WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 9, 87-92. Research Article ISSN 2277– 7105

VIROLOGIC RESPONSE IN THE TREATMENT OF INFECTION WITH ANTIVIRAL DRUGS

Oblokulov A.R.*, Oblokulov Z.I., Elmuradova A.A. and Farmanova M.A.

Bukhara State Medical Institute Named After Abu Ali Ibn Sino.

Article Received on
05 July 2020,

Revised on 24 July 2020,
Accepted on 14 Aug. 2020,

DOI: 10.20959/wjpr20209-18035

***Corresponding Author**
Oblokulov A.R.
Bukhara State Medical Institute Named After Abu Ali Ibn Sino.

ABSTRACT

There were studied epidemiological features of patients with HCV-infection who were under dispensary observation in clinics located in Bukhara Region, number of patients was 319, 110 (34.5%) of them were men and 209 (65.5%) were women. Etiological diagnostics of Chronic Hepatitis C was performed by the development of RNA and genotype of HCV infection in blood serum by the method of real-time polymerase chain reaction. It was detected that 63.9% (n. 204) of the patients had first, 0.5% (n = 18) of them had second, 21.9% (n=70) – third, 0.8% (n=27) – fourth genotype of the virus. Before antiviral therapy, in 22 (20%) in the main group of patients it was detected F0 fibrosis, so in 30 (27%) patients F1, in 36 (31.8%) patients F2 and in 23 (21%) patients F3. Fibrosis of F4 stage was revealed only in 2 (0.2%) patients. With the use of NS5B and NS5A RNA polymerase inhibitors, rapid virologic response was observed in 195 (95.6%) patients, early virological response – in 204 (100%), 200 (98%) of the patients achieved complete elimination of HCV RNA.

KEYWORDS: *HCV-infection, fibroscan, NS5B and NS5A RNA polymerase inhibitors.*

According to published data in the world from 110 to 177.5 million people have antibodies to hepatitis C virus (HCV), of which 80-119 million suffer from chronic hepatitis C (CHC).[7] In 60-80% of cases, HCV infection leads to the development of a chronic form of infection, 10-25% of them result in the development of liver cirrhosis (CP) and hepatocellular carcinoma (HCC).[6] The effectiveness criterion and the goal of HCV therapy is to achieve a stable virologic response (SVR), defined as the absence of a detectable HCV RNA in the patient's blood serum 12 or 24 weeks after the end of the course of treatment. SVR indicates the elimination of the virus from the body and predicts the subsequent probable stop of the

fibrotic process in the liver.[3,7] Thanks to advances in molecular biology, new antiviral drugs have been developed that target specific stages of the HCV life cycle by suppressing the function of non-structural proteins of the virus. These groups of drugs are designated as direct antiviral drugs (DAAs), their appearance in 2011 marked the beginning of a new era of treatment for chronic hepatitis C.[7]

Since then, the arsenal of drugs for the treatment of hepatitis C has begun to expand rapidly. After boceprevir, telaprevir (first-generation drugs) entered the market, then, two years later, sofosbuvir (the first of the second-generation drugs).[3,7] The main goal of antiviral therapy for HCV is to cure the infection, that is, to achieve a stable virological response, which means the absence of virus RNA detected by the polymerase chain reaction (PCR) in blood serum, after treatment is completed and this result is saved 12 or 24 weeks after completion of antiviral therapy.[4]

The formation of a stable virological response is equivalent to eradication of HCV infection, more than 99% of patients have long-term resistance to aviremia, lack of detection of HCV RNA in liver tissues and peripheral mononuclear cells, normalization of aminotransferase, improved histological data and, most importantly, reduced incidence of cirrhosis due to survival.[1,2] A great achievement of modern AVT HCV was the development of the algorithm “AVT based on the virologic response”, reflecting an individualized approach to treating patients based on the prognostic significance of the HCV genotype and the kinetics of viral load during treatment.[1,5]

OBJECTIVE: To study the virological clinical and immunological efficacy of antiviral therapy for chronic hepatitis C using direct antiviral drugs in real clinical practice.

MATERIALS AND METHODS

The study included 319 adult patients aged 18 to 71 years with chronic hepatitis C, caused by HCV genotypes 1, 2, 3, who had not previously received antiviral treatment. The criteria for inclusion in the study were serological confirmation of the presence of antibodies against chronic hepatitis C by ELISA, qualitative and quantitative determination of HCV RNA by polymerase chain reaction (PCR), the absence of changes in the hematopoietic organs, the number of neutrophils in the kidneys, thyroid gland more than 3x109 / l, platelets 100x109 g / l, Hb more than 110 g / l in women; Hb more than 120 g / l in men, normal creatinine and TSH. Etiological verification of hepatitis was carried out by serological methods with the

detection of anti-HCV-core, unprotected proteins NS3, NS4, NS5, PCR genotype IQ5 CUCLER at the time of amplification of the nucleic acid. This level of liver fibrosis (according to the METAVIRF-0, F-1, F-2, F-3, F-4 scale) by ultrasonic liver elastometry. In the treatment of patients with identified genotype, drugs containing NS5B and NS5ARNA polymerase inhibitors were prescribed.

Patients showed a quick viral response within 4 weeks, and an early virological response after 12 weeks. Antiviral efficacy was assessed by the presence of a rapid virologic response - reduction of viremia by 100 times or more (> 2 log10) from the initial level after 4 weeks of therapy, early virological response - reduction of viremia by 100 times or more (> 2 log10) from the initial level after 12 weeks of therapy.

RESULTS AND DISCUSSION

The results of a comprehensive examination, including clinical, biochemical, virological instrumental methods, of 319 patients with a preliminary diagnosis of chronic hepatitis C, including 110 (34.5%) men and 209 (65.5%) women aged 18 to 70, were analyzed. years old. Significant age differences between men and women were not noted (Fig. 1).

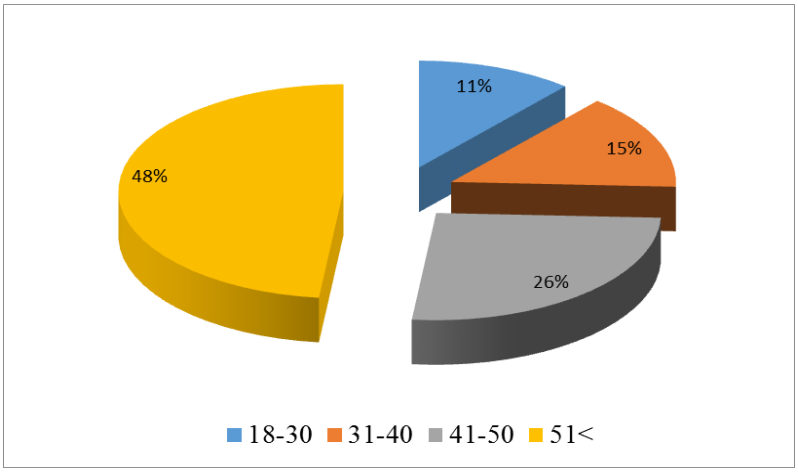

Figure 1: Age distribution of patients with viral hepatitis C Patients were divided by territory and by gender, the patients were distributed as follows: in the city of Bukhara, 50 patients were examined, of which 72% were women and 28% were men, and in the Gijduvan region 36 patients, 69.4% and 30.6%, respectively. Bukhara region 29 people, 62%, 38%, in the Peshkun region 31 patients, 51.6% and 48.4%. Bukhara region 29 people, 62%, 38%, in the Peshkun region 31 patients, 51.6% and 48.4%. Low incidence rates were noted in Karaulbazar district - 7 patients, 42.8% and 57.2%, as well as in Shafirkan region - 10 patients, 70% and 30%, respectively (Fig. 2).

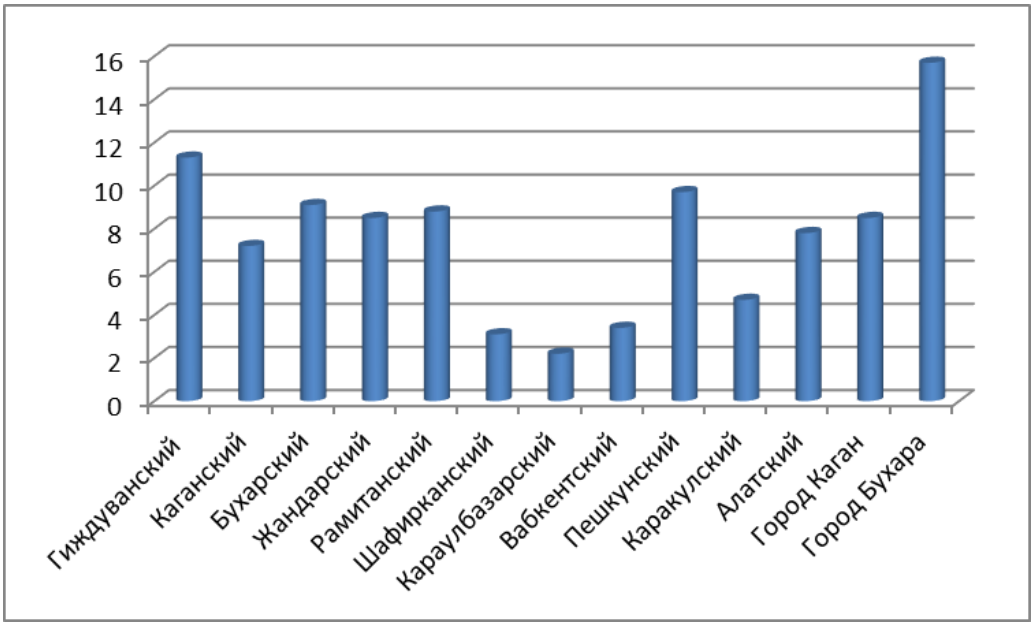

Figure 2: Epidemiological indicators of viral hepatitis C in cities and regions of the region.

Analysis of the results of PCR diagnostics showed that in 204 patients with chronic hepatitis C, a 1-genotype was detected, in 18 patients a 2-genotype, in 70 patients a 3-genotype, and in 27 patients - non-genotyped. In the study of the genotype subtype, genotype 1A was detected in 15 (7.4%) cases, 1B 185 (90.7%) and 1AB in 4 cases (1.9%) in patients with 1 genotype. Among the observed patients, a high viral particle (400,000 IU / ml) was observed in 9 patients (43%), a low viral particle in 12 patients (57%). Most patients had a low content of viral particles (Fig. 3). Assessment of liver fibrosis in chronic hepatitis C is primarily important for clinical trials, as well as for the diagnosis and prognosis of liver status. In addition, morphological criteria in these patients are often used to evaluate treatment outcomes.

Before the start of antiviral therapy, 113 patients were examined. Fibrosis of F-0 level was detected in 22 patients (20%), F-1 in 30 patients (27%), F-2 in 36 patients (31.8%), F- in 23- (21%) 3. F-4 degree fibrosis developed in 2 patients (0.2%) (Fig. 4) Patients with F-2 and F-3 fibrosis levels made up the majority in the group.

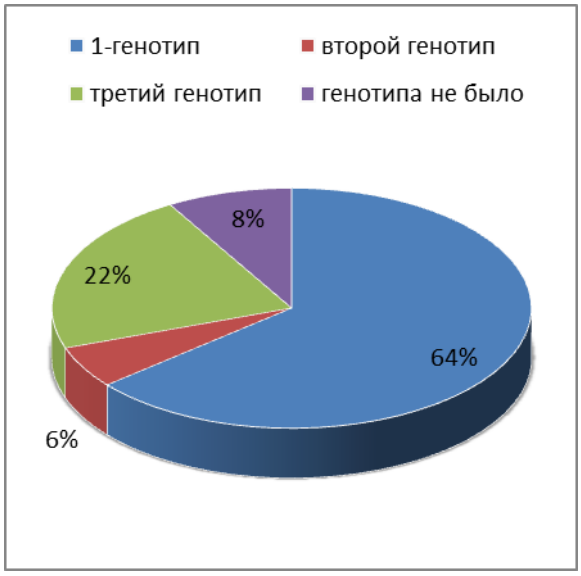

Figure 3: Distribution of patients.

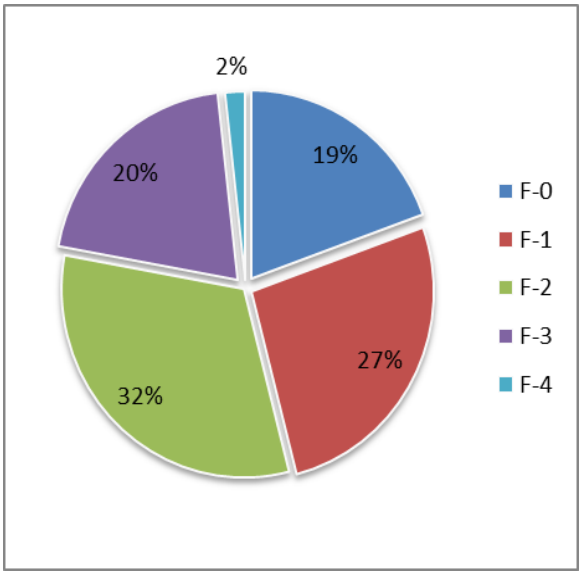

Figure 4: Distribution of patients by genotyping according to the degree of fibrosis.

Patients with a 1 genotype received direct-acting antiviral drugs - Sofosbuvir + Ledipasvir (group 1) and the remaining 2 and 3-genotype Sofosbuvir + daclatasvir (2 group) for 12 weeks. Fast virologic response in patients was evaluated after 4 weeks. after treatment. After a 4-week treatment in patients with a 1-group, 90 (44.1%) patients did not detect HCV RNA, and in 90 (44.1%) other patients, a 2-log reduction in viral load was observed. In 195 patients (95.6%) a rapid virologic response was achieved. When analyzing an early 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. An early virological response in this group was recorded in all patients (100%).

When analyzing a stable virologic response (within 24 weeks from the start of treatment), complete eradication of HCV RNA was observed in 196 (96%) patients.

CONCLUSIONS

1. Most HCV registered in the region are caused by genotypes 1 of hepatitis C.
2. The effectiveness of the antiviral drug Sofosbuvir + Ledipasvir, which has a direct effect during outpatient treatment of patients with chronic hepatitis C, leads to the elimination of viruses, causing an early virological response in 98% of patients.

REFERENCES

1. Oblokulov A.R., Elmurodova A.A., Farmonova M.A. et al. Virological response for HCV infection with antiviral drugs. // New day in Medicine, 2020; 1(29): 306-309. Sapronov G.V. New perspectives for personified therapy of chronic viral hepatitis C // G.V. Sapronov, L.I. Nikolaeva // Epidemiology and Infectious Diseases, 2013; 3: 27-36.
2. Syutkin V.E. New opportunities to increase the effectiveness of antiviral therapy for patients with chronic hepatitis C. // Infectious diseases, 2009; 2: 55-58. Arase Y, Kobayashi M, Suzuki F, et al. Effect of type 2 diabetes on risk for malignancies includes hepatocellular carcinoma in chronic hepatitis C. Hepatology, 2013; 57(3): 964-973. doi: 10.1002/hep.26087.
3. Fried M.W. et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection // N. Engl. J. Med., 2002; 347(13): 975982.
4. Hadziyannis S.J. et al. Peginterferon-a2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. // Ann. Intern. Med., 2004; 140(5): 346355.
5. Dore G.J., Matthews G.V., Rockstroh J. Future of hepatitis C therapy: development of direct-acting antivirals // Curr. Opin. HIV AIDS, 2011; 6(6): 508-513.