ABOUT THE PROBLEM OF COMBINED FORMS OF HIV INFECTION AND HEPATITIS B AND C

A.A. Jakovlev, N.I. Lapteva

In the article the literature data on the results of virological, immunological and clinical studies of combined forms of HIV and hepatitis B and Care given. The necessity of a systematic approach to the study of co-infections and research on the population level of the epidemic process is shown.

Keywords: combined infection, hepatitis B and C, HIV infection.

Combined infection (synonyms: mixed infection, associated infection, satellite infection) - an infection caused by two or more kinds of microorganisms. It may be viruses, protozoa, fungi, bacteria, mycoplasmas, spiroheta, rickettsiae, chlamydiae. According to V. Pokrovsky [9] of mixed infection should say when the infective process caused by the first one, then the activator in various stages of (or in conjunction with the launch of the first) can be associated with infectious process different etiology. According to some reports in the structure of mixed infections account for up to 50% with viral etiology – up to 30% of cases [1]. The main outcomes were possible interaction of two or more agents in the process of mixed infections: 1) independent reproduction; 2) exaltation-increased reproduction of one and all associants; 3) interference-suppressed reproduction of one or all associants; 4) complementation - specific dependence of reproduction of one associants from another. The latter is especially prevalent in associations of oncogenic viruses [2].

One of the features of the modern period is the increase in infections in the structure of the infectious pathology of combined forms of different etiology [11]. However, the reason for this is understudied. According to A. A. Selivanov [10] the occurrence of infections of mixed etiology should be considered from the environmental perspective of interspecies, not just as a coincidence arising associants. It is important to emphasize that the vital strategy of viruses is the quest for survival and replication, which is a modification of the human immune system, a high rate of mutations (appereance of quasispecies). Perhaps a combination of viruses in one organism contributes to these processes [12]. By of studies A.A. Yakovlev, E.S. Pozdeeva combined infections is a factor contributing to the self-regulation systems in the generated antropoparasitic system of biocenosis.

In the characterization of combined infection is important to the order of: simultaneous (coinfection) or serial (superinfection). In mixed infections when the body develops multiple

pathogens, the relationship is complicated mechanism of various pathological processes that are extremely difficult to timely diagnosis, etiological decoding and selection of optimal therapies [2, 4].

Development problems of mixed infections, including elucidation of interactions in microbial associations, including bacterial and bacterial (intraspecific, interspecific, intergeneric etc.), bacterial and viral, viral and viral, bacterial and viral with the simplest and other pathogens, the study mechanisms of pathogenesis and immunity, the development of diagnostic, immunization, treatment, risk factors, and role in the development of the epidemic process have independent theoretical and practical significance [2, 14]. It is important to emphasize that the problem of mixed infections should be considered in line with the developed back in the 30's of the last century the theory of parasitocenosis E.N. Pavlovsky, according to which in infectology be aware that in the patient parasites are in a complex and varied relationship between themselves and the host organism [8].

Viral hepatitis and HIV infection as separate diseases have a worldwide distribution and considerable social importance. This is facilitated by a single haemocontact mechanism of transfer for them, which is being actively implemented parenteral, sexual and vertical ways, especially groups with a high risk of infection from these infections [16, 34, 40]. Viral hepatitis B (HBV) and C (HCV), HIV infection are among the ten leading causes of death from infectious diseases in the world. R. Weber et al. [49] note that in the era of antiretroviral therapy for HIV infection of liver disease are 14.5% of deaths of patients of combined infection. Actual fatality rates from liver disease in HIV-infected persons, apparently higher than registered [17].

Also the increased risk of transmission of HBV, HCV and HDV vertical and sexually in the presence of concomitant infection with human immunodeficiency virus. In particular, HCV transmission from mother to fetus is observed in the 15 - 36% of cases of coinfection with HIV and not more than 5 monoinfection% of HCV, which may be associated with increased sensitivity to hepatotropic viruses with immunosuppressive conditions [13].

If HBV in patients with HIV infection is the leading reason for the liver disease, HIV infection after virus hepatitis B causes a high risk of developing chronic hepatitis B [7]. Among the 15,728 people living with HIV in 498 (8.7%) had HbsAg and 3.6-fold increase in deaths compared with HbsAg-negative patients [30].

Since the HB and HC, as well as HIV infection, have a common mode of transmission, coinfection is quite often and is becoming a serious public health problem in all countries of the world [6, 30]. Last 10 years mixed infection (HIV and parenteral hepatitis) have become

widespread in our country, as a result of additional risk factors for social and behavioural character [7]. Also there is a hidden currents, as evidenced by the HB only DNA detection of HB, anti-HBc, in the absence of HbsAg. Approximately 9% of HIV-positive patients from industrialized countries are carriers of HbsAg [31, 46]. The prevalence HC rate among HIV-infected persons is 40% or more, varying in different risk group [20]. M. Sulkowski et al., [40] believe that GW is shown as an opportunistic infection in HIV-infected persons. In this connection, it should be noted that, among human pathogens microorganisms that hepatitis b virus is one of the most common worldwide. HIV and virus of hepatitis B have much in common, although cytotoxic T- lymphocytes in we are able to eliminate the virus from the body, assuming that most patients virus of hepatitis B remains in the body for a lifetime. Therefore, reactivation of infection can occur after many years of infection, such as immunocompromised patients with advanced HIV infection or chemotherapy, regardless of the spectrum of antibodies to hepatitis B, detected in the patient.

It should be emphasized that the possible interference as HB and HC on the course and outcome of HIV infection, and the last - for the development of parenteral hepatitis. In particular, for a mixed HBV/HIV - infection is characterized by rapid decline swarm of anti-HBs, and progression to cirrhosis of the liver [39, 41]. Hepatocellular carcinoma in this population begins to develop at a young age and is more aggressive [38]. Causes of progression of liver disease in HIV/HBV-associated infections remain unclear. Although the immune response of the host is an important trigger of liver disease in patients with HB, it cannot always explain the aggressive disease course. So in HIV-infected persons with evidence of chronic hepatitis B in reduction of CD4 + T-lymphocytes and CD4 : CD8 ratio violation. The decrease in the number of CD4 + T - lymphocytes especially expressed in patients with chronic active hepatitis. HIV infection reduces the clearance of HbsAg and HBeAg and stimulates DNA virus HBV in HIV-infected persons [50, 27].

Immunosuppression caused by HIV, it may reduce the levels of AlAt [32]. In patients with mixed form of HIV/HBV increased replication of HBV and have a low incidence of seroconversion to HBeAg [25]. It stresses the role of HIV - infection and virus-induced interference in the damage of the liver parenchyma [19].

Results of clinical studies on effect of HC for HIV infection more contradictory. On the one hand, according to some researchers, chronic HCV infection is the cause of death of coinfected persons [17]. There is evidence that HIV infection is clinically 2-5 times faster progression to AIDS in the presence of the virus HS [23]. This effect is the high risk of developing cirrhosis of the liver, the more frequent prevalence of cirrhosis in these patients, rapid decompensated liver disease,

culminating in the death of patients [7, 26]. The presence of the virus in the blood, how HC and RNA of HIV increases risk of death from AIDS [35]. But is the value of viral load and its influence on the mortality of combined infection [24]. On the other hand, studies of a number of authors have shown that high levels of RNA virus HC of blood not only stimulates the progression of HIV infection, but also worsens the response to treatment active antiretroviral therapy and histological picture of liver [7, 15].

HIV infection substantially modifies the natural history of HCV infection, increasing levels viremia of HCV [23]. It affects all stages of infection the HC by reducing the frequency of spontaneous recovery from HCV infection [48, 36].

The degree of influence of the HC on the course and outcome of HIV infection depends on the path of infection by these viruses. In HIV-positive persons infected through blood transfusions and the introduction of drugs, the rate of liver cirrhosis in the first 15 years of follow-up was 15-25 % and in HIV-negative significantly less - 2.6 – 6.5% [42]. Many persons from among drug addicts and alcohol have combined HIV and HC. The progression process of HIV infection has taken place against a background of high content RNA of virus HC in blood serum [23] and reduced the number of CD 4 cells. An inverse correlation between the level of RNA virus HC and CD 4 cell count. At high levels of RNA observed reduced CD4, low - increased [47, 28]. In 87.3% of patients with HC in the presence of detection of HIV increased levels of activity AlAt and in 72.8% - fibrosis of the liver varying degrees. However, in patients with normal transaminases fibrosis is found only in 38.5%. Moreover, in patients with combined infection in 2.5 times more often marked the third genotype HC [7].

The influence of the HC on the progression of HIV infection is less certain. At the same time the risk of progression of HIV infection may be insufficient antiretroviral therapy. However, R.S. Nershow et al. [29] for long-term observation of a large group of HIV-infected women found no effect of HCV infection on the progression of the process. Moreover, there are reports that in HIV-coinfected patients have spontaneous GS climate Rens virus GS [44] and its frequency depends on the route of infection [45].

Thus, as the analysis of literary publications, the priority in the study of co-infections belong clinical, immunological and virological studies, where as epidemiological - very few [7, 5]. To some extent, this is due to the lack of official registration mix - forms of viral hepatitis with HIV infection. Moreover, in-depth study of the co-infections is just beginning. Undoubtedly, the importance of the study of cell-level interactions of the parasite and the host, as the only habitat of many pathogens is the host cell (from prokaryotes to man). «Here in my home they are

evolutionarily developed their parasitic forms of existence, including biological properties as items of pathogenicity, aggressiveness, invasiveness and others. It evolved and intraspecific fighting and synergies and satellizm and much more» [1]. At the same time, in accordance with a systematic approach to the study of epidemic process as complex multilevel system, the processes at the cellular, molecular levels, reflected in epidemic forms, that is at the population level [3,11,13]. Consequently, it is epidemiological studies can adequately integrate and interpret the data obtained from both clinical and virological surveillance.

Used literature:

1. Baroyan O.V. The problem of mixed infections / O.V. Baroyan, D.R. Porter // International and national aspects of modern epidemiology and microbiology. - M. – 1975. – P. 152 - 191.

2. Belaya O.F. The problem of mixed infections and their diagnostics / O.F. Belaya, Y.A. Belaya // Mixed infections. – M. – 1986. – P. 45-52.

3. Belyakov V.D. The problem of self-regulation of parasitic systems and mechanism of development of the epidemic process / V.D. Belyakov // Bulletin of the AMS of the USSR. – 1983. – N.3. – P. 3-5.

4. Zinovev A.S. Some results of the study of the pathogenesis of mixed infections / A.S. Zinovev, V.F. Marenko, L.S. Egorova // Mixed infections and invasions. – Omsk. – 1981. – P. 4-13.

5. Lapteva N.I. Epidemiologic evaluation factors that influence the development of combined forms of HIV infection with parenteral viral hepatitis among the population of the Sakha Republic (Yakutia) / N.I. Lapteva, A.A. Yakovlev // Yakutsk medical journal. - 2012. – N.2. - P.64-66.

6. Nechaev V.V. Epidemiology of viral hepatitis and HIV infection of tuberculosis patients / V.V. Nechaev, A.K. Ivanov, Le Thanh Toan et al. // Socially significant infections. – SPb.- 2007. – P. 22-25.

7. Nechaev V.V. Socially significant infections. Part II (mixed infection) / V.V. Nechaev, A.K. Ivanov, A.M. Panteleev – SPb: LLC «Birch». - 2011. - 312 p.

8. Pavlovsky E.N. Common problems of parasitology and zoology / E.N. Pavlovsky – M.: Publishing House AS of the USSR. - 1961. – 120 p.

9. Pokrovsky V.I. Infection diseases in the Russia / V.I. Pokrovsky // New medical journal. - 1995. – N.1. - P.3-4.

10. Selivanov A.A. Infection of the mixed etiology - chance or regularity / A.A. Selivanov // Patterns of epidemic process: Proceedings of the Institute by name Pasteur. - V.61. -1983. - P.47-49.

11. Cherkassky B.L. Guidance on the general epidemiology / B.L. Cherkassky – M.: Medicine. – 2001. -558 p.

12. Sherlock Sh. Diseases of the liver and biliary tract / Sh. Sherlock, J. Dooley // A practical guide: Trans. from English (Edited by Z.G. Aprosinoy, N. A. Mukhina) – M.: GEOTAR Medicine. - 1999. - 864 p.

13. Yakovlev A.A. Need for a systemic approach to the problem of combined viral hepatitis / A.A. Yakovlev, E.S. Pozdeeva // Epidemiology and infection dis. – 2010. – N.4. – P. 54-57.

14. Yakovlev A.A. Integrative epidemiology of hepatitis B and C in the Primorye Territory / A.A. Yakovlev, E.S. Pozdeeva. - Vladivostok: Medicine Far Eastern. - 2011. - 116 p.

15. Adinolli L.E. Serum HCVRNA levels with histological liver damage and concur with steat osisin progression of chronic hepatitis C / L.E. Adinolli, R. Utili, A. Andreana et al. // Dig. Dis. Sci.- 2001.- Vol. 46.- P. 1677-1683.

16. Alter M.J. Epidemiology of viral hepatitis and HIV co-infection / M.J. Alter // J. Hepatology. -2006. - Vol. 44. - P. 6-9.

17. Bica G. Increasing mortality due to end stage liver disease in patients with human immunodeficiency virus infection / G. Bica, Mc B. Govern, R. Dhar et al.// Clin.Infect.Dis. – 2001. - Vol. 32. - P. 492-497

18. Brau N. Presentation and outcome of hepatocellular car¬cinoma in HIV-infected patients: a US-Canadian multicenter AIDS study / N. Brau, R. Fox, P. Xiao et al. // J. Hepatology. - 2007. - Vol 47- P. 527-537.

19. Buti M. Influence of human immunodeficiency virus infection on cell-mediated immunity in chronic D hepatitis / M. Buti, R. Esteban, M. Espanol et al. // J. Infect. Dis. - 1991. - Vol. 163.- P.1353.

20. Dieterich D.I. Activity of combination therapy with in¬fection alfa-2b plus ribavirin in chronic hepatitis C patients co-infected with HIV / D.I. Dieterich, J.M. Parow, R. Rajapaksa // Semin. Liver Dis. - 1999. - Vol. 19. - P. 87- 94.

21. Di Martino V. Influence of HIV infection on the re¬sponse to interferon therapy and the long-term outcome of chronic hepatitis B / Di V. Martino, T. Thevenot, J.F. Colin et al. // Gastroenterology. - 2002.- Vol. 123.- P. 1812-1822.

22. Eyster M.E. Natural history of hepatitis C virus infection in multitransfusion hemophiliacs. Effect co-infection with HIV / M.E. Eyster, L.S. Diamondstone, J.M. Lien et al. // J. AIDS. - 1993. - Vol. 6. - P. 602-610.

23. Eyster M.E. Increasing hepatitis C virus RNA levels in hemophiliacs: relationship to

human immunodeficiency virus infection and liver disease / M.E. Eyster, M.W. Fried, Di A.M. Bisceglie et al. // Blood. - 1994. - Vol. 84. - P. 1020-1023.

24. Goldert J.J. Lack of association of hepatitis C virus load and genotype with risk of end-stage liver disease in patients with human immuno¬deficiency virus coinfection / J.J. Goldert, A. Hatzaris, K.E. Sherman et al. // J. Infect. Dis. - 2001. - Vol. 184.- P. 202-205.

25. Gilson R.J. Interaction between HIV and hepatitis B virus in homosexual men: effects on the natural history of infection / R.J. Gilson, A.E. Hawkins, M.R. Beechaman et al. // AIDS. - 1997 - Vol. 11. - P. 597-606.

26. Graham C.S. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis / C.S. Graham, L.R. Baden, E. Yu et al. // Clin. Infect. Dis. - 2001. – Vol. 91. - P. 562-569.

27. Hadler S. C. Outcome of hepatitis B virus infection in homosexual men and its relation to prior human immunodeficiency virus infection / S.C. Hadler, P.O. Judson, P.M. Malley et al. // J. Infect. Dis. - 1991. - Vol. 163. - P. 454-459.

28. Herrero-Martinez E. The prognostic value of a single hepatitis C virus RNA load measurement taken early after human immunodeficiency virus seroconversion / E. Herrero-Martinez, C.A. Sabin, J.G. Evans et al. // J. Infect. Dis. - 2002. - Vol. 186. - P. 470-476.

29. Hershow R.C. Hepatitis C virus coinfection and HIV Load CD4 + cell percentage, and clinical progression to AIDS or death among HIV- infected women: women and infants transmission study / R.C. Hershow, P.T. Driscoll, E.D. Handlsman et al. // Clin. Infect. Dis. - 2005. - Vol. 40. - P. 859-866.

30. Konopnicki D. Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA Cohort / D. Konopnicki, A. Macroft, de S. Wit et al. // AIDS. - 2005. - Vol. 19. - P. 2117-2125.

31. Kellerman S.E. Prevalence of chronic hepatitis B and incidence of acute hepatitis B infection in human immunodeficiency virus-infected subjects / S.E. Kellerman, D.L. Hanson, A.D. Me Naghten, R.L. Fleming // J. Infect. Dis. - 2003. - Vol. 188. - P. 571-577.

32. Kregsgaard K. The influence of HTLV-III infection on the natural of hepatitis B virus in male homosexual HBsAg carriers / K. Kregsgaard, B.O. Lindhardt, J.O. Nilsen et al. // Hepatology. - 1987. - Vol. 7. - P. 37-41

33. Klein M.B. The impact of hepatitis C virus coinfection on HIV progression before or antiretroviral therapy / M.B. Klein, R.G. Lalonde, S. Suisse // J. Aquir. Immune Syndr. - 2003. -Vol. 33. - P. 365-372.

34. Lodengo H. Hepatitis B and C virus infections and liver function in AIDS patients at Chris Hani aragwanath Hospital, Johannesburg / H. Lodengo, B. Schoub, Ally R. et al. // East. Afr. Med. J. - 2000. - Vol. 77. - P. 13-15.

35. Mellars J.W. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma / J.W. Mellars, C.R. Rinaldo, P. Gupta et al // Science.- 1996. - Vol. 272.- P. 1167-1170.

36. Netski D.M. CD4+T cell-dependent reduction in hepatitis C virus-specific humoral immune responses after HIV infection / D.M. Netski, T. Moshruger, J. Astemhorski et al. // J. Infect. Dis. - 2007. - Vol. 195. - P. 857-863.

37. Palella K. Mortality in the highly active antiretro-viral therapy era: changing causes of death and disease in the HIV outpatient study / K. Palella, R. Baker, A. Moorman et al. // Acquir. Immune Defic. Syndr. - 2006. - Vol. 43.- P. 27-34.

38. Puoti M. Hepatocellular carcinoma in HIV-infected patients: epidemiological features, clinical presentation and outcome / M. Puoti, R.Bruno, V. Soriano et al. // AIDS. - 2004. -Vol. 18. - P. 2285-2293.

39. Puoti M. Natural history of chronic hepatitis B in co-infected patients / M. Puoti, C. Torti, R. Bruno // J. Hepatology.- 2006.- Vol. 44.- P. 65-70.

40. Sulkowski M.S. Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection / M.S. Sulkowski, D.L. Thomas, R.E. Chaisson et al. // JAMA. - 2000. - Vol. 283. - P. 74-80.

41. Soriano V. Care of patients with chronic hepatitis B and HIV co-infection recommendations from an HIV-HBV international panel / V.Soriano, M. Puoti, M. Bonacini //AIDS.- 2005. -Vol. 19. - P. 221-240.

42. Soto B. Human immunodeficiency virus in¬fection modities the natural history of chronic parenterally-acquired hepatitis C with an unustially rapid progression to cirrhosis / B. Soto, A. Sanchez- Quijano, I. Rodrigo et al. // Hepatology.- 1997.- Vol. 26. - P. 1-5.

43. Selik R.M. Trends in diseases reported on US death cer¬tificates that mentioned HIV infection, 1987-1999 / R.M. Selik, R.H. Byers, M.S. Dworkin // J. Acquir. Immune Dene. Syndr - 2002. - Vol. 29. - P. 378-387.

44. Sherman K.E. Comparison of methodologies for quanti¬fication of hepatitis C virus (HCV) RNA in patients coinfected with HCV and human immunodeficiency virus / K.E. Sherman, S.D. Rouster, P.S. Horn // Clin. Infect. Dis. - 2002.- Vol. 35.- P. 482 -487.

45. Shores N.J. Sexual transmission is associated with spontaneous HCV clearance in HIV-infected patients / N.J. Shores, I. Maida, V. Soriano, M. Nunez // J. Hepatology. - 2008. - Vol. 49. -

P. 323-328.

46. Thio C.L. Multicenter AIDS Cohort Study. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort study / C.L. Thio, E.G. Seaberg, R.J. Skolasky et al. // Lancet - 2002. - Vol. 360. - P. 1921-1926.

47. Thomas D.L. Effect of human immunodeficiency virus on hepatitis C virus infection among injecting drug users / D.L. Thomas, J.W. Shin, H.J. Alter et al. // J. Infect. Dis. - 1996. - Vol. 174. - P. 690-695.

48. Thomas D.L. The natural history of hepatitis C virus infection: host, viral and environmental factors / D.L. Thomas, J. Assemborski, R.M. Rai et al. // JAMA. - 2000. - Vol. 284. - P. 450 - 456.

49. Weber R. Liver-related deaths in persons infected with the HIV: the D: A: D study / R. Weber, C. Sebin, N. Friis-Moller et al. // Arch. Intern. Med. - 2006. - Vol. 166. - P. 1632-1641.

50. Weller I.V. Spontaneous loss of HBeAg and the preva¬lence of HTLV-III-LAV infection in a cohort of homosexual hepatitis B virus carriers and the implications for antiviral therapy / I.V. Weller, A. Brown, B. Morgan et al. // J. Hepatology. - 1986. - Vol. 3. - P. 9 - 16.

Information about the authors:

1) Anatoly Yakovlev - the doctor of medical sciences, the professor, the professor of chair of epidemiology and military epidemiology of the Vladivostok State Medical University, Vladivostok, Russian Federation, E-mail: yakovlev-epid@yandex.ru,

2) Nurgustana Lapteva -post-graduate student of epidemiology and military epidemiology of the Vladivostok State Medical University, leading specialist-expert of the part epidemical department of Administration of the Rospotrebinspection of Sakha (Yakutia) Republic, Yakutsk, Republic Sakha (Yakutia). E-mail: lapteva.nurgusta@mail.ru.