiving eplerenone + L-ornithine L-aspartate + glutathione on the basis of the second, i.e. complex treatment of liver cirrhosis, total protein and albumin were 53±1.32 g/l and 27.77±1.03 g/l, respectively, before treatment. and after treatments were 66.16±1.4 g/l and 36.7±1.07 g/l, respectively, and highly reliable changes were found in both parameters ($r<0.001$). Urea indicators in the first group from 13.8±0.53mmol/l to 11.7±0.54mmol/l ($p<0.05$), in the second group from 13.5±0.6mmol/l to 8.7±0 High reliable changes were noted with a decrease of 0.4 mmol/l ($r<0.001$). There were no reliable changes in glucose values in both groups ($r>0.05$).

The values of alanine aminotransferase and aspartate aminotransferase in the first group were 83.87±1.6Ed/l and 115.8±2.2Ed/l before treatments, and 66.4±1.5Ed/l and 92.63±2, 66.4±1.5Ed/l after treatments. It was 17 Ed/l. In the second group, 2.16 times from 87.67±1.94 Ed/l to 40.67±1.87 Ed/l and from 119.9±2.43 Ed/l to 61.07± It decreased by 1.96 times to 2.7Ed/l, and highly reliable changes were observed in both groups ($r<0.001$). Total bilirubin decreased by 1.2 times in the first group ($r>0.05$) and 3.1 times in the second group ($r<0.001$). Alkaline phosphatase in the first group was 90.73±2.12 Ed/l before and after treatment. decreased to 86.7±2.15 Ed/l ($r>0.05$). In the second group, these indicators were 86.23±2.34 Ed/l and 74.5±2.35 Ed/l, respectively, and highly reliable changes were detected ($p<0.001$). There were no significant changes in total cholesterol in both groups ($r>0.05$).

The indicators of collagen IV in urinalysis obtained after complex treatment procedures with various components in patients with advanced liver cirrhosis due to chronic hepatitis B were also studied.

After the treatment, collagen IV values in the group of patients who received L-ornithine L-aspartate and glutathione with the standard treatment of liver cirrhosis were 245.37 ± 5.2 μg before the treatment and 224.6 ± 6.4 μg after the treatment. was ($p<0.05$). In patients receiving only L-ornithine L-aspartate with standard treatment of liver cirrhosis, it was 239.3 ± 5.7 μg and 231.8 ± 6.1 μg before and after the treatments, respectively ($p>0.05$).

The results of collagen IV in patients with advanced liver cirrhosis due to chronic hepatitis C were more reliable than in patients with advanced liver cirrhosis due to chronic hepatitis C after various complex treatment regimens.

In the group of patients who received eplerenone + L-ornithine L-aspartate and glutathione with the standard treatment of liver cirrhosis, collagen IV values decreased from 256 ± 4.2 μg to 224 ± 4.2 μg before and after the treatments, and the differences were highly reliable ($p<0.001$). In the second group of patients, the indicators before and after treatment were 263 ± 5.7 μg and 244.2 ± 5.13 μg, respectively, and reliable differences were noted ($p<0.05$). In patients with

developed hepatorenal syndrome, the main indicator determining its severity is BFZ. BFZ was determined before and after procedures in all patients in our follow-up.

Functional reserves of kidneys before and after complex treatment of patients with advanced liver cirrhosis due to chronic hepatitis B were evaluated. We can see a significant decrease in BFZ indicators in patients regardless of treatment procedures. In the first group of patients, BFZ decreased from 4.34 ± 0.13 % to 3.7 ± 0.2 % before and after treatments, respectively. In the second group, it was 4.23±0.3% and 4±0.2% ($p<0.05$). The fact that BFZ did not appear in patients can be explained by the fact that the hepatitis B virus has an aggressive effect on the liver and kidneys, causing irreversible changes in them.

Positive changes were noted in both groups after treatment with various components in patients with liver cirrhosis due to chronic hepatitis C. In the first group of patients, the indicators before and after treatments increased from 4.09 ± 0.15% to 4.54 ± 0.13%, but they did not develop BFZ. In the second group of patients, this indicator was 4.1 ± 0.2% and 5.09 ± 0.14%, respectively, before and after treatment, and high reliable changes were noted ($p<0.001$).

CONCLUSIONS

1. Hepatic encephalopathy (80%) and ascites syndrome (10%) are more often observed in liver cirrhosis developed on the basis of hepatitis B, and hemorrhagic syndrome (38%) and bleeding from esophageal veins (67%) are more often observed in its C form ;

2. The indicators of the functional reserve of the kidneys, determined by the use of creatinine in the blood and loading of 0.45% sodium chloride solution, are equal to 4.3±0.17% in liver cirrhosis developed on the basis of viral hepatitis B, and 4.1±0.12% in its C form. 'lib they did not reliably differ from each other (R>0.05) and the indicators indicated that there was no reserve;

3. The values of collagen IV in urine were 242.33 ± 3.85 μg in liver cirrhosis developed on the basis of viral hepatitis B, and 259.48 ± 3.55 μg in its S form, they reliably differed from each other (R<0.001) and After the indicators, it was confirmed that the group was higher in liver cirrhosis. This shows that fibrosis processes are more rapid in liver cirrhosis developed on the basis of viral hepatitis C;

4. Complex treatment negizidaeplerenone + L-ornithine L-aspartate and glutathione in advanced liver cirrhosis due to hepatitis B virus decreased the functional reserve of kidneys from 4.23 ± 0.3% to 4.0 ± 0.2%, but the differences are not reliable it has been. In liver cirrhosis developed on the basis of hepatitis C, these numbers were 4.1 ± 0.2% and 5.09 ± 0.14%, respectively, and reliable changes were noted (p<0.001);

5. Collagen IV indicators decreased from 245.37 ± 5.2 μg to 224.6 ± 6.4 μg after the complex treatment of negizidaeplerenone + L-ornithine with the addition of L-aspartate and glutathione in liver cirrhosis developed due to hepatitis B virus. was reliable (p<0.05). In cirrhosis of the liver developed on the basis of hepatitis C, these numbers were 256 ± 4.2 μg and 224 ± 4.25 μg, respectively, and reliable changes were noted (p<0.001). This can be attributed to the antifibrosis effect of eplerenone and glutathione drugs.

PRACTICAL RECOMMENDATIONS

1. Determination of renal functional reserve on the basis of serum creatinine in liver cirrhosis allows early diagnosis of hepatorenal syndrome in patients;

2. It is recommended to use eplerenone and glutathione drugs in complex medical procedures in order to reduce the exacerbation of fibrosis processes in the kidneys in patients with advanced liver cirrhosis due to chronic hepatitis B and C viruses.

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LIST OF CONDITIONAL SYMBOLS AND TERMS

ALT- alaninaminotransferaza

ACT-antiHCValaninaminotransferaza

GSK -hepatocellular carcinoma

HBV -viral hepatitis B

HCV- viral hepatitis C

HCV-RNK- RNA virus hepatitis C

GGTP-gamma-glutamiltranspeptidaza

IF-ishqoriyfosfotaza

IgG-immunoglobulinG

OZ-optical density

ENaC-epithelial sodium channel

ANA-antinuclear antibodies