Arabian Journal of Science

ISSN:2308-5703

Impact factor:13.5 *International Multidisciplinary Online Journal* July, 2026

DEVELOPMENTS IN ANTIVIRAL THERAPY AND DIAGNOSIS FOR CHRONIC HEPATITIS C

Axmadaliyeva Umidaxon Qobiljonovna
Andijan State Medical Institute Assistant of the Department of Outpatient and Polyclinic Therapy
https://orcid.org/0000-0003-2397-832X
Doi: https://doi.org/10.5281/zenodo.21223214

Abstract: Hepatocellular carcinoma, cirrhosis, fibrosis, and chronic inflammation are all consequences of the progressive viral infection known as chronic hepatitis C (HCV). The hepatitis C virus, an RNA virus belonging to the Flaviviridae family, is the cause of the illness and is mostly spread via blood contact. The introduction of direct-acting antivirals (DAAs), which precisely target viral replication pathways, has revolutionised the treatment of HCV thanks to advances in molecular virology.

Due to their superior tolerability, reduced treatment time, and high sustained virologic response (SVR) rates, these medicines have supplanted conventional interferon-based regimens. To eradicate the virus and avoid problems, early diagnosis, genotyping, and optimal medication selection are crucial. Reducing disease burden and transmission still requires comprehensive care, which includes lifestyle change, patient education, and routine monitoring.

Key Words: Chronic hepatitis C; Hepatitis C virus (HCV); Antiviral therapy; Direct-acting antivirals (DAAs); Interferon; Ribavirin; Liver fibrosis; Cirrhosis; Viral eradication; Sustained virologic response (SVR).

Introduction

The C virus (HCV) is one of the most common causes of chronic liver damage. Over 71 million people worldwide suffer from this ailment. Our understanding of the biology of chronic hepatitis C (CHC) and its effects has significantly expanded as a result of recent scientific advancements. This has enabled the development of effective diagnostic methods, the identification of crucial therapeutic approaches, and a significant improvement in prognosis. Thanks to extremely potent antiviral drugs made possible by the continuous worldwide development of new drug classes, hepatitis C can now be treated.

By achieving a sustained virological response-that is, the absence of viral RNA as determined by the polymerase chain reaction (PCR) method in the blood serum after treatment is completed and maintenance of this result 12 or 24 weeks after treatment is finished-antiviral therapy for HCV aims to cure the infection. A sustained virological response is typically associated with normalisation of liver enzyme activity, improvement or resolution of liver inflammation, and stability of fibrosis in individuals without cirrhosis.

According to recent data examining the impact of a sustained virological response on the risk, patients with chronic hepatitis C who have a sustained virological response have a significantly lower risk of primary liver cancer than those who do not. Reaching undetectable serum RNA levels also reduces the risk of serious consequences in patients with advanced fibrosis or cirrhosis. Unfortunately, a durable virological response may not completely reduce the risk of primary liver cancer in patients with cirrhosis and chronic hepatitis C, especially when cofactors such as metabolic syndrome, chronic drinking, and concurrent hepatitis B are present. Achieving an undetectable level of RNA in the blood

serum while taking antiviral medicine reduces the risk of dying from extrahepatic manifestations of chronic hepatitis C and eliminates their clinical symptoms.

First and foremost, early antiviral medication commencement improves efficacy and shortens treatment time. It is necessary to establish a causal link between hepatitis C virus infection and liver damage prior to starting therapy for chronic hepatitis C. Finding such a connection aids in ruling out liver damage brought on by concomitant conditions (such as autoimmune illnesses, metabolic syndrome, and persistent drinking). Assessing the degree of liver damage-that is, figuring out whether the patient has cirrhosis-is essential before starting treatment. Its presence might change the antiviral treatment plan. An evaluation of renal function by measuring serum creatinine and glomerular filtration rate, together with the identification of extrahepatic HCV symptoms, is a prerequisite for treatment.

The selection of an antiviral therapy regimen is predicated on an evaluation of the treatment regimen's projected effectiveness, safety, and economic viability. The high cost of direct-acting antiviral medications now prevents the Russian Federation from implementing new interferon-free treatment regimens. Consequently, the adoption of combination treatment regimens for HCV that combine interferon medications with ribavirin is still important, given the restricted financial resources.

A diagnosis of viral hepatitis C, verified by the PCR method's detection of HCV RNA in blood serum, is a sign that antiviral medication should be started. Due to the potential for spontaneous recovery, the Russian recommendations for the diagnosis and treatment of adult patients with hepatitis C (2017) permit patients with acute hepatitis to postpone starting antiviral medication for eight to twelve weeks from the commencement of the illness. Interferon monotherapy without ribavirin is administered to patients with acute hepatitis C (AHC) for a duration of 24 weeks. At 12 and 24 weeks following treatment completion, efficacy is assessed. AHC can also be treated with a pangenotypic regimen of direct-acting medications, which consists of a combination of daclatasvir and sofosbuvir for eight weeks.

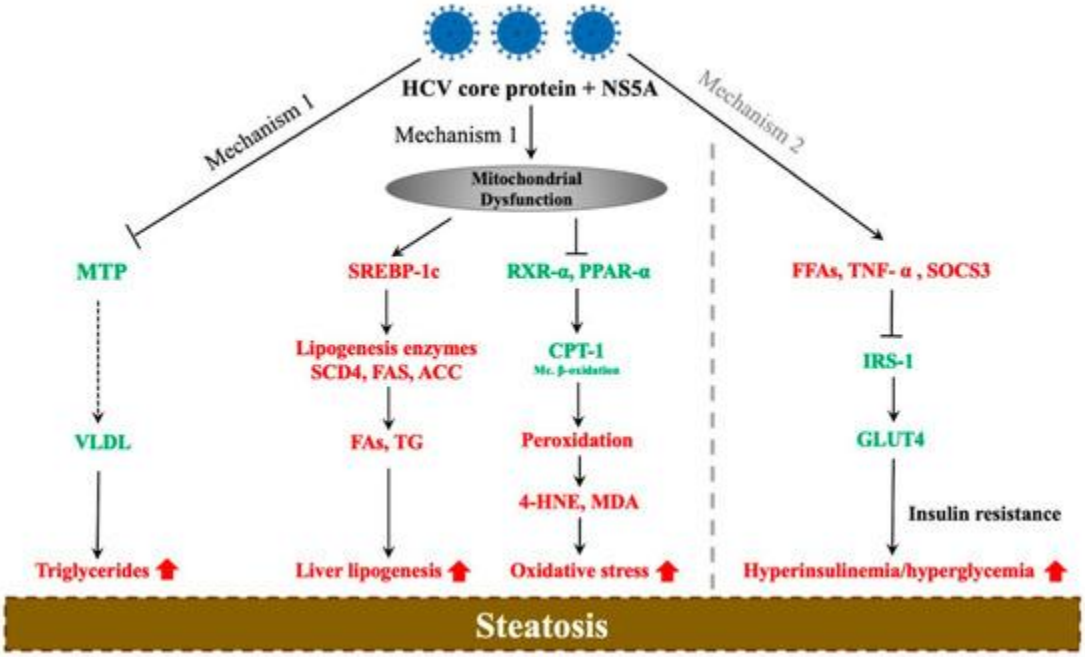


Figure 1 shows how the hepatitis C virus affects the development of hepatic steatosis. Green and red, respectively, show downregulation and upregulation. Hepatitis C virus (HCV); microsomal triglyceride transfer protein (MTP); very-low-density lipoprotein (VLDL); sterol regulatory element-

binding protein (SREBP-1c); sterol CoA dehydrogenase 4 (SCD4); fatty acid synthase (FAS); acetyl-CoA carboxylase (ACC); and peroxisome proliferator-activated receptor alpha (PPAR-α); CPT-1 stands for carnitine palmitoyltransferase-1; 4-HNE for 4-hydroxynonenal; MDA for malondialdehyde; FFAs for free fatty acids; TNF-α for tumour necrosis factor alpha; SOCS3 for suppressor of cytokine signalling 3; IRS-1 for insulin receptor substrate signalling; Mc. β-GLUT-4: glucose transporter type 4; oxidation: mitochondrial β-oxidation.

The term may be prolonged to 12 weeks if HIV infection or HCV RNA levels are more than 1 million IU/mL. In order to achieve maximum effectiveness and guarantee the safety of antiviral therapy, patients with chronic hepatitis C must undergo virological tests (to determine the level of HCV RNA, the genotype and subtype of HCV, to identify the presence of hepatitis B and D viruses), assess the degree of liver damage using elastometry on the FibroScan device or using FibroTest, and be evaluated to rule out concomitant diseases.

The "therapy according to virological response" idea guides the administration of antiviral therapy for treating chronic hepatitis C with interferon (IFN) preparations. In other words, the time it takes to get a virological response, which is measured at the fourth week of treatment (fast virological response), the twelfth week (early virological response), and the twenty-fourth week (slow virological response), determines the length of the course of therapy. Patients with genotype 2 of the virus with a viral load below 800,000 IU/ml may receive treatment for 16 weeks if a response is seen at the 4th and 12th weeks from the beginning of therapy; patients with genotype 3 and the same viral load may get treatment for 24 weeks.

The ideal course of treatment is 72 weeks for viral loads greater than 800,000 IU/ml, independent of the virological response and virus genotype. The initial virological response in individuals with a viral load larger than 800,000 can only be observed at week 24; if this is the case, a 72-week course of treatment is advised. There are currently reports of a novel genotype 2 variation circulating among chronic hepatitis C patients. The hepatitis C virus's genotype 1 and genotype 2 were combined to create this genotype variation, which also gained traits from genotype 1. A combined genotype variation is referred to as genotype 2 by diagnostic test methods.

In this sense, it is advised that patients with genotype 2 get antiviral therapy with IFN medications for the same length of time as those with genotype 1 HCV. In the course of antiviral treatment for persistent hepatitis C, dynamic clinical monitoring consists of two parts: tracking the emergence of adverse events and evaluating the efficacy of treatment. To ascertain the metabolic reaction, ALT activity is measured concurrently with HCV RNA. Two and four weeks after the commencement of treatment, as well as every four weeks until the conclusion of treatment, a complete blood count (CBC) with platelet and other blood cell counts is carried out. Every three months, levels of free thyroxine and thyroid-stimulating hormone are assessed.

If side effects occur, such as depression, a drop in the absolute neutrophil count below 750/mm3, or a drop in the platelet count below 50,000/mm3, the IFN dosage is lowered. IFN is stopped if the platelet and neutrophil counts drop below 25,000/mm3 and 500/mm3, respectively. If the patient's haemoglobin level is less than 100 g/L, the ribavirin dosage is lowered by 200 mg every dose; if it is less than 85 g/L, the medication is stopped. If the haemoglobin level falls by more than 20 g/L from the baseline in patients with cardiovascular disorders, the ribavirin dosage is lowered.

Combining interferon therapy with direct-acting antiviral medications can boost its efficacy, decrease its duration, and, as a result, greatly lower the frequency of side effects. Medications like narlaprevir (24-week course) and simeprevir (48-week course) are used in individuals with HCV genotype 1. Compared to narlaprevir, the combination of IFN and simeprevir is less severe and does not cause adverse effects that necessitate stopping treatment. Patients with HCV genotype 1 may

receive weekly PegIFN in addition to daily doses of ribavirin, daclatasvir, and asunaprevir for 24 weeks.

This therapeutic strategy can be used by those without hepatic cirrhosis as well as those with compensated cirrhosis. The effectiveness of antiviral therapy with direct-acting antiviral drugs should be assessed using very sensitive test methods. Therefore, treatment is stopped if, during the fourth week of interferon therapy plus simeprevir, the HCV RNA level is more than 25 IU/ml.

The best and least harmful treatment for chronic hepatitis C is direct-acting antiviral medication. An examination of the patient's possible course of therapy for concurrent disorders is a prerequisite for their use. Drug interactions between direct-acting antivirals and the patient's existing drugs must be taken into consideration. If at all feasible, it is advised to stop or lower the chance of negative drug interactions and replace prescription drugs for coexisting diseases. Co-administration of direct-acting antiviral medications with medications whose clearance is dependent on cytochrome P450 is not recommended. The concentration of direct-acting medications is greatly decreased by interactions with these medications, which lowers the efficacy of treatment.

Direct-acting antiviral treatment is a combination therapy, which entails the prescription of two medications or a single combination medication, each of which targets a distinct aspect of HCV replication. For instance, daclatasvir, the medication it is taken with, is an NS5A complex inhibitor, whereas sofosbuvir is a polymerase inhibitor. Antiviral treatment is less successful when medications with comparable effects on HCV replication are used. The metabolism of direct-acting antiviral medications must be taken into account while prescribing them. It is not recommended to utilise medications in people with renal dysfunction if the kidneys are the primary organ responsible for their excretion.

Before direct-acting antiviral medications are prescribed, the degree of liver damage must be assessed. Sadly, a combination of sofosbuvir and daclatasvir is the only direct-acting antiviral treatment regimen available in the Russian Federation for patients with decompensated liver cirrhosis. Determining the genotype subtype is essential for administering direct-acting antiviral medications (DAAs) without interferon to patients with HCV genotype 1. The genetic subtype determines the length of treatment and its efficacy. The training lasts between eight and twelve weeks for genotype 1b. It takes eight weeks for those without cirrhosis and twelve weeks for those who do. Genotype determination is not necessary while using pangenotypic antiviral treatment. Additionally, the length of the therapy varies from 8 weeks for individuals without cirrhosis to 12 weeks for those who have.

Patients with concurrent hepatitis B are treated according to the same protocols as those with HCV monoinfection. Simeprevir, narlaprevir, asunaprevir, dasabuvir, and ombitasvir + paritaprevir + ritonavir are NS3/4A protease inhibitors for HCV genotype drugs. Effective against genotypes 1 and 4 NS5A complex inhibitor daclatasvir, Pangenotypic drug Polymerase inhibitor sofosbuvir, Pangenotypic drug. Combination medication: pibrentasvir (NS5A inhibitor) + glecaprevir (NS3/4A protease inhibitor), Pangenotypic medication Sofosbuvir + simeprevir +/- ribavirin, HCV genotype 1. Paritaprevir/ritonavir + ombitasvir + dasabuvir HCV genotype 1 Daclatasvir + asunaprevir Daclatasvir + sofosbuvir +/- ribavirin All genotypes Glecaprevir + pibrentasvir

Reactivation can happen during or after therapy. Patients are recommended nucleoside analogue treatment if this happens. The period of treatment for hepatitis B should be at least 12 to 24 weeks when using direct-acting medications and addressing extrahepatic symptoms. Direct-acting antiviral medications are often well tolerated by patients. There are very few serious adverse effects that necessitate stopping therapy. The most frequent symptoms from patients are tiredness, headaches, nausea, and weakness.

During treatment, direct-acting antiviral medication is not monitored for efficacy. However, the 2017 guidelines for the diagnosis and treatment of adult patients with hepatitis C in Uzbekistan [9]

advise measuring HCV RNA in serum prior to treatment, at week 2 (assessment of treatment adherence), at week 4, 12, or 24 (at the end of treatment for patients treated for 12 or 24 weeks, respectively), and at week 12 or 24 following treatment completion. At week 48, the final evaluation is completed. Patients without liver cirrhosis who have normal ALT levels and undetectable blood RNA levels, as determined by PCR on extremely sensitive test equipment (< 15 IU/ml), may be excluded from follow-up based on the results of the sustained virological response (SVR) evaluation at week 48 following the conclusion of therapy.

Due to the possibility of primary liver cancer, patients with liver cirrhosis are still under monitoring. They get an annual alpha-fetoprotein test and an abdominal ultrasound as part of their follow-up. Alpha-fetoprotein levels are multiplied by baseline levels. A visit with a liver surgeon is advised for further testing to rule out primary liver cancer if a follow-up abdominal ultrasound shows a homogenous mass in the liver or if the alpha-fetoprotein rise is greater than 1-1.5 times the baseline.

Conclusion

Direct-acting antivirals (DAAs) have revolutionised the treatment of hepatitis C virus (HCV) infection, making interferon-free regimens the accepted standard of care worldwide. Regardless of the viral genotype, these treatments produce sustained virological response (SVR) rates of 95–98% and are distinguished from interferon-based methods by better safety profiles, shorter treatment durations, and increased patient adherence.

The lack of detectable HCV RNA for at least 48 weeks after treatment completion is known as a sustained virological response, which is commonly considered a virological cure. Regression of liver inflammation and fibrosis, a lower chance of cirrhosis, a lower incidence of hepatocellular cancer, and an overall increase in patient longevity and quality of life are all linked to achieving SVR.

However, the chance of illness recurrence is not completely eliminated by effective antiviral medication. Even though late relapse is uncommon, it cannot be totally ruled out, and reinfection is still a concern, especially in high-risk groups. Therefore, even after reaching SVR, long-term follow-up, including clinical, biochemical, and virological monitoring, remains crucial.

There are still gaps in availability to DAA-based regimens despite their obvious benefits, especially in low- and middle-income nations. Due to financial limitations and the scarcity of more recent medicines, interferon-containing regimens may still be used in certain situations.

A customised, interdisciplinary strategy led by skilled medical specialists is necessary for the best management of hepatitis C. To maximise therapeutic effectiveness and minimise problems, careful patient selection, evaluation of liver disease stage, concomitant illnesses, and potential medication interactions are essential.

Literature

1. Polaris Observatory HCVC. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modeling study. Lancet Gastroenterol Hepatol. 2017;2 (3):161-176. doi : 10.1016/S2468-1253(16)30181-9.
2. Arase Y, Kobayashi M, Suzuki F, et al. The 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. Bruno S, Di Marco V, Iavarone M, et al. Survival of patients with HCV cirrhosis and sustained virologic response is similar to that of the general population. J Hepatol . 2016;64 (6):1217-1223. doi: 10.1016/j.jhep.2016.01.034.
4. Kew MC. Interaction between hepatitis B and C viruses in hepatocellular carcinogenesis. J Viral Hepat. 2006;13 (3):145-149. doi: 10.1111/j.1365-2893.2005.00686.x.

5. Kew MC, Yu MC, Kedda MA, et al. The relative roles of hepatitis B and C viruses in the etiology of hepatocellular carcinoma in southern African blacks. Gastroenterology. 1997;112(1):184-187. doi : 10.1016/S0016-5085(97)70233-6.
6. Eslam, M.; Newsome, P.N.; Sarin, S.K.; Anstee, Q.M.; Targher, G.; Romero-Gomez, M.; Zelber-Sagi, S.; Wai-Sun Wong, V.; Dufour, J.F.; Schattenberg, J.M.; et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J. Hepatol. 2020, 73, 202–209.