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Serum cholinesterase activity in viral hepatitis

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Abstract: Serum cholinesterase (CHE) activity was assessed in a group of patients with different types of viral hepatitis. Serum samples from 120 patients with such a diagnosis (37 with hepatitis A, 48 with hepatitis B and 35 with hepatitis C virus infection) were analysed. As compared to 66 serum samples from uninfected controls, the hepatitis C virus-infected patients showed significantly higher CHE activity ($p < 0.001$), whereas diminished activity was detected in patients with either hepatitis A or hepatitis B virus infection ($p < 0.001$ for both groups). There was a correlation between CHE activity and other serum viral markers. The significance of this variation in CHE activity among different viral hepatitis infections should be established.

Introduction: Viral hepatitis represents a worldwide health problem that is caused by at least five different viruses [1]. Clinically, the disease is characterised by impaired liver function, which can be monitored by changes in the activity of liver enzymes, such as the aminotransferases, and in the levels of other liver proteins, mainly albumin. These viral infections comprise a wide range of acute and chronic liver diseases, each with a characteristic biochemical and virological profile [1,2].

Serum cholinesterase (EC 3.1.1.8) has been associated with liver disease, cancer and lipoprotein metabolism as well as exposure to organophosphates [3]. The measurement of serum cholinesterase activity in the diagnosis and/or management of hepatic disease is controversial and varies extensively in different countries. Several authors have found useful the addition of CHE measurement in the monitoring of viral hepatitis [4] whereas others have not found any significant contribution of the enzyme to disease evaluation [3].

In the present report we describe the patterns of serum CHE activity in a group of patients with different types of viral hepatitis, and evaluate its correlation with other viral markers.

Patients and methods: A group of 120 patients with diagnosis of viral hepatitis infection was selected for this study. They were divided into 37 individuals infected with hepatitis A virus (HAV), 48 with hepatitis B virus (HBV) and 35 with hepatitis C virus (HCV). Serum from 66 individuals with no evidence of viral infection or liver disease were used as controls.

Viral markers screening in the selected population was assessed using standard assays. These tests included markers for HAV infection (IgM anti-HAV, Hepanostika, Organon Teknika, Turnhout, Belgium), HBV infection (IgM or IgG anti-HBcAg, anti-HBsAg, anti-HBeAg, HBsAg and HBeAg, Hepanostika, Organon Teknika, Turnhout, Belgium) and HCV infection (anti-HCV, third generation, Ortho Diagnostics, Neckkargemünd, Germany). Additionally, HBV-DNA and HCV-RNA detection in serum samples was evaluated by PCR following the methods of Kaneko *et al.* [5] and Inchauspe *et al.* [6] respectively.

We excluded any patient with other unrelated viral infections, liver failure or other chronic diseases (such as diabetes, renal disorders and cardiopathies).

Cholinesterase was measured using a kit from the Sigma Chemical Company (St Louis, MO, USA) according to the method of Rappaport and coworkers [7]. A standard curve using acetic acid was used to calculate the units (Rappaport units mL^{-1}) of cholinesterase detected in the samples.

The results were compared using paired Student's *t*-test, and ANOVA analysis.

Results: Table 1 shows the percentage of positiveness of the different viral markers in the population studied. 100% of HAV-infected patients were positive for IgM anti-HAV. A high prevalence of IgG anti-HBcAg, HBsAg, HBeAg and HBV-DNA was detected in the HBV-infected population. 27% of these patients were simultaneously positive for HBsAg, HBeAg and HBV-DNA. 91% of HCV-infected individuals were positive for HCV-RNA.

Figure 1 shows the serum cholinesterase levels of the population studied. As compared to uninfected controls, significantly higher CHE activity was observed in the group of patients infected with the hepatitis C virus ($p < 0.001$) whereas those patients infected with either hepatitis A or hepatitis B virus had diminished activity of this enzyme ($p < 0.001$ for both groups).

In the HBV-infected population, a higher CHE activity was found in those patients who were positive for HBV DNA in serum (mean ± SD, 38.32 ± 14.96 for HBV DNA positive patients *vs* 26.81 ± 13.72 for HBV DNA negative patients, $p < 0.02$). Although only two HCV infected patients were negative for HCV RNA in serum, their levels of CHE did not differ significantly from those in patients

Table 1: Viral markers in a group of individuals with a diagnosis of hepatitis A, B or C

Viral marker	% positiveness		
	Hepatitis A	Hepatitis B	Hepatitis C
IgM anti-HAV	100		
IgM anti-HBcAg		8	
IgG anti-HBcAg		46	
IgG anti-HBsAg		16	
IgG anti-HBeAg		19	
HBsAg		35	
HBeAg		27	
HBV-DNA		27	
IgG anti-HCV			100
HCV-RNA			91
No. patients	37	48	35

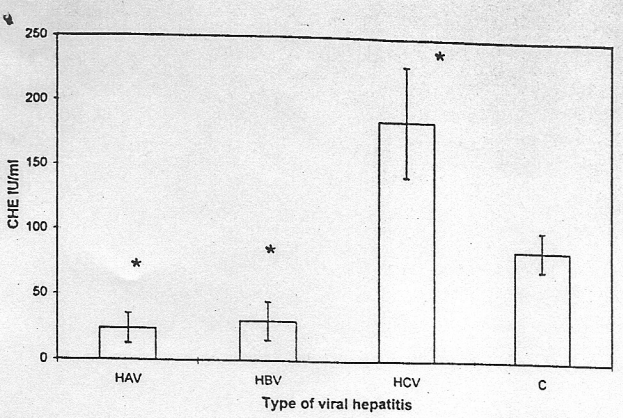

*Figure 1: Serum cholinesterase levels in individuals with hepatitis A virus (HAV), hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, and in uninfected controls (C). *As compared with controls, $p < 0.001$.*

positive for this viral marker. There was no correlation between CHE activity and other serum viral markers in any group of patients examined.

Discussion: Cholinesterase is an enzyme that has been widely implicated in different hepatic disturbances. Its use as a biochemical marker for the diagnosis and management of hepatic diseases remains controversial [3]. Thus serum CHE levels has been used extensively in Germany, Italy and Japan whereas in North America and other countries it is not considered a useful clinical marker [3,4].

In the present study, we evaluated serum CHE activity in a group of individuals with a diagnosis of viral hepatitis A, B or C. We found significantly higher CHE activity in HCV-infected patients as compared with controls whereas patients with HAV or HBV infection had a lower activity. Like other liver enzymes, CHE levels may be modified by the degree of inflammatory activity and hepatocyte damage as a consequence of viral infection. In this sense, low CHE activities have been reported in different stages of viral hepatitis and this seems to correlate with the degree of hepatic injury [8]. For instance, in HBV infection progression from chronic disease to liver cirrhosis is accompanied by a decline in CHE levels and enzyme activity [8].

Viral replication could also condition liver function and liver enzyme activities [9]. Our results show a higher CHE activity in HBV-infected patients positive for HBV DNA as compared to those patients negative for this viral marker. This difference was not seen in the HCV-infected group since 92% of the serum samples examined were positive for HCV RNA.

Raised serum CHE activity in the HCV-infected group may reflect a clinical and histopathological condition, characteristic of this type of patient, which differs from other viral hepatitis infections. This issue needs further evaluation in order to clarify the value of measuring CHE activity as a diagnostic and management tool for this viral infection.

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