Metabolic Profile and the Histological Changes in Patients with Chronic Viral Hepatitis

Crăciun P[1], Oltean G[2], Georgescu D[3], Crăciun Lucia[4]

[1] Chronic Haemodialysis Center, Tîrgu Mureş
[2] County Emergency Clinical Hospital Tîrgu Mureş, Medical Clinic I
[3] County Emergency Clinical Hospital Tîrgu Mureş, Clinic of Gastroenterology I
[4] Sighişoara Municipal Hospital, Integrated Specialty Dispensary

Objective: To evaluate the incidence of steatosis and its correlation with lipidic profile changes comparing the patients with HVB to those with HVC.

Material and method: We enrolled a number of 87 patients who were diagnosed with viral hepatitits B and C between 2004–2008 in Medical Clinic I from Tîrgu Mureş, based on positive test results for HBs antigen and HCV antibody, on the presence of HCV-ARN and on histological features. To all patients it was performed hepatic biopsy and we determined cholesterol, triglyceride, glucose, ALT and AST blood levels.

Results: Steatosis had a higher incidence in patients with HCV infection. The steatosis is correlated with necroinflammation and fibrosis in patients with HVC. In the case of patients with HVB there was no correlation between the steatosis and the grade of fibrosis. The HVC group yielded lower mean values of cholesterol, triglycerides and glicemia than the HVB group. The values of the aminotransferases were increased in patients with hepatic steatosis in both groups.

Conclusions: Hepatic steatosis appears with a higher incidence in patients with HVC and it is correlated with the necroinflammatory and fibrosis scores. There is no correlation between the steatosis and fibrosis stage in HVB patients. Both in HVB and HVC the steatosis is correlated with high values of serum aminotransferases.

Keywords: B and C virus infection, steatosis, cholesterol, triglycerides

Introduction

The injury of hepatocytes in the course of a chronic infection with hepatic B virus (HBV) and hepatic C virus (HCV) follows different patterns. In HBV patients the lesion is most frequently immune mediated and it is due to the low production of free radicals, without the implication of the iron dependent hepatic metabolic system.

On the other hand, in patients with HCV infection, the lesions are very well correlated with the presence of micro- and macrovacuolar steatosis and with the activation of the glutation metabolism, which represents the physiological response to peroxidative injury [1,2].

Hepatic steatosis represents the fat loading of hepatocites and it appears most frequently in the form of macrovacuolar distrophy with lipidic vacuoles pushing the nuclei of hepatocytes to the periphery. In the case of viral hepatitis C the steatosis appears with a higher frequency and represents an important cofactor in the growth of necroinflammatory grade and also in the outcome of fibrosis [3].

In hepatitis B the clinical significance of hepatic steatosis is not completley clarified, because there are not enough trials that investigate the relationship between steatosis and hepatitis B, and how this influences the course of the disease [4].

The aim of this study is to evaluate the incidence of steatosis and its correlation with the changes of the lipidic profile, comparatively in patients with HBV and HCV hepatitis.

Material and method

The study included a number of 87 patients who were diagnosed with viral hepatitits B and C between 2004–2008 in Medical Clinic I from Tîrgu Mureş, based on the positive test results for HBs antigen and HCV antibody, on the presence of HCV-ARN and on histological features. We included patients with ages between 18 and 65 years and with an alcohol intake lower than 20 g/day.

We excluded patients with previous hepatotoxic drug consumption, those with congenital jaundice, autoimmune hepatic disease, or hepatic storage diseases with regular or excessive alcohol intake. The exclusion of patients with high alcohol intake was based on anamnesis, completion of the ESPAD questionnaire and gama glutamil transpeptidase (GGT) values.

After the patients signed an informed consent, we performed a hepatic biopsy in each patient. The obtained samples were fixed in 4% formaldehyde. The determination of necroinflammatory and fibrosis scores was made using the Knodell scoring system. Micro- and macrovacuolar steatosis changes were also observed and for each patient we determined cholesterol, triglycerides, glycemia, glutamic pyruvic transaminase (GPT) and glutamic oxalic transaminase (GOT) levels.

The total number of patients was divided in 2 groups: group 1 – 56 patients with HCV and group 2 – 31 patients with HBV. These two groups were divided in 2 subgroups by the presence or absence of steatosis on the histopatological examination.

Table I. The incidence of necroinflammation and fibrosis in pacients with HCV and HBV, with or without steatosis

	No. of patients	Mild necro-inflammation	Moderate necro-inflammation	Severe necro-inflammation	Mild fibrosis	Moderate fibrosis	Severe fibrosis
HCV with steatosis	39	10 (25.6%)	18 (46.1%)	11 (28.2%)	14 (35.8%)	17 (43.5%)	8 (20.5%)
HCV without steatosis	17	8 (47%)	7 (41.1%)	2 (11.7%)	6 (35.2%)	8 (47.0%)	3 (17.6%)
HBV with steatosis	9	2 (22.2%)	6 (66.6%)	1 (11.1%)	1 (11.1%)	7 (77.7%)	1 (11.1%)
HCV without steatosis	22	8 (36.3%)	12 (54.5%)	2 (9.0%)	3 (13.6%)	15 (68.1%)	4 (18.1%)

Table II. Mean values of cholesterol, triglyceride and glycemia in HVB and HCV patients

	HCV	HBV
Cholesterol	187.4±17.6	202.75±19.8
Triglycerides	97±14.77	101.5±22.26
Glycemia	101.6	102.6±6.86

Table III. Mean values of aminotranspherases in HCV and HBV patients, with or without steatosis

	HCV with steatosis	HCV without steatosis	HBV with steatosis	HCV without steatosis
GPT	119.42±11.83	63.17±10.56	114.83±16.48	80.94±12.01
GOT	82.53±7.84	49.62±6.94	95.66±13.8	50.54±8.3

Results

From the total number of patients included in the study 63.2% were female and 36.7% were male. In the HCV group 71.4% of the patients were female and 28.5% male, while in the HBV group 48.3% were female and 51.6% male. Analyzing the two groups we have found that in the HCV group 39 patients (69.6%) had steatosis, while only 13 patients (41.9%) had steatosis in the HBV group.

Analyzing the necroinflammatory score in the HCV group based on the presence or absence of steatosis, 25.6% of the patients had mild necroinflammation, 46.1% moderate necroinflammation and 28.2% severe necroinflammation, compared with patients without steatosis where severe necroinflammation was observed in a much smaller percentage – 11.7% (Table I).

In the HBV group we observed a higher percentage of patients with moderate necroinflammation in both subgroups. In the case of fibrosis we observed a low percentage of patients with severe fibrosis and hepatic steatosis, so we are not able to sustain a correlation between the two processes.

As far as serum lipid values are concerned, in the HCV group we obtained a mean value of 187.4±17.6 mg% for cholesterol and 97±14.77 mg% for triglycerides. In the HBV group the mean value of cholesterol was 202.75±19.8 mg% and the mean value of triglycerides 101.5±22.26 mg%. For glycemic values we obtained a mean value of 101.6±5.42 for the HCV group 102.6±6.86 in the HBV group (Table II).

The mean values of cholesterol, triglycerides and glicemia were lower in the HCV group than in the HBV group. The aminotransferares mean values were significantly reduced in patients with HCV without steatosis compared with patients with HCV and steatosis on the histological examination (Table III).

Discussions

According to some trials hepatic steatosis in HBV hepatitis is independently associated with high glycemia and it is not correlated with the grade of fibrosis [5].

In our study the steatosis was significantly more frequent in chronic hepatitis C cases. In different trials the reported incidence of steatosis in patients with HCV may be between 50–80% depending on the features of the studied population, on the incidence of diabetus mellitus and obesity. If the risk factors are excluded, the incidence of steatosis is around 40%. This suggests that hepatitis C virus may be the a direct cause of steatosis [6].

We encountered severe necroinflammation and fibrosis in a higher proportion of patients with HCV and steatosis, which means steatosis can represent an aggravating factor of hepatic injury. The effect of steatosis on the histological changes in HBV patients is not completely understood. Steatosis in chronic hepatitis B virus infection is associated with the host metabolic factors and is not associated with the intensity of the histological lesions [7]. Comparing the mean value of serum lipids we have obtained lower values in HCV patients compared with HBV patients. This could be due to the pathophysiology of the HCV infection. The hepatitis virus C may induce steatosis through 3 ways: impaired lipoproteic secretion, impaired lipid degeneration and increased lipogenesis [8].

Conclusions

1. Hepatic steatosis appears with a higher incidence in patients with HCV compared with HBV.
2. In HCV the steatosis is correlated with the necroinflammatory and fibrosis scores, representing an aggravating factor of the hepatic injury.
3. It can't be sustained there is a correlation between steatosis and the stage of fibrosis in HBV patients.
4. Both in HBV and HCV the steatosis is correlated with high values of serum aminotranspherases.
5. HCV patients have lower serum cholesterol and triglyceride values compared with HBV patients, probably due to the direct effect of the hepatitis C virus.

References

1. Hu KQ, Kyulo NL, Esrailian E, Thompson K, Chase R, Hillebrand DJ, Runyon BA – Overweight and obesity, hepatic steatosis, and progression

of chronic hepatitis C: a retrospective study on a large cohort of patients in the United States, J Hepatol. 2004 Jan; 40(1): 147–54

2. Hu SX, Kyulo NL, Xia VW, Hillebrand DJ, Hu KQ – Factors associated with hepatic fibrosis in patients with chronic hepatitis C: a retrospective study of a large cohort of U.S. patients, J Clin Gastroenterol. 2009 Sep; 43(8): 758–64
3. Szanto P, Grigorescu M, Dumitru I, Serban A – Steatosis in hepatitis C virus infection. Response to anti-viral therapy. J Gastrointestin Liver Dis 2006; 15 (2): 117–24
4. Peng D, Han Y, Ding H, Wei L – Hepatic steatosis in chronic hepatitis B patients is associated with metabolic factors more than viral factors: J Gastroenterol Hepatol. 2008 Jul; 23(7 Pt 1): 1082–8
5. Tsochatzis E, Papatheodoridis GV, Manesis EK, Chrysanthos N, Kafiri G, Archimandritis AJ – Hepatic steatosis in chronic hepatitis B develops due to host metabolic factors: a comparative approach with genotype 1 chronic hepatitis C: Dig Liver Dis, 2007, 39(10): 936–942
6. Negro F – Mechanisms and significance of liver steatosis in hepatitis C virus infection: World J Gastroenterol, 2006, 12(42): 6756–6765
7. Thomopoulos KC, Arvaniti V, Tsamantas AC, DImitropoulou D, Gogos CA, Siagris D, Theocharis GJ, Labropoulou-Karatza C – Prevalence of liver steatosis in patients with chronic hepatitis B: a study of associated factors and relationship with fibrosis: Eur J Gastroenterol Hepatol, 2006, 18(3): 233–237
8. Popescu CI, Dubuisson J – Role of lipid metabolism in hepatitis C virus assembly and entry: Biol. Cell (2010) 102, 63–74