UDC 616.36-002.1.2.

CHARACTERISTICS OF THE DEGREE OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C

S.G. Xudoydodova, M.A. Farmanova

Bukhara State Medical Institute

✓ ***Resume***

319 patients aged 19-60 years with HCV infection were under observation, including 110 (34.5%) male patients and 209 (65.5%) women. All patients were under dispensary supervision in polyclinics of the Bukhara region. The first genotype of the virus was detected in 63.9% (n=204) patients, 0.5% (n=18) the second genotype; 21.9% (n=70) the third genotype, 0.8% (n=27) the fourth genotype. Before antiviral therapy in the main group of patients, fibrosis F0 was detected in 22 (20%), F1 in 30 (27%), F2 in 36 (31.8%), and F3 in 23 (21%) patients. Fibrosis F4 stage was noted in 2 (0.2%) patients. With the use of antiviral therapy, an early virological response was noted in 204 (100%) patients, of which 200 (98%) patients confirmed the absence of recurrence of HCV RNA viremia, a rapid virological response was noted in 195 (95.6%) patients. In parallel with the improvement of the results of HCV antiviral therapy, there was also a decrease in the progression of liver fibrosis.

Keywords: HCV infection, elastometry, antiviral therapy, carcinoma, treatment dynamics.

ХАРАКТЕРИСТИКА СТЕПЕНИ ФИБРОЗА ПЕЧЕНИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕПАТИТОМ С.

Худойдодова С.Г, Фарманова М.А.

Бухарский Государственный Медицинский институт

✓ ***Резюме***

Под наблюдением находились 319 пациентов в возрасте 19-60 лет с HCV–инфекцией, из них 110 (34,5%) больных мужчин и 209 (65,5%) женщин. Все больные были под диспансерным наблюдение в поликлиниках Бухарской области. Выявлены у 63,9% (n=204) больных первый генотип вируса, 0,5% (n=18) второй генотип; у 21,9% (n=70) третий генотип, 0,8% (n=27) четвертый генотип. До противовирусной терапии в основной группе больных у 22 (20%) выявлен фиброз F_0, у 30 (27%) F_1, у 36 (31,8%) F_2, у 23 (21%) больных F_3. Фиброз F_4 стадии отмечен у 2 (0,2%) пациентов. С применением препаратов противовирусная терапия ранний вирусологический ответ отмечено у 204 (100%) пациентов, из них 200 (98%) пациентов подтверждено отсутствие рецидива виремии РНК HCV, быстрый вирусологический ответ отмечено у 195 (95,6%) пациентов. Параллельно с улучшением результатов лечения ХГС антивирусной терапии, также отмечено снижение прогрессирования фиброза печени.

Ключевые слова: HCV- инфекция, эластометрия, антивирусная терапии, карцинома, динамика лечения.

СУРУНКАЛИ ВИРУСЛИ ГЕПАТИТ С БЕМОРЛАРДА ЖИГАР ФИБРОЗИНИНГ ТАВСИФИ

Худойдодова С.Г, Фарманова М.А.

Бухоро давлат тиббиет институти

✓ ***Резюме***

Назоратимиз остида 19-60 ешдаги 319 (19%) нафар беморлар, шулардан 110 (34,5%) эркак ва 209 (65,5%) аёллардан иборат. Кузатувдаги беморлар вилоят оилавий поликлиникаларида диспансер назоратида туради. Вируснинг биринчи генотипи 63,9% (н=204) нафар беморларда, 0,5% (n=18) иккинчи генотип; 21,9% (n=70) учинчи генотипда ва 0,8% (n=27) тўртинчи генотипда аниқланди. Беморларнинг асосий гуруҳида antiviral терапиядан олдин фиброз ф0 22 (20%), Ф1 30 (27%), Ф2 36 (31.8%) ва Ф3 23 (21%) беморларда аниқланди. Фиброз Ф4 босқичи 2 (0,2%) беморларда қайд этилди. Вирусга карши препаратларининг кулланиши билан эрта вирусалогик натижа 204 (100%) нафарида кузатилиб, шулардан 200 (98%) нафарида виремия РНК HCV рецидиви кузатилмаганлиги, тез суръатдаги вирусалагик ижобий натижа эса 195 (95,6%) нафар беморларда аникланган.

СГС вирусга карши препарат терапиясининг натижаларини яхшилашга паралел равишда жигар фиброзининг ривожланишида ҳам пасайиш кузатилди.

Калит сўзлар: HCV- инфекция, эластометрия, вирусга карши терапия, карцинома, даволаш.

Relevance

Infection caused by hepatitis C virus (HCV) is one of the most common infectious diseases. To date, the number of people infected with hepatitis C virus (HCV) in the world has reached more than 180 million, most of them develop chronic hepatitis, less often CP (cirrhosis of the liver), hepatocellular carcinoma. Due to the lack of an effective vaccine, it is unlikely to expect a significant decrease in the incidence of HCV, which determines the importance of developing and improving antiviral therapy regimens [1,2]. Chronic viral hepatitis is a risk of developing cirrhosis of the liver (CP) and its complications, hepatocellular carcinoma (even without the formation of CP) [3-6]. Therefore, a clinician who has identified chronic HCV infection in a patient for the first time needs to evaluate the possible individual prognosis of the patient and indications for antiviral therapy. Currently, the standard of antiviral therapy (HTP) for chronic hepatitis C (HCV) is a combination of pegylated interferon - alpha (Peg – INF – alpha) and ribavirin, which provides 40-50% in the frequency of achieving a persistent viral response when infected with HCV genotype 1 with a duration of treatment for 48 weeks and 70-90% when infected with HCV genotypes 2 and 3 and treatment for 24 weeks.

The standard antiviral therapy (AVT) for chronic hepatitis C is pegylated-interferon-Alpha and ribavirin, and with HCV-1 genotype, treatment for 48 weeks is 40-50%, or with HCV-2 and 3 treatment for 24 weeks reaches 70-90% effectiveness. The formation of a stable virological response is currently equated with the eradication of HCV infection, >99% of patients have long-term resistance to aviremia, lack of detection of HCV RNA in liver tissues and peripheral mononuclear cells, normalization of the amount of aminotransferase, improvement of histological data and, most importantly, a decrease in the frequency of liver cirrhosis [7-9].

A great achievement of modern AVT is the development of the algorithm "fundamentals of the virological response of AVT" in HCV, which will be presented based on an individual approach to the treatment of patients, the prognostic value of the HCV genotype and the amount of virus in the dynamics of treatment [10,11].

The purpose of the study: To identify an early and persistent virological response, as well as the development of fibrosis with the use of combined antiviral drugs (sofosbuvir, ledipasvir) in patients with chronic hepatitis C on an outpatient basis.

Materials and methods of the study: RNA-positive patients with HCV (319) aged 18-71 years, caused by HCV genotypes 1, 2, 3, who had not previously received antiretroviral therapy, were examined. Those who applied to urban and rural family polyclinics 2018-2019. 110 of them are men, 209 women, the average age is 32.5 (25-40) years. The duration of the disease is from 8 to 15 years, on average 9.5 (9-11) years. Patients with a body mass index of more than 30, alcoholic, drug-induced liver damage, as well as patients with pulmonary, cardiac and renal insufficiency of more than 1st degree are excluded. The patients underwent a standard examination, including the collection of complaints and anamnesis for major and concomitant diseases, a medical examination with a targeted assessment of possible "liver" signs and signs of fibrosis using elastomertics (fibroscan). During the biochemical examination, the indicators of cytolytic, cholestatic, mesenchymal-inflammatory syndrome and impaired liver synthetic function were

determined. The criteria for inclusion in the study are serological confirmation of the presence of hepatitis C antibodies by ELISA, qualitative and quantitative determination of HCV RNA by polymerase chain reaction, absence of changes in hematopoietic organs, the number of neutrophils in the kidneys, thyroid gland more than 3 * 109 g / l, platelets 100 * 109 g / l, hemoglobin more than 110 g / l in women, more than 120 g/ l in men, normal creatinine and Thyroid-stimulating hormone. Etiological verification of hepatitis was carried out by serological methods, with the detection of anti HCV-core, unprotected NS3, NS4, NS5 proteins, molecular polymer chain reaction of the IQ5 cucler genotype at the moment of nucleic acid amplification. This level of liver fibrosis (according to the METAVIR scale F0, F1, F2, F3, F4) by ultrasound elastometry of the liver. In the treatment of patients with the identified genotype, drugs containing Sofosbuvir and Ledipasvir (Sofoled, sofas, Virpas) were prescribed.

Patients have a rapid viral response within 4 weeks, and a late virological response after 12 weeks. The effectiveness of antiviral therapy in the presence of an early virological response is an increase in viremia by 100 times or more (> 2 log10) 4 weeks after treatment, a late viral response by 100 times or more (> 2 log10) treatment for 12 weeks absence of HCV-RNA immediately after the end of antiviral therapy (24 or 48 weeks, depending on the genotype of viral hepatitis C). The results of the study and their discussion. 319 patients selected for clinical trials were examined from an epidemiological point of view and the data are presented in the table. According to the information given in the table, 110 of the patients under control were men (34.5%) and 209 (65.5%) were women.

The study of the degree of liver fibrosis in 319 patients with HCV, depending on the magnitude of the viral load, duration of the disease, enzymatic activity, body mass index (BMI) and elastometry indicators (IQR and the percentage of reliably performed studies on the apparatus). According to the results, the distribution of patients into groups with minimal, moderate and severe AF (groups 1,2,3) determined the duration of the disease, age, body mass index, MD, spleen area, de Rites coefficient, cholesterol, alkaline phosphatase, fibrinogen, PTI, thrombin time (Table 1).

Table 1. The most significant indicators of routine research methods in HCV infection.

Indicators	Function	
	1	**2**
Duration of the disease, years	0,367	0,074
Age, years	-0,030	-0,080
Body mass index, kg/m2	0,177	-0,364
liver density	-0,156	0,172
The area of the spleen, cm2	0,066	-0,076
De Ritis Coefficient	1,336	2,183
Cholesterol, mol/l	-0,333	-0,664
Alkaline phosphatase, Units/l	0,003	0,011
Fibrinogen, g/l	-5,502	-5,612
PTI%	-0,072	0,029
Thrombin time, with	0,131	0,438

When analyzing the PCR data presented in the table, 204 patients had 1 genotype, 18 had the second genotype, 70 had the third genotype, and 27 had no genotype. In the study of genotype subtypes, genotype 1A was detected in 15 (7.4%) cases, 1B 185 (90.7%) and 1B in 4 cases (1.9%) in patients with genotype 1. Of the 3, 3 genotypes were detected in 20 (28.6%), 3 in 15 (21.4%), 3 in 22 (31.4%) subtypes, and 13 (18.6%) subtypes were not detected. Among the control patients, a high viral particle (400,000 IU/ml) was observed in 9 patients (43%), a low viral particle in 12 patients (57%). The majority of patients in the control group had a low content of viral particles.

As a non-invasive assessment of liver fibrosis, patients underwent elastometry. According to elastometry data, patients with chronic HCV infection have significant differences (p0.05) in elastometry indicators depending on the stage of liver fibrosis (AF) of the HCG stage (stages 1-3 according to Metavir) and CP (stages 4 according to Metavir). Before the start of antiviral therapy, 113 patients (61%) were examined in the control group: 22 patients (20%) had F0 fibrosis, 30

patients (27%) had F1 level, 36 patients (31.8%) had F2 level, 23 patients (21%) had F3 level. Grade F4 fibrosis developed in 2 patients (0.2%). The early virological response in patients was evaluated 4 weeks after treatment. During 4 weeks of treatment, 90 (44.1%) of the observed patients did not detect HCV RNA, and 90 (44.1%) patients had 2 logarithmic decreases in viral load: 195 patients (95.6%) achieved an early virological response.

When analyzing the later virological response (within 12 weeks from the start of treatment), complete eradication of HCV RNA was observed in 200 patients (98%), with 2 log and a greater decrease in viral load in 4 patients; A decrease in the stage of fibrosis was noted in more than half of the patients. Also, it was revealed that a long-term persistent viral response reduces the risk of developing late complications of chronic hepatitis C.

Conclusions

1. The majority of chronic viral hepatitis reported in the region are caused by genotypes 1 of the hepatitis C virus. 2. The effectiveness of the antiviral drug - sofosbuvir + ledipasvir, leads to the elimination of viruses, causing a persistent virological response in 98% of patients. which has a direct impact on outpatient treatment

3. It is important to substantiate approaches to conducting AUTH in chronic viral hepatitis based on non-invasive monitoring of the dynamics of liver fibrosis by elastometry. Also, non-invasive methods of diagnosing liver fibrosis in outpatient practice can be used not only for diagnosis, but also for monitoring patients.

LIST OF REFERENCES:

1. Ivashkin V.T., Pavlov C.S. How to assess and reduce the risk of fibrosis, cirrhosis and hepatocellular carcinoma (HCC) in patients with chronic infection with hepatitis B (HCV) and C (HCV) viruses. Russian Journal of Gastroenterology, Hepatology, Coloproctology 2007; 17(5): 16-23
2. Bogomolov, P. O. Effectiveness of treatment of patients with chronic hepatitis C with the 1st genotype of the virus with standard interferon a / P. O. Bogomolov, A. O. Bueverov, N. V. Dubinina // Clinical prospects of gastroenterology and hepatology. - 2011. -No. 6. - pp. 17-22.
3. Sapronov G. V. New perspectives of personalized therapy of chronic viral hepatitis C // G. V. Sapronov, L. I. Nikolaeva // Epidemiology and infectious diseases. - 2013. - No. 3. - pp. 27-36.
4. Syutkin, V. E. New opportunities to increase the effectiveness of antiviral therapy in patients with chronic hepatitis C / V. E. Syutkin // Infectious diseases. - 2009. - No. 2. - pp. 55-58.
1. Oblok ulov A.R., Khudoydodova S.G., Farmanova M.A. Effektivnost' antivirusnoy terapii i kharakteristika stepeni fibroza pecheni u bol'nykh khronicheskim gepatitom S // Voprosy nauki i obrazovaniya. 2020. - №10 (94). S. 23-31.
5. EASL Recommendations on Treatment of Hepatitis 2014. April 2014 [Electronic resource]. - URL: htpp: // files.easl.eu/easl-recommendations-on-trearment-of-hepatitis-C.pdf.
6. Khudoydodova S.G., Farmanova M.A. Intrauterine infections and their clinical and neurological manifestations in young children // Achievements of science and education. 2020. -No.5 (59). P. 60-62.
7. EASL Recommendations on Treatment of Hepatitis C 2015. European Association for Study of Liver // J. Gastroenterology. - 2015. - Vol. 63 (1). - P. 199-236.
8. Obloqulov A.R., Oblokulova Z.I., Elmurodova A.A., Farmanova M.A. Virologic response in the treatment of infection with antiviral drugs // World Journal of Pharmaceutical Research. 2020. P.87-92
9. Oblokulov A.A., Obloqulov A.R., Ergashov M.M. Clinical and laboratory criteria for spontaneous bacterial peritonitis in liver cirrhosis of viral etiology //Central Asian Journal of Medical and Natural Sciences. 2021. P. 172-177
10. Oblokulov A.A., Obloqulov A.R., Elmurodova A.A. The importance of the level of procalcitonin in blood serum for early diagnosis of ontaneous bacterial peritonitis in patients with decompensated liver cyrrosis of viral ethiology //Europe's Journal of Psychology. 2021. -Vol. 17(3). P.156-161.

Entered 09.11.2021