Clinics and Peculiarities of the Course of Combined Viral Hepatitis

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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.

Since the second half of the 20th century, viral hepatitis (VH) has become the most common infection, second only to acute respiratory viral infections and, in some periods, acute intestinal infections. The tension of the epidemiological situation persists at the beginning of the 21st century. The number of reported cases of viral hepatitis is 50-60 times less than the number 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 tendency of some forms of viral hepatitis to chronic course, development of cirrhosis and even liver cancer [1,2,3,5J.

Uzbekistan, according to WHO, belongs to the territories endemic for viral hepatitis. In the dynamics of the incidence of viral hepatitis in 2000-2019, there were 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 rate was 882.0 per 100 thousand of the population, in subsequent years there was a dynamic decrease in the incidence, but in 2005 and 2007 there was an abrupt 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 100,000 population. In 2001, the first among the Central Asian states in the Republic of Uzbekistan, immunization of newborns against viral hepatitis B was introduced into healthcare practice, as a result of which, compared with 2000, in 2009, the incidence of viral hepatitis B, as a whole in the republic, decreased almost 60 times, amounting to 2.6 versus 155.9 per 100 thousand of the population [4,5,6J.

There are a number of unresolved issues, in

particular, specific diagnostic methods (ELISA) are not implemented everywhere, therefore, HAV and HBV diagnoses are mainly established on the basis of clinical, biochemical and epidemiological data, without taking into account other etiological forms of HB, combined (mixed) hepatitis are not detected.

Purpose of the study. Determine the etiological structure of CH, the level and, in part, the clinic of combined (mixed) forms of CH in children.

Materials and methods. Under observation were 1400 children with acute viral hepatitis from 0 to 14 years old, who were admitted to hepatitis departments during the year. A complete serological examination was carried out to identify the etiology of hepatitis and the level of mixed forms among them. Known markers of hepatitis viruses were determined in blood sera in enzyme immunoassay with test systems of JSC ROSH (Russia-Switzerland) and NPO Diagnostic Systems (Nizhny-Novgorod, Russia).

Results and discussions. During a planned serological examination of 400 children admitted to hepatitis departments during the year, the etiological structure of CH in children was established. At the same time, the share of HA was 37.3%, HS - 8.01%, GS - 9.5%, GE - 1.0% and TTV - 1.6%, combined forms (VG-mix) were found in 40.0%. Of these, 10.3% were a combination of HS with HS, 7.0% - HA with HS, 5.8% - HS with HD. 3.5% - HS with TTV, 3.0% - HS with GE. 2.0% - HW with TTV and 1.5 - HW with GE. In 7.5% of cases, the detection of combined infections with the detection of markers of 2, 3, and even 4 types of VH.

In accordance with the objectives of the work, 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. HBeAg anti-HCVc test systems of the second generation) were analyzed. Control groups with monoinfections amounted to 40 children patients with OV and 56 with AVHS.

In the epidemiological history of patients with HBV, 9.3% of children had a transfusion of blood and its components, 18.1% had information about various parenteral manipulations (injections, blood sampling, dental procedures, circumcisions, and others). At the same time, 18.2% of children with HB had information about contact with a patient with HB-virus infection (acute chronic HB, HBsAg carriers) in the family. At the same time, in 53.4% of patients, there is no information about parenteral manipulations and contact with patients with hepatitis B.

In the group of children with mixed HB+HC infection in the epidemiological history, there were similar data with the group of children with HC (transfusion of blood and its preparations - 78.14, various parenteral manipulations - 12.5%, contact in the family - 6.2%, and no 3.1% of children had information). With regard to the severity and course of the disease, with mixed HCV infection, compared with patients with HBV, moderate and severe forms became somewhat more frequent ($P<0.05$). The difference in severity forms compared with the group of patients with HCV 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 indicators in the dynamics of manifest forms of mixed hepatitis B + C are interesting. During the peak of the disease, a significantly earlier onset of HBcAg/anti HBc seroconversion was established, and hence the cessation of active HBV replication in hepatitis B+C compared 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 of 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 in 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, the presence of a depressing effect from HBV was also assumed. Detection of antibodies to the 4th non-structural protein on average in half of the patients with both hepatitis C (51.2%) and hepatitis B+C (56.1%) indicated the chronic nature of HCV infection.

Taking into account the fact that during the height of hepatitis B+C, HBV DNA was detected in the blood serum of 70% of patients, while HCV RNA was detected only in 16% ($p<0.05$), we can confidently speak about the dominant role of HBV in the development clinical manifestations in combined HBV / HCV - liver damage. The extremely rare simultaneous indication of the genomes of both viruses indicated the possibility of their mutual suppression. Control studies of serum HBV markers conducted during the convalescence period showed that HBeAg/anti HBe seroconversion occurred in all patients with mixed hepatitis B+C, while HBsAc continued to be detected in some patients with monohepatitis B (3.8%). Moreover, HBsAg (88.4 and 95.2%; $p<0.05$) and HBV DNA (23.9 and 52.4%; $p<0.05$) were registered significantly more frequently also in the comparison group.

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

Thus, a comparative analysis of the results of serological and molecular biological studies suggested that during the infectious process of 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, which to a greater extent was due to the manifest clinical picture of the disease. 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 patterns.

Among the combined HA+HB, the combination of AVHA+AVHB was detected in 39 (18.5%) AVHA against the background of HBsAg-carriage in 70 (33.2%) and AVHA against the background of CVHB - in 102 (48.3%). When analyzing the severity of the disease, it was found that with GA in carriers of HBsAg. there was no difference in the forms of severity compared with the group of patients with AVHA (PO.G5). as for the combined course of AVHA with OVHV and OVH A with CHBV. then there is an increase in moderate (respectively 46.0 and 42.0% versus 37.2%) and severe forms (respectively 13.0 and 9.0% versus 2.7%).

In restore; in the new period of the combined course of AVHA + AVHB and AVHA against the background of HBsAgc carriage, there was a significant slowdown in recovery with a 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 (chic 2 years) dispensary observation, in no group of patients did the process become chronic. Out of 294 patients undergoing OVHV. 51 patients were diagnosed with acute delta-virus infection. In 16 of them (5.4) co-infection was noted, in 45 (15.4%) - superinfection in HBsAg carriers. Such separation using modern methods of laboratory verification of the diagnosis allowed us to identify a number of clinical features and differences in IOP in co-infection and superinfection. In the first case, the percentage of severe form increased (19.0%). Fulminant hepatitis occurred in 25.0% of cases, with three deaths (19.0%). Chronic hepatitis was noted in 12.0% of patients, against 9.1% with HBV. In the second case, fulminant hepatitis occurred in 13.0% of patients with three fatal outcomes (7.0%), and the formation of chronic hepatitis occurred in 76.0% of cases. As for the nature of the relationship between HBV and HDV, it is determined not only by the use of HBsAg to form the outer shell of HDV, but also by other interactions that are not completely common, so HDV inhibits HBV replication, which leads to a decrease in the expression of HBsAg and HBsAg and inhibition of DNA polymerase activity during acute infection. One of the possible announcements of this fact is data on the stimulation of HDV intracellular synthesis of interferon, which inhibits HBV replication. Thus, a delta-virus infection, both in co-infection and superinfection, can cause a aggravated and prolonged course of hepatitis B.

Conclusion. Thus, the use of a highly sensitive IFD method makes it possible to clearly carry out the etiological diagnosis of CH in children and, thereby, to find out the true ratio of CH in children, the presence of combined forms of the

disease. This allows predicting the incidence with various forms of CH in the region and contributes to the implementation of rational measures to reduce the incidence of CH.

Bibliography

1. Azimov Sh.T. "Changes in cellular and humoral immunity in children with viral hepatitis B and C'", Med. journal of Uzbekistan, Tashkent 2005, No. 2, pp. 20-22.
2. Gromova N.I., Gordeychuk I.A. | Clinical significance of HGVy RNA detection in patients with chronic viral hepatitis. Journal of Epidemiology and Infectious Diseases, 2012, No. 2, pp. 35-41.
3. Zakirkhadzhaev A, Kh,, Tadzhiev B. M. "Viral hepatitis", Tashkent, 2009, S. 26-50
4. Kudasheva L, V. "Organizational basis for the fight against viral hepatitis in the Republic of Uzbekistan", Journal "Infection, Immunity and Pharmacology", 2010 No. 1-2 P. 124-128
5. Matkarimov B.D., Tursunova D.A. “On the epidemiology of viral hepatitis “B” in the Republic of Uzbekistan”, Journal “Infection, Immunity and Pharmacology”, 2010 No. 1-2 C136-139
6. Mukasheva G.K. "Clinical and laboratory characteristics of the course of HCV - infection in children", Journal "Epidemiology and Infectious Diseases", Moscow 2012 No. 2 S. 46-50.