

The changes of plasma lipoproteins in patients with viral hepatitis

Yavuz BAYKAL¹, Bayram KOÇ¹, Gülsüm ÖZET², Refis MAS¹, Üçler KISA¹,
Murat ŞALK¹, Mustafa YILMAZ¹, Tahir ÜNAL¹, Fikri KOCABALKAN¹

Dept. of, internal Medicine, Gülhane Military Medical School, Dept. of internal Medicine, Numune Hospital, Ankara, TURKEY

We investigated the changes in plasma cholesterol, triglyceride, LDL-Cholesterol (LDL-C), VLDL-Cholesterol (VLDL-C), HDL-Cholesterol (HDL-C) levels in the patients with Hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, chronic active hepatitis, or chronic persistent hepatitis. In addition, we investigated the change in plasma Apo-A1 and Apo-B in 30 patients with chronic active hepatitis. Thirty patients with HBV infection, 14 patients with HCV infection, 44 patients with chronic active hepatitis, 13 patients with chronic persistent hepatitis and 34 controls with matching ages and sexes enrolled the study. Age range was 25-34 years. As a result, we have determined a decrease in the levels of total cholesterol, LDL-C, VLDL-C, triglycerides, and increase in HDL-C levels in all the patient groups. Additionally, Apo-A1 and Apo-B levels were decreased in patients with chronic active hepatitis [Turk J Med Res 1996; 14(3): 106-109]

Keywords: Viral hepatitis, Lipoproteins, Triglycerides, Apo- lipoproteins, Chronic active hepatitis, Chronic persistent hepatitis, Cholesterol

The apoprotein component of the lipoproteins has an important role in the transportation of cholesterol, phospholipids and triglycerides in blood. The amount, composition and synthesis of plasma lipoproteins are influenced by various factors in hepatic diseases (1). Hepatocellular diseases are with increases in both triglycerides and LDL-cholesterol levels which is more prominent in the latter.

The insufficiency in the synthesis of apoproteins can cause defects in hepatic clearances of VLDL and triglycerides (2).

Some studies have reported apolipoproteins and LDL receptors are suppressed in hepatic diseases and increased in the number in the case of regeneration (3). There are several studies focused on the changes in lipid profiles in hepatic diseases. Some studies report cholesterol and phospholipids are metabolized in different ways (2). It was also reported that apoprotein H

and annexin V on the surface of hepatocyte may have role on the onset of infection by facilitating the binding of 5 protein of HBsAg to the membrane of hepatocyte (4).

A patient, we have followed up from ischemic heart disease, had stenosis of 80 percent or more in right coronary artery screened by angiography. Stenosis was regressed to 30% by angioplasty. The patient who had been negative for HBsAg before angioplasty was found to be positive for HBsAg 3 months after angioplasty. Control angiography that was performed one year later showed near-total opening in stenotic lumen and better laminated surfaces in the distal parts of it. This inspired us to study the lipid fractions of serum in patients with hepatitis to see whether the changes in patients with viral hepatitis have anti-atherogenic effects.

MATERIALS AND METHODS

One hundred one patients, 30 with hepatitis B infection (18 males, 12 females), 14 with hepatitis C (8 males, 6 females), 44 with chronic active hepatitis (25 males, 19 females), 13 with chronic persistent hepatitis were included in the study.

Received: Jan. 16,1996

Accepted: May. 11,1996

Correspondence: Yavuz BAYKAL

Dept. of Int. Med., Gulhane Mili. Med. School
Ankara, TURKEY

Thirtyfour people with matching ages sexes weight were taken as controls. Patients with any disease which might affect the results were excluded from the study.

Fasting blood samples were obtained from the patients and kept at-27°C in deep freeze after extraction of plasm.

Diagnosis of HBV infection and HCV infection were based on anti HCV IgM positivity, anti HBCAg IgM positivity, HBsAg positivity and high levels of ALT. Diagnosis of chronic active hepatitis and chronic persistent hepatitis were based on the histopathologic examination of the needle biopsy of liver.

Levels of cholesterol and triglycerides were determined by enzymatic methods and that of HDL-cholesterol by heparine-Manganese chloride sedimentation method defined by Berstein and Samaille. Level of LDL-cholesterol was estimated by the formula of LDL-cholesterol = total cholesterol- (HDL+VLDL), and VLDL by the division of triglycerides level by five.

po-A1 and Apo-B levels were determined by nephelometric immunoassay with Behring Nephelometer 100 apparatus.

The results were analyzed by Student's t-test and Mann Whitney U test.

RESULTS

There was no significant difference between patient and control groups in comparison of their ages, sexes and weight. Mean values of data for both groups are shown in Table 1.

Cholesterol levels were lower in patient groups, notably in chronic active hepatitis (CAH) patients, than that of control group. Triglyceride levels also tended to be lower in patients groups.

HDL-cholesterol levels were increased in all the patient groups, especially in the group of patients with HCV infection.

Table1. The mean values of data for both control and patients groups (mg/dl).

Parameters	Control (n:34)	HBV Inf. (n:30)	HCV Inf. (n:14)	CPH (n:13)	CAH (n:44)
Age	34.42±12.58	32.19±14.40	35.62±11.95	34.83±13.45	36.41 ±12.31
Weight	67.19±19.73	62.41±18.11	66.90±16.23	69.18±15.71	61.93±17.73
Cholesterol	208.11 ±31.00	190.16±54.00	203±54	192.80±39.00	181.08±33.60
Triglycerides	190.02±84.00	155.83±83.00	163.46±83.6	126.1±50.4	102.55±41.10
HDL	37.55±6.40	40.66±11.10	49.4±5.2	38.6±4.9	45.17±1.00
LDL	138.4±27.4	119.33±58.60	122.6±54.6	133.5±39.3	115.42±34.40
VLDL	38.4±17.4	31.08±16.00	32.6±17	25.2±15.3	20.4±8.1

HBV: hepatitis B virus, HCV: hepatitis C virus, CPH: Chronic (Persistent hepatitis, CAH: chronic active hepatitis

Table2. The mean values chronic active hepatitis and control groups (mg/dl).

Parameters	CAH group (n=30)	Control Group (n=34)	
Cholesterol	183.08±33.60	208.11 ±53.40	p>0.08
Triglycerides	102.55±41.10	190.02±84.00	p<0.001
HDL-Cholesterol	47.37±10.41	37.55±6.40	p<0.001
LDL-Cholesterol	112.64±33.90	138.52±27.40	p<0.005
VLDL-Cholesterol	20.6±8.2	38.4±7.4	p<0.001
Apo-A1	76.92±37.40	146.32±17.40	p<0.001
Apo-B	82.96±35.00	138.5±27.3	p<0.001

CAH: chronic active hepatitis

LDL-cholesterol levels were decreased in all the patient groups especially in CAH patients.

Though cholesterol and triglyceride levels decreased lesser in CAH patients than chronic persistent hepatitis (CPH) patients, it was not significant ($p>0.05$). HDL increased higher ($p<0.05$) and LDL decreased lower ($p<0.005$) in CAH patients cholesterol and triglycerides levels lower in HBV group compared to the HCV group ($p>0.5$). HDL levels, though not significant, were higher in HCV group and LDL was lower in HBV group ($p>0.05$).

Cholesterol levels were lower in CAH group compared to that of group with HCV infection ($p>0.05$). The decrease was more significant in triglycerides ($p<0.01$). HDL was insignificantly higher in HCV group ($p>0.1$), and LDL insignificantly lower in CAH group ($p>0.5$).

Comparison of CAH group with group with HBV infection disclosed lower cholesterol levels in CAH group ($p<0.05$) along with a more significant decrease in triglycerides ($p<0.005$). HDL increase was significantly higher in HBV group in ($p<0.05$) and LDL was significantly lower in CAH group ($p>0.5$).

Both cholesterol and triglycerides were lower in CPH group than that of group infected by HCV ($p>0.1$). HDL was higher ($p<0.005$) and LDL was lower in group with HCV infection ($p>0.1$).

Cholesterol levels were similar in CPH group and group with HBV infection. Triglycerides were lower in CPH group ($p<0.05$). HDL cholesterol was higher ($p<0.05$) and LDL was insignificantly lower in HBV group ($p>0.5$).

Apo-A1 and Apo-B levels of controls and CAH group, which was determined in only 30 patients with CAH, are shown in Table 2. Mean value for apo-A1 was 76.92 ± 37.4 in CAH group and 146.32 ± 17.4 in control group ($p<0.001$). Mean value for apo-B was 89.96 ± 35 in CAH group and 138.5 ± 27.3 in control group.

DISCUSSION

Liver has an important role in the metabolism of lipids. The amount, composition and structure of plasma lipoproteins vary depending on various factors in liver diseases. Decreases in HDL and VLDL levels depending on the decrease in the activity of plasma lecithin cholesterol acyl transferase (LCAT) in acute and chronic hepatic diseases and increased in levels of LDL and triglycerides were reported (1). B lipoproteins

that bind to viral particles may facilitate the viral infection of hepatocytes by behaving as if the LDL receptors were ligands for hepatocytes (5).

Goal et al. reported that they determined the triglyceride levels to be increased in patients with viral hepatitis and following the recovery the levels decreased to the normal levels (6). They determined LDL cholesterol level to be increased, VLDL level to be decreased and no significant change in cholesterol level. They suggested the decrease in HDL might be a prognostic criterion in patients with viral hepatitis. Carre et al. determined the levels of apoprotein B and plasma cholesterol decrease in patients with chronic viral hepatitis (7).

We determined decreases in cholesterol, triglycerides, LDL, VLDL, apo-A1 and apo-B levels and increase in HDL levels in patients with CAH in our study.

Kryška et al, determined significant decreases in HDL-cholesterol levels in patients with chronic active hepatitis (8). On the other hand, we determined significant increase in HDL levels. Ahaneku et al determined cholesterol levels to be decreased in patients with viral hepatitis and Zuberi et al determined the reverse that is increased levels of cholesterol (9). Taylor et al did not find any significant change in cholesterol levels (10).

Camps et al. reported considerable increases in the levels of apo-CIII in patients with hepatitis and decreases in the levels of apo-A1 and apo-B in patients with cirrhosis (11). Chen et al, determined in carriers of chronic hepatitis that that levels returned back normal when the patients recovered (12). We determined decreases in the levels of Apo-A1 and Apo-B in the current study.

In evaluation of the changes in lipid fraction as a whole, we see a general trend to decrease in atherogenic fractions (total cholesterol, LDL-Cholesterol, apo-A1 and apo-B) and to increase in anti-atherogenic fractions (total cholesterol, apo-A1 and apo-B) and to increase in anti-atherogenic fractions (HDL-cholesterol). When we consider those changes in lipid fractions and the case we present in the third paragraph together, we noticed a probable antiatherogenic quality of hepatitis viruses.

We could not find any reports about lipid fractions and apoproteins in hepatitis patients divided into four different groups just as we have done. Therefore a complete comparison was impossible. Besides that, we did not find any reports demonstrating the anti-atherogenicity that we disclosed.

As a result, significant changes in the lipid fractions of patients with hepatitis occur. These changes may not be explained by the defects in lecithin metabolism, decrease in LCAT activity, defects in the level of membrane receptors or the changes in hepatic synthesis metabolism well enough. However, there is no reports in literature demonstrating that hepatitis virus has such an effect. If it really has what is the mechanism?

If HBV has an ant-iatherogenic effect, is it possible to determine a new strategy for the treatment of ischemic heart disease based on virus antigens? We wish to notice such a possibility in our study.

Hepatitji hastaların serum lipidlerinde meydana gelen değışiklikler

Bu çalışmamızda, Hepatit B, Heatit C virüs enfeksiyonu, kronik aktif hepatit (KAH) ve kronik persistan hepatit (KAH) vakalarında plazma total kolesterol, trigliserid, LDL-kolesterol, Apo-A1 ve Apo-B değışikliklerini inceledik. Çalışma yaş ve ağırlık bakımından uygun 34 kontrol vakası ile 30 HBV enfeksiyonu, 14 HCV enfeksiyonu, 44 KAH'li, 13 KPH'li hasta da yapıldı. Sonuç olarak bütün hasta gruplarında, kontrol grubuna göre total kolesterol, trigliserid, LDL-kolesterol ve VLDL-kolesterol düzeylerinde azalma, HDL-kolesterol düzeylerinde yükselme tespit ettik. Ayrıca KAH'li hastalarda kontrol grubuna göre Apo-A1 ve Apo-B düzeylerinde azalma mevcuttu. fTurk J Med Res 1996; 14(3): 106-109]

REFERENCES

1. Sherlock S. Diseases of the Liver and Biliary System. Ninth Edition 1993; 24-5.
2. Ahaneku JE, Olubuyde ID, Agbedan GD, et al. Changes in plasma high density lipoprotein cholesterol and phospholipid in acute viral hepatitis Int Med 1991;229:17-21.
3. Fukishim N, Yamamoto K, Osaki I, et al. Apolipoprotein A-1, E, CIII and LDL receptor mRNA expression in liver diseases. Nippon-Rinsho 1993; 51 (2): 407-13.
4. Neurath AR, Strick N. The putative cell receptors for hepatitis B Virus, Annexin V, and Apolipoprotein H, Bind to lipid Components of HBV. Virology 1994:204; 475-7.
5. Kodama T, Reddy P, Kishimoto C, et al. Purification and characterization of a bovine acetyl LDL receptor. Proc Natl Acad. Sei, 1988:85: 9238-42.
6. Goal VK, Mehrotra TN, Srivastave SS, et al. Observation of lipid profile and lipoproteins in viral hepatitis and hepatic coma. J Assos Physic 1993; 41(10): 651-2.
7. Carre D, Boucher E, Tuzlin B, et al. Decrease of cholesterolemia and apolipoprotein B in chronic viral hepatitis C with masive steatosis. Gastroenteral Clin Biol 1994; 18 (10): 899-900.
8. Kryska A, Jusaczyk J, Berszynska I, et al. Evaluvation of lipid metabolism in patient with chronic active hepatitis Pol-yg-lek 1991; 46(8); 159-60.
9. Zuberi SJ, Hussain SS. Lipid pattern in liver disease. J Med Assoc 1982; 32:275-8.
10. Taylor GOL, Bamgboya AE. Serum cholesterol and disease in Nigerians. Am J Clin Nutr 1979; 32:2540-5.
11. Camps J, Pizarro I, Prts E. Plasma lipopretin alterations in patients with chronic hepatocellular liver disease resulting from alcohol abuse. J Hepatol 1994; 21(5):- 704-9.
12. Chen Z, Keech A, Collins R, et al. Prolonged infection with hepatitis B virus and association between low blood cholesterol concentrations. BMJ 1993; 306:390-4.