Original article

CHRONIC RENAL FAILURE ASSOCIATED WITH HEPATITIS B AND C VIRUSES AS A THERAPY PROBLEM

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The presence of infections caused either by hepatitis B or C viruses or both of them complicates the evolution of chronic renal failure considerably.The aim of our investigation was to determine the presence of hepatotropic viral markers, clinical and laboratory characteristics, as well as therapeutic possibilities for examined patients.

Our investigation included 136 patients who had had regular dialysis tretment. Based on the presence of viral markers, all the patients were divided in three groups: (I) HBV positive patients; (II) HCV positive patients, (III) HBV and HCV positive patients. All the patients were subdivided in two groups: those with an acute form and those with a chronic form based on the clinical course of the disease.The laboratory analysis did not show a clear correlation with the course of the disease, especially in those patients with a chronic disease. These finding allow us to draw the following conclusions: a significant number of patients have been infected with hepatitis B and C viruses; laboratory analysis in patients with a chronic course did not always correlate with the evolution of the disease; the clinical course is mostly mild.

Introducing antiviral therapy gives a much better perspective to all categories of patients. *Acta Medica Medianae 2008;47(3):5-8.*

Key words: *viral B hepatitis, viral C hepatitis, chronic renal failure, haemodialysis*

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Introduction

The liver disese caused by hepatitis B and C viruses has become the important cause of morbidity and mortality in patients with chronic renal insufficiency.

Infections by hepatitis B and C viruses had a different outcome by the end of the last millenium. With the development of diagnostic tests as well as carrying out prevention measures, the decresing of incidence and prevalence of hepatitis B infection has been reached. On the other side, liver damage caused by hepatitis C virus has different characteristics. The main characterictics of hepatitis C are transmission without common risk factors, absence of biohemical indicators in spite of viremia and false negative serological tests (1). Prevalence of anti-HCV positivity in patients on hemodyalisis are differentely manifested, from 8.9% to 75% (Moldavia).The main characteristic of prevalence is big geografic and individual variability among hemodialisis centers (2). With the aim of authentic follow-up of patients, it is necessary to examine a blood sample to HCV RNA before starting the hemodyalisis.

Acute infection of HCV in hemodialysis patients is followed by moderate increasing of ALT level and returnig to normal level. The beginning of viremic phasis is associated with ALT activity (till 74 IU/I), prior to anti-HCV seroconversion, then is followed by persistant viremia, normal ALT activity and anti-HCV positivity. However, investigations and experiences showed that around 25% of patients with HCV infection had had normal values of ALT (till 74 IU/I), and not only patients on hemodyalisis (1,3,4). Forty percents of patients had minimal dissenting from normal ALT values (5).

Relation of ALT level and histological finding is not often in correlation, so the decision on starting with the treatment is based on presence of fibrosis grade after liver biopsy. (6,7). Administration of recombinant alfa-2a interferon or pegilated interferon is indicated in the treatment of patients in terminal stage of renal insufficency(8). New preliminary results have shown that interferon application is safe in patients coinfected with HBV and HCV infections, untill Ribavirin administration is contraindicated (8). The aims of the administered therapy for hepatitis B viral infection (interferon, lamivudin, adefovir) as well as for hepatitis C viral infection (pegilated interferon) are stable eradication of virus, regression of chronic hepatitis, prevention

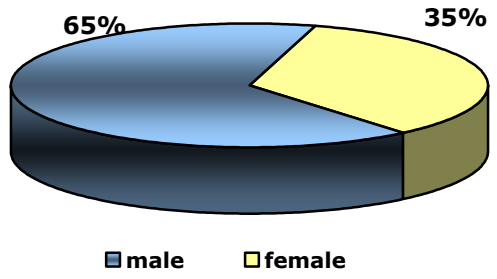
of terminal stage of disease (liver cirrhosis) and hepatocellular carcinoma (10).

Material, methods and aim of the study

The investigation involved 136 patients on hemodialysis programme, during 2004 and the beginning of 2005. All examined patients were devided by scrining tests (ELISA test) in three groups on the basis of the presence of HBs Ag and anti-HCV antibodies. ELISA test was done in serological laboratory of the Infectious Diseases Clinic. The first group included HBs Ag positive patients on hemodialysis programme (29/136). The second group were patients with combinated HBV and HCV infection (18/136). The aims of the investigation were numerous and included clinical and biochemical analyses of patients, determination of presence of HBV and HCV markers and consideration of therapeutic investigations.

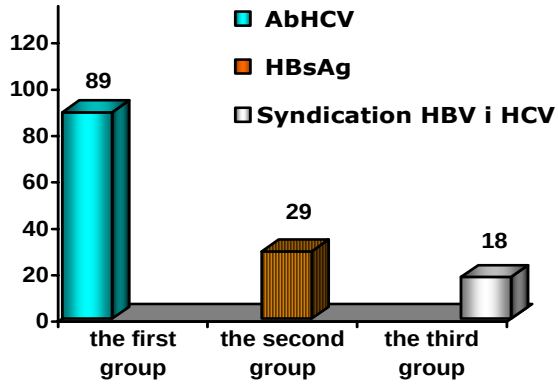
Results

During 2004 and the beginning of 2005 there were 136 patients tested, with terminal renal inuffi-cency on the hemodialysis programme by ELISA.



Picture 1. Patients distribution by sex

The screening tests for diagnosis HBV and HCV infections were done. The patients made heterologous group (age from 23 to 82). Most of the patients (48) belonged to age group from 65 to 74 years, the smallest number of patients (4) were younger than 35 years. Sex distribution showed the predominance of male sex.

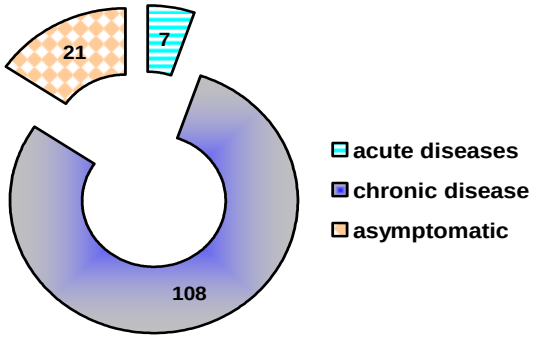


Picture 2. Presence of hepatitis markers

Regarding the results, all patients were divided into three groups. The first group were patients anti-HCV positive (89/136)-more numerous than other groups. The second group were HBs Ag positive (29/136). The third group were patients coinfected with HBV and HCV (18/136). The duration of hemodalysis programme were various, from 1 to 13 years (Picture 2).

The clinical picture was acute disease (7) (Picture 3) with finding HBs Ag, high level of bilirubines (≥ Xsr 209 mmol/l), elevated values of gama-GT (Xsr=230 UI), aminotransferasis (AST Xsr=430 U/l, ALT Xsr=710 U/l) and LDH (Xsr=760 U/l više). Zika Biochemical aspect of illnes is manifested by dyspeptic problems, discoloured urine, icterus with severe pruritus, hepatomegaly and splenomegaly as main clinical presentation of infection. Other patients, with HbsAg, AtHCV or conjoined infection were almost asymptomatic except some light form of pruritus, hepatomegaly or fatigue. The levels of aminotranspherasis,well-known as a leading biochemical marker of liver malfunction, were differently detectable. The scale was expanded from normal or subnormal values to lightly alterated. (AST Xsr =52 U/l), (ALT Xsr= 62 U/l). Sometimes, these analyses could be misdiagnosed at first sight. Analysed patients often had pathological values of gama glutamyl transferase up to Xsr=96 U/l. Within these patients, there`s a little group of patients who had had the liver biopsy performed with the aim of kidney transplantation and antiviral treatement (5).

Pathohistological findings showed active form of chronical hepatitis (HAI 5-11) and moderately active chronic hepatitis (fibrosis O-2).



Picture 3 . Clinical picture of HBV and HCV infections

Discussion

Analysed patients showed very heterogenic group. Most of them had monoviral infection (118), but 18 had the so-called dual infection. Clinical manifestation of acute liver disease in hemodialysed patients corresponeded to clinical manifestations in the rest of population.

Chronic forms of hepatitis B and C infections have asymptomatic course with light symptoms as fatigue, pruritus or hepatomegaly. This asympto-matic course could be a reason for misdiagnosis and delayed treatment.

The tests that have been done had a big epidemiological and therapeutical importance because of administration of current antiviral therapy on time.

The chronic dialysis program patients have a similar interferon therapy response as the other with chronic hepatitis C form (8). Everyday high-doses interferon therapy is not recommended in practice. Kidney malfunction does not have influence on apsorption, distribution and elimination of pegilated interferon, so it is a therapy of choice in chronic C hepatitis (11,12). Ribavirin is not indicated as a drug of choice in HCV infections because of possible red cells hemolysis (8,9). Patients with transplanted kidneys as well as with HBV infections should be treated by lamivudine (10).

Newly found patients with HBV were in so-called „negative apparatus" group, with valid data about regular immunisation against HBV infection. More detailed epidemiological investigation showed that they had been incompletely vacinated agains hepatitis B, before hemodialysis was started. Analyses of aminotranspherasis activity showed that its levels ranged from normal to slightly higer, which corresponds to the literature data (2,3,4,5,6).

Conclusion

Hemodialysis program patients are in high percentage infected with hepatitis C virus, hepatitis B virus, or both. Clinical presentation is mostly mild with very low or normal activity of aminotranpherase enzimes. HBV and HCV infected patients should be treated adequatly before kidney transplantation is planned.

Antiviral therapy has its own limits, but offers brighter perspective for this kind of chronic patients.

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HRONIČNA BUBREŽNA INSUFICIJENCIJA UDRUŽENA SA VIRUSIMA HEPATITISA B I C KAO TERAPIJSKI PROBLEM

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Prisustvo infekcije izazvane virusima B i C, pojedinačno ili udruženo, u značajnoj meri komplikuje evoluciju hronične bubrežne insuficijencije. Cilj našeg ispitivanja bio je određivanje prisustva markera hepatotropnih virusa, kliničkih i laboratorijskih karakteristika hroničnog hepatitisa B i C, kao i terapijskih mogućnosti kod ispitivanih bolesnika.

Ispitivanjem je obuhvaćeno 136 bolesnika sa programa hronične hemodijalize. Na osnovu prisustva virusnih markera svi bolesnici su podeljeni u tri grupe: I sa HBV, II sa HCV i III grupa sa udruženom infekcijom prethodna dva virusa. Na osnovu kliničkog toka ispitanici su podeljeni na bolesnike sa akutnim i hroničnim oblikom bolesti, pri čemu je klinički tok hronične bolesti asimptomatski. Laboratorijske analize nisu u jasnoj koleraciji sa tokom bolesti, naročito kod hronične bolesti. Ovakav nalaz dozvoljava da zaključimo da su bolesnici u značajnom broju inficirani virusima B i C, da laboratorijske analize hroničnih bolesnika nisu uvek u korelaciji sa evolucijom bolesti i da je klinički tok bolesti uglavnom blag. Uvođenjem antivirusne terapije nudi se jasnija perspektiva ovoj kategoriji bolesnika. *Acta Medica Medianae 2008;47(3):5-8.*

***Ključne reči**: Hepatitis viralis B, Hepatitis viralis C, hronična bubrežna insuficijencija, hronična hemodijaliza*