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CLINICS AND FEATURES OF THE COURSE OF COMBINED VIRAL HEPATITIS

Abstract: *Conducted clinical and serologic examination of 1400 children aged 0-14 with acute viral hepatitis in order to reveal the etiology of hepatitis and the number of combined forms among them was performed. During our investigation we revealed some peculiarities in clinical course, clinical symptoms and aggravation of the disease in case of combined course of VHB and VHC. In case of combination of AVHA+AVHB and AVHA associated with HBSAg significant prolongation of remission was noted. Among 294 patients with A VHB acute delta-viral infection was revealed in 51 persons. It gave the possibility to determine some clinical peculiarities and differentiations of VHD in case of co-infection and super infection. The obtained data allows to prognosticate frequency of different forms of VH in the region and help to perform rational measures on decreasing YH morbidity.*

Keywords: combined hepatitis, morbidity, clinical peculiarities, course, serologic examination.

Beginning in the second half of the 20th century, viral hepatitis (VH) became the most common infections, second only to acute respiratory viral infections and, in some periods, to acute intestinal infections. The intensity of the epidemiological situation persists in the beginning of the XXI century. The number of reported cases of viral hepatitis is 50-60 times less than the number of cases of influenza and acute respiratory infections, but their average duration is 3-5 times longer, and the severity of the course is much more pronounced, not to mention the propensity of some forms of viral hepatitis to chronic, the development of cirrhosis and even liver cancer [1,2,3,5].

Uzbekistan, according to the WHO, belongs to the territories endemic for viral hepatitis. In the dynamics of the incidence of viral hepatitis in the years 2000-2019, there have been years of rise and fall in the incidence. During the observed period, relatively high incidence rates of viral hepatitis were observed in 2000, when the incidence rates were 882.0 per 100 thousand population, in subsequent years there was a dynamic decrease in the incidence, but in 2005 and 2007 there was a sharp increase in the incidence of viral hepatitis. At the same time, the incidence of viral hepatitis "B" was characterized by a dynamic decline, from 155.9 in 2000 to 29.5 in 2001 per 100 thousand population. In 2001, among the Central Asian states in the Republic of Uzbekistan, the first to introduce immunization of newborns against viral hepatitis B into the practice of health care, as a result, compared with 2000 in 2009, the incidence of viral hepatitis B in the republic as a whole decreased 60 times, making up 2.6 against 155.9 per 100 thousand population [4,5,6].

There are a number of unresolved issues, in particular, specific diagnostic methods (ELISA) have not been introduced everywhere, therefore, diagnoses of HAV and HBV are mainly established on the basis of clinical, biochemical and epidemiological data, without taking into account other etiological forms of HG, combined (mixed) hepatitis is not detected.

The aim of the study was to determine the etiological structure of VH, the level and, in part, the clinic of combined (mixed) forms of VH in children.

There were 1,400 children under observation with patients with acute viral hepatitis from 0 to 14 years old, who were admitted to the hepatitis wards during the year. A complete serological survey was conducted to identify the etiology of hepatitis and the level of mixed forms among them. In blood sera, well-known markers of hepatitis viruses were determined in an enzyme immunoassay with test systems of Rosh JSC (Russia-Switzerland) and NPO Diagnostic Systems (Nizhny-Novgorod, Russia).

During a routine serological examination of 400 children admitted to the hepatitis wards during the year, the etiological structure of VG in children was established. At the same time, the share of HA was 37.3%, HB - 8.01%, HS - 9.5%, GE - 1.0% and TTV - 1.6%, 40.0% revealed combined forms (SH-mixed). Of these, 10.3% were the combination of HS with HS, 7.0% - HA with HS, 5.8% - HS with DG. 3.5% - HS with TTV, 3.0% -GS with GE. 2.0% - GW with TTVi 1,5 - GW with GE. In 7.5% of cases, the detection of co-infections with the identification of markers of 2, 3-x and even 4 types of VG.

In order to study the clinical picture of mixed B + C infections, 32 cases verified by the detection of serological markers of both infections (HBsAg. Anti-HBc, IgM. HBeAgantn-HCVc test systems of the second generation) were analyzed. The mono-infection control groups comprised 40 children of patients OB and 56 - with OVGS.

In the epidemiological history of HBV patients 9.3% of children had a transfusion of blood and its components, 18.1% had I information about various parenteral I manipulations (injections, blood draw, dental procedures, circumcisions, and others). Moreover, 18.2% of children with HB had information about contact with a patient with HBV infection (acute chronic HBV, HBsAg carriage) in the family. However, in 53.4% of patients there is no information about parenteral manipulations and contact with patients with HB.

In the group of children with mixed HB + HS infection in the epidemiological history, there were similar data with a group of children with HS (transfusion of blood and its drugs - 78.14 different parenteral manipulations - 12.5%, contact in the

family - 6.2%, and It was reported in 3.1% of children). With regard to the severity and course of the disease, with mixed HB infection compared with a HBV patient, moderately severe and severe forms (P <0.05) became somewhat more frequent. The difference in the forms of severity compared with the group of HCV patients showed a significant increase (P < 0,001) severe forms of the disease.

Thus, with a mixed course of HBV and HCV, it was possible to identify a number of features in the clinical course, the severity of the disease, the severity of individual clinical symptoms, which must be taken into account in practical work.

The results of a comparative analysis of virological indices in the dynamics of manifest forms of mixed hepatitis B + C are interesting. At the height of the disease, the onset of seroconversion HBcAg / anti HBc was established significantly, and hence, the termination of active HB replicationV in hepatitis B + C in comparison with monohepatitis B (61.2 and 46.7%; p <0.05). A possible reason for this could be the simultaneous presence in the patient's body and the hepatitis C virus, which to some extent inhibits the hepatitis B virus. In addition, there were statistically significant differences in the registration of serum HCV markers. First of all, a rarer indication for hepatitis B + C compared with hepatitis C is anti HCVcorcIgM (13.2; 37.9% and 24.2%; p <0.05), and HCV RNA (15.7 and 24 %; p <0.05) indicating active HCV replication. In turn, assumed the presence of a suppressive effect on the part of HBV. On average, half of patients with hepatitis C (51.2%) and with hepatitis B + C (56.1%) detected antibodies to the 4th nonstructural protein, indicating the chronic nature of HCV infection. Given the fact that during the height of hepatitis B + C, HBV DNA was detected in serum in 70% of patients, while HCV RNA was only in 16% (p <0.05), we can confidently speak of the dominant role of HBV in development clinical manifestation with combined HBV / HCV - liver lesions. The extremely rare simultaneous indication of the genomes of both viruses indicated the possibility of their mutual suppression. Control studies of serum markers of HBV, conducted during the recovery period, showed that HBeAg / anti HBe seroconversion occurred in all patients with mixed hepatitis B + C, while in some patients with monohepatitis B, HBsAc was still detected (3.8%). Moreover, HBsAg (88.4 and

95.2%; p <0.05) and HBV DNA (23.9 and 52.4%; p <0.05) were recorded significantly more often also in the comparison group.

The ego showed that elimination from the patient's body occurred more quickly at the simultaneous presence of HCV in patients with mixed hepatitis during the recovery period was generally comparable to that of monohepatitis C. In both groups, total antibodies continued to be detected, as well as with similar frequency of HCV RNA (17.4 and 21.2%; p <0.05). Apparently, this situation was determined further by the persistence of HCV.

Thus, a comparative analysis of the results of serological and molecular biological studies suggested that during the infection process of the combined HBV / HCV etiology, there was a mutual suppression of the activity of hepatotropic viruses. At the same time, at the beginning the hepatitis B virus dominated, and to a greater extent the manifest clinical picture of the disease was caused. Subsequently, HBV was eliminated from the patient’s body, and more rapidly in the presence of the hepatitis C virus. The subsequent course of the actual HCV infection continued in accordance with its inherent regularities.

Among the combined HA + HB, the combination of OVGA + OVHV was detected in 39 (18.5%) of OVGA against the background of carriage of HBsAg- in 70 (33.2%) and OVGA against the background of CVHV - in 102 (48.3%). When analyzing the severity of the disease revealed that with HA in carriers of HBsAg. no difference in forms of severity compared with the group of patients with AHA was detected (PO.G5). with regard to the combined course of OVGA with OVHV and OVG A with HVGV. there is an increase in moderately severe (respectively 46.0 and 42.0% versus 37.2%) and severe forms (respectively 13.0 and 9.0% versus 2.7%).

In the recovery period of the combined course of OVGA + OVHV and OVGA, on the background of the HBsAgc carriage, there was a significant slowdown in recovery with more frequent formation of a protracted course of the disease (10.0 and 8.0% vs. 4.5%; P <0.001). With a long-term (more than 2 years) follow-up observation in any group of patients, the process did not become chronized. Of the 294 patients suffering from AVHV, 51 had acute delta viral infection. In 16 of them

(5.4), there was an acute infection, in 45 (15.4%) - supernifction in HBsAg carriers. This separation using modern methods of laboratory verification of the diagnosis allowed us to identify a number of clinical features and differences in IOP during co-infection and superinfection. In the first case, the percentage of severe forms increased (19.0%). Fulmnnant hepatitis occurred in 25.0% of cases, with three deaths (19.0%). Chronicity of hepatitis was noted in 12.0% of patients, against 9.1% with HBV. In the second case, fulminant hepatitis occurred in 13.0%, patients with three fatal outcomes (7.0%), and the formation of chronic hepatitis occurred in 76.0% of cases. Regarding the nature of the relationship between HBV and HDV, it is determined not only by using HBsAg to form the outer shell of HDV, but also by other, not completely spread interactions. HDV inhibits HBV replication, which leads to a decrease in HBsAg and HBsAg expression and inhibition of DNA polymerase activity during acute infection. One of the possible announcements of this fact is the data on the stimulation of HDV intracellular synthesis of interferon, which inhibits the replication of HBV. Thus, a delta-viral infection, as with co-infection, and superinfescion can be a cause of aggravated and prolonged HBV.

Thus, the use of a highly sensitive method of IFD allows you to clearly conduct the etiological diagnosis of VH in children and thus, find out the true correlation VG in children, the presence of combined forms of the disease. This allows us to predict the incidence of various forms of HS in the region and contributes to the implementation of rational measures to reduce the incidence of SH.

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