

EFFECTIVENESS OF ANTIVIRAL THERAPY IN VIRAL HEPATITIS

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Abstract

Viral hepatitis (VH) is a large group of diseases that differ in etiology, epidemiology, and clinical presentation with predominant liver damage.

Currently, the following independent forms of VG are known, which are usually denoted by letters of the Latin alphabet: A, B, C, D, E, G, TTV. The greatest importance for practical health care is represented by hepatitis with parenteral (or hemocontact) infection and, above all, hepatitis caused by viruses B, C, D. This is due to the fact that when infected with these viruses, the course of the disease is usually more severe than with hepatitis A and E, lightning-fast (malignant) infections are possible variants of the course with a fatal outcome.

Introduction. The frequency of chronic acute hepatitis C infection reaches 80%, acute hepatitis B-in 10- 15% of cases, and in B+D infection-up to 90%. Progression of chronic hepatitis b to cirrhosis occurs with varying frequency and varies with HS and HS in 40-60% of patients, with GO-in 90% of patients with acute hepatitis (Sherlock S., 2001). Patients with chronic hepatitis have a high risk of developing hepatocellular carcinoma, which kills more than a million people worldwide every year. Chronic hepatitis is a prolonged (more than 6 months) pathological process in the liver caused by the persistence of hepatitis B, C, and D viruses, with a genetically determined deficiency of cellular and macrophage immunity. It should be noted that clinical symptoms may not always serve as a reliable criterion for assessing the severity of chronic viral hepatitis (CVI). In many cases, they are poorly expressed and poorly specific. Often, obvious clinical signs (malaise, weakness, fatigue, decreased appetite, nausea, heaviness in the right hypochondrium, abdominal pain, muscle or joint pain, enlarged liver) are found only at a far advanced stage of the disease and even with cirrhosis. In the 70s and 80s of the XX century, the search for etiotropic therapy of viral hepatitis was launched, aimed at suppressing the replication of pathogenic viruses and eliminating them. First of all, these drugs include interferon preparations, which have been the basic ones for the treatment of acute and chronic viral hepatitis for the past 20 years. The mechanism of action of IFN in viral hepatitis is primarily related to its antiviral and immunomodulatory effects. Due to this systemic effect, viral replication suppression is achieved (reduction of adsorption, inhibition of deproteinization, induction of cell nucleases and proteases, stimulation of interferogenesis) with simultaneous stimulation of HLA hepatocytes, amplification of killer cells and cytotoxic T-lymphocytes, and production of neutralizing antibodies.

Antiviral drugs used for the treatment of VH, as well as their effective delivery

Antiviral drugs used in the treatment of viral hepatitis

Type of drug	Drug group	Medication	The effect of the drug
IFNS Natural and recombinant α -IFN R-IFN	Antiviral Immunomodulatory IFN Inductors	Fluorenones Acridanones Amixin Cycloferon	Neovir Immunostimulators
Immunomodulators	Cytokines Interleukin-1 Interleukin-2 Interleukin-12	Tumor Necrosis Factor	Immunomodulatory

Recombinant interferons include IFN α -2a (roferon-A, Switzerland), interferon- α >2b (intron-A, USA), human leukocyte IFN- α (reaferon, Russia), and viferon. The list of IFN drugs offered for the treatment of VH is constantly expanding. There are new drugs - alfaferon (alfa-wasserman, Italy), recombinant α -2 IFN- heberon- α -R. Introduction of long-acting (pegeled) recombinant alpha- IFN drugs-pegasys (Switzerland) and Peg Intron (USA) - into clinical practice is very promising, which makes it convenient to administer (once a week) and individually select the dose taking into account the patient's weight.

Indications for the appointment of etiotropic therapy for PRand viral hepatitis are: laboratory and morphologically proven hepatitis B or C presence of markers of hepatitis B virus replication (determination of HBV and HBeAg DNA in blood serum) or hepatitis C virus (determination of RNA of the virus and its genotypes) ; if possible, of viruses in the blood persistently elevated ALT level absence of decompensated portal hypertension. Contraindications to the use of alpha-IFN are: hypersensitivity to any of the components cirrhosis and decompensation of liver disease severe cardio vascular diseases severe renal failure epilepsy previously long-term immunosuppressive therapy autoimmune disease in the anamnesis (hepatitis, thyroiditis); diabetes mellitus, drug addiction. But the appointment of IFN is associated with certain difficulties, namely, the side toxic effect of the drug: flu-like syndrome, leuko and thrombocytopenia, hypo or hyperthyroidism, the formation of neutralizing antibodies to IFN, and deterioration of liver function indicators. Depending on the dose and individual sensitivity, weakness, drowsiness, fatigue, and delayed reaction may occur. The severity and persistence of these events may require a dose reduction, and sometimes a change in the rhythm of drug administration. As a rule, these phenomena can be corrected or disappear on their own. Insufficient effectiveness of IFN in the treatment of VH can be

observed in cholestasis (results improve with simultaneous administration), excessive iron deposition in liver tissue (removal of iron by repeated bloodletting increases the effectiveness of treatment), the formation of antibodies to IFN. The presence of severe steatosis, alcoholism, drug addiction, mixed hepatitis, infection with the HS 1b genotype virus, high viremia, the presence of genetic variability, and low ALT worsen the prognosis of treatment. In chronic hepatitis B infection with a mutant strain (HBe-negative), mixed infections with delta virus or HS also worsen the effectiveness of interferon therapy. According to the literature, it is promising not only to find ways to overcome interferon resistance in the reactivation phase, but also to prescribe it early in the acute phase. In CHC, positive treatment results are achieved in the first year of clinically manifest therapy. stages. In the latent phase of HCV infection, although it precedes the reactivation phase, patients are refractory to interferon.

The greatest effect of treatment with interferon GS can be achieved when it is prescribed as early as possible after infection. To increase the effectiveness of interferon therapy in patients with chronic hepatitis (CH) with a low degree of activity, a short preliminary course of corticosteroid treatment (0.5-1 mg/kg) is recommended for 2 weeks with their rapid cancellation, which leads to the so-called immune "rebound", i.e. restoration of immune competence necessary for virus elimination. Tables 2 and 3 show the dosage and administration regimens of the most commonly used drugs for the treatment of IH. The results of the effectiveness of interferon therapy are evaluated by biochemical and virological tests, namely, the result of treatment is considered positive if: normalization of ALT, disappearance of HBeAg and the appearance of antibodies to HBe (seroconversion), disappearance of HBV-DNA in HB and HCV- PHK in HS, reduction of the phenomena of lymphohistiocytic infiltration along the portal tracts during morphological examination. In evaluating the effectiveness of interferon therapy, the time factor is of great importance, since it is important not only to obtain a response to treatment, but also to maintain it stably. Therefore, the biochemical and virological response to treatment is evaluated twice: immediately after the end of treatment and after a certain time after its completion (at least 6 months). It should be remembered that IFN often induces the formation of antibodies (in 20-60% of cases). In the treatment of acute HS, the positive effect of intron A treatment is achieved in 95-97% of cases, whereas only 30-40% of patients with CHB and CHC have a stable response (lack of viral replication and normal ALT levels 6 or more months after the end of antiviral therapy). The sustained response to intron A treatment in patients with XГ-D is about 10%. Given the insufficient effectiveness of IFN monotherapy, an intensive search led specialists to use a number of chemotherapy drugs, in particular nucleoside analogues, for VH.

Their mechanism of action consists in blocking the synthesis of viral DNA and RNA by replacing natural nucleosides and, thereby, inhibiting viral replication. These

include lamivudine and ribavirin (virazol, rebetol, ribamidil, vidarabine, etc.). The most studied of these drugs is lamivudine (zeffix, UK), used for the treatment of HBV. The mechanism of action of lamivudine is based on its ability to inhibit the synthesis of RNA-dependent HBV DNA polymerase. Lamivudine can be used as monotherapy, but after its withdrawal, the relapse rate is too high. The effectiveness of antiviral therapy increases with the appointment of combined treatment-lamivudine (100-300 mg /day. within 12 weeks) + interferon. In the treatment of hepatitis C, combination therapy is most often used-IFN (intron A) with ribavirin (virazol).

Ribavirin is prescribed at a dose of 1000-1200 mg /day. in 2 doses for 12-24-48 weeks. The drug is well tolerated. In the initial period of acute hepatitis C, the appointment of phosphogliv is justified (domestic drug), which has not only hepatoprotective properties, but also. It also has antiviral properties. Phosphogliv is prescribed 1-2 capsules 3 times a day for 1 month. Extensive systemic tests of a group of IFN inducers of various types (cycloferon, amixin, neovir, ridostin) have shown that their antiviral activity generally coincides with the previously identified activity of endogenous IFN. Cycloferon is administered intramuscularly or intravenously once a day in a dose of 2 ml (250 mg) on the 1st-2nd-4th- 6th-8th-10th- 12th day of the course of treatment. To consolidate the effect, it is possible to repeat the course of treatment.

Intravenously, the drug is prescribed in 4 ml - 500 mg according to the same scheme. For children, cycloferon is prescribed at the rate of 10 mg / kg of body weight once a day with an interval of 48-72 hours, a course of 15 to 30 injections. In OGV, the average duration of treatment is 23 days (1 course - 10 injections), in chronic hepatitis - 70 days (3 courses of 10 injections of 4 ml-500 mg, IV). Amixin is the first oral inducer of endogenous interferons α , β , and γ . As a polyclonal stimulator, amixin induces the synthesis of IFN types 1 and 2 in T lymphocytes, penetrates the blood-brain barrier, and induces interferon in brain cells.

For the treatment of acute hepatitis B, C, B+C, amixin is prescribed in one course according to the scheme: on the first day - 2 tablets of 0.125 mg, then every 48 hours 0.125 mg (10-12 tablets per course). For the treatment of chronic hepatitis B, C, and B+C, 4 to 6 courses of 10-12 tablets are prescribed (the total number is from 40-48 to 60-72 tablets). In pediatric practice, only viferon is widely used, since it is the only drug from the IFN group that is approved for the treatment of children (including newborns) with various infectious and inflammatory diseases. Other IFN drugs are prescribed to older children with parental consent. In children, the use of combined therapy regimens is considered promising - simultaneous administration of IFN and an IFN inducer (for example, viferon + cycloferon) in order to prevent "slipping remission", which is often achieved immediately after treatment. Thus, the treatment of viral hepatitis in children is a complex and urgent task, but even now many

researchers claim that the future belongs to the combined use of medicines, in which we cannot disagree with them.

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