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Professional paper

Prognosis for the Patients with Alcoholic and Nonalcoholic Liver Disease

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A B S T R A C T

The purpose of this investigation was to determine the role of alcohol in development of progressive liver disease. For this purpose, 41 alcoholic patients were followed up for 5 years. Criteria for alcohol abuse was that the patients were enjoying 20 g alcohol daily in a period of 5 years for females and respectively 60 g daily for males. In the same time a group of 51 nonalcoholic patients with histologically proven chronic liver disease were investigated. In all 92 patients chronic liver disease and progression of the disease was proven by liver biopsy during a 5-years follow-up. In sera of all patients the markers of hepatitis viruses B, D and C were continuously determined and chronic viral hepatitis was excluded. Also, autoimmune chronic hepatitis was excluded. The results of the investigation showed that alcoholics develop cirrhosis hepatitis, in most cases 78.04%. The most progressive chronic liver diseases – cirrhosis and hepatocellular carcinoma – are significantly present among nonalcoholics ($p \leq 0.05$). In the mentioned investigation a large group of 51 patients with severe chronic hepatitis without a proven ethiology of disease was found and it deserves priority in future research.

Introduction

Although in the past few decades hundreds of scientists have been concerned with chronic viral hepatitis, alcohol as a cause of liver disease remains the most frequent ethiologic factor. In spite of long-years researches, the role of alcohol in development of chronic liver diseases is not entirely clear; present are also genetic factors, gender, quantity and duration of alcohol abuse, immunological events in the liver. We are still surprised by the uncleared fact that only 15% to 20% of alcoholics develop liver disease and that female population is more sensitive to alcohol consumption. Since we follow up many patients with chronic liver diseases

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of different causes, we wanted to determine the role of alcohol in development of progressive liver chronic diseases[1–3].

Patients and Methods

In a group of 41 patients with the history of alcohol abuse and with histologically proven chronic liver disease, we checked anamnestic data of the patients who were continuously taking alcohol after a period of 48 months. Criteria for alcohol abuse was that the patients were enjoying 20 g alcohol daily in a period of 5 years for females and 60 g daily for males. In the same time, we investigated a group of 51 patients with histologically proven chronic liver disease, but without history of alcohol abuse. In that whole group of 92 patients, at the moment of the first liver biopsy, we excluded the infection by B, D and C hepatitis virus in their sera.

After 48 months we performed a control liver biopsy. After that, we followed the whole group during 12 months and every four months during clinical control we determined HBV markers in their sera. Testing of the sera markers HbsAg, anti- HBs, anti-HBC, HbeAg, anti-Hbe, was performed by the commercial methods RIA and EIA (BEAD test) Abbot Laboratories, North Chicago, Illinois, USA. HBV-DNA-PCR was performed by the Roche-Amplicor test. Anti-HCV Elisa test by the Ortho Clinical Diagnostic, Rharitan, USA was used. Anti-Hd was tested by the RIA Abbot commercial test. In the sera of our patients we also determined ANA (anti-nuclear) and SMA (anti-smooth muscle antibodies) by immunoflorescence. Histological diagnosis was made according to the accepted classification of CPH (chronic persistent hepatitis), CAH (chronic active hepatitis), CH (cirrhosis hepatis), HCC (hepatocellular carcinoma), N (normal finding)[4–6]. The history of previous acute and blood transfusion was taken. Hemochromatosis and Wilson disease were excluded in all patients. All the patients with cirrhosis hepatis at the beginning of the investigation had Child Pugh A degree. All results were statistically computed: a test of significance X with the Yates correction for small numbers was used. X was significant if higher than 3.841, p 0.05. As well the 95% interval of confidence was used for results expressed in percentage. The numbers in brackets mean upper and lower limits of the 95 % interval of confidence.

Results

In 92 patients, 59 male and 33 female, chronic liver disease was histologically proven. Among 41 of them, 44.56% (29–62%) were alcoholics and 78.04% (60–91%) of these alcoholics had cirrhosis hepatis. In 51 patients who were not alcoholics 33.3% (12–61%) had CH and 21.6% (3–57%) had CAH.

After 48 months we performed 17 control biopsies. 7 patients with CAH developed CH in the group of nonalcoholics. Among alcoholics 5 patients with CPH developed CH and 2 developed CAH. In the same group 3 patients with previous normal findings developed CPH and 2 developed CAH. All 92 patients were serologically negative for markers of B, C and D hepatitis virus during a period of the next 12 months. ANA and SMA were positive in 27.17% (11–47%) patients.

However, no one among the patients had criteria for autoimmune liver disease and there was no statistical difference of ANA and SMA between alcoholics and nonalcoholics[8]. After 12 months of serological and clinical follow-up in 13 patients a control biopsy was performed. Two patients with CAH and one with CH developed HCC in the group of nonalcoholics. Among alcoholics one patient with CH had a regression into CAH and 9

patients with CH again had the same disease.

After 5 years of follow-up 6 (52%) patients died: three nonalcoholics with developed HCC and three alcoholics with CH. Although the alcoholics had very severe hepatic disease, there was a significant statistical difference in relation to nonalcoholics (X^2 = 8.4212, p 0.05).

Because of such unexpected result we compared this group of patients with the patients with HBV chronic hepatitis. There was a significant difference between severe chronic hepatitis of alcoholics without markers of HBV and chronic hepatitis in nonalcoholics, but HBsAg positive (X^2 = 8.2407, p 0.05). However, the patients with chronic HBV hepatitis and with markers for viral replication had significant difference in relation to alcoholics without HBV markers (X^2 = 4.0502 p 0.05). It means that our nonalcoholic patients without markers for viral hepatitis viruses developed the most progressive forms of liver disease.

Discussion

The mechanism of development of chronic liver disease among alcoholics is multifactorial[9]. In one of our previous investigations out of 401 patients with histologically proven chronic liver disease 48.9% (41–54%) were alcoholics. Among 196 alcoholics 44.4% (33–56%) were negative for serological markers of HB virus. In this group 25.4% (16–33%)[10] had CH. Alcoholic cirrhosis is a very severe chronic hepatitis with a bad prognosis.

In a prospective study of 270 cirrhotics more than a half died within 48 months and 1/3 of these patients had a combination with alcohol hepatitis[11]. The results of our investigation demonstrate that the majority of our alcoholic patients have CH, but after a 5-year follow-up the mortality was not so high. Nevertheless, alcohol abuse in our patients causes significantly more severe chronic hepatitis compared to the patients with chronic HBV nonalcoholic hepatitis.

Alcohol abstinence is the only attenuating factor since the five-year survival of cirrhotics who continue drinking is 50%. According to that fact, therapy against alcohol abuse could have an effect to the reduction of alcoholic liver disease. Liver transplantation among alcoholics is also questionable because it is recommended for abstinent patients and the relaps of disease in transplant patients who continue to drink is more often[12,13].

It is well known that in spite of the use of many diagnostic methods, 10% of patients have severe chronic liver disease with significant progression, still without a proven ethiology of disease. Mortality among such patients is increased in 75% of the cases. Our results correspond to such investigations because they show that our nonalcoholic patients without any viral infection have significant severe chronic hepatitis. Among them, after a 5-year follow up, hepatocellular carcinoma developed[14–18].

In conclusion, alcoholism is one of the most important causes of chronic liver disease in our patients and has to be resolved together with all other aspects. Along with that, the patients with severe chronic hepatitis, but of unknown ethiology, have priority in our future research. Through this investigation we perceived that keeping up with up-to-date knowledge on liver diseases we are very often occupied by the problems which are not decisive in our national pathology. Therefore, we have to check exactly every individual patient with chronic liver disease in order to give him/her optimal treatment.

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PROGNOZA U ALKOHOLNOJ I NEALKOHOLNOJ KRONIČNOJ BOLESTI JETRE

SAŽETAK

Cilj ispitivanja bio je utvrditi utjecaj alkohola na razvoj kronične bolesti jetre. U tu svrhu praćen je tijekom 5 godina 41 bolesnik s utvrđenim alkoholizmom. Alkoholizam je utvrđen anamnestičkim podatkom o konzumaciji etila 20 g dnevno kroz 5 godina za žene, te 60 g dnevno kroz 5 godina za muškarce. Istodobno je praćena grupa od 51 nealkoholičara s kroničnim hepatitisima. U svih 92 bolesnika bolest jetre je utvrđena histološkom verifikacijom, a progresija bolesti dokazana je također bioptički tijekom petogodišnjeg praćenja. U svih 92 bolesnika kontinuirano su u serumu određivani biljezi hepatitis virusa B, D i C, kao i ANA i AMA, te je u svih isključena virusna kronična bolest jetre ili autoimuni hepatitis. Rezultati ispitivanja pokazali su da u alkoholičara prevladava ciroza jetre u 78,04 % slučajeva, ali da su teški oblici kroničnog hepatitisa, odnosno ciroza i karcinom jetre statistički značajno prisutni u nealkoholičara (p 0,05). Navedenim ispitivanjem iznađena je velika grupa od 51 bolesnika s progresivnim oboljenjima jetre kojima nije utvrđena etiologija oboljenja čime je postavljen ozbiljan zadatak istraživanja uzročnika njihove bolesti.