

Association of Caffeine Clearance with Serum AST/ALT Ratio in Chronic Liver Disease

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Background: Serum AST/ALT ratio more than one (>1) was seen to be the first manifestation of cirrhosis in chronic liver disease. It was considered to be due to increased serum AST level by its release from the mitochondria of massive number of necrosed liver cells with a simultaneous decrease in serum ALT level due to decreased production by reduced number of living hepatocytes. It increases with increasing degree of fibrosis. Caffeine clearance test measures the hepatic microsomal function quantitatively. The aim of the present study was to find a correlation between caffeine clearance and AST/ALT ratio in patients of cirrhosis to prove the efficacy of caffeine clearance test to measure the extent of liver fibrosis.

Methods: Forty (40) hospitalized patients of chronic liver disease were included in this study. According to Child Pugh scoring, twenty-seven (27) patients belonged to Child class A and thirteen (13) to Child class B. A baseline blood sample was drawn after an overnight fast immediately followed by oral administration of 200 mg caffeine. Three more blood samples were drawn after three hours intervals. Caffeine concentration was measured by High Performance Liquid Chromatography (HPLC). 6 hours and 9 hours samples were used to measure caffeine clearance. Serum AST and ALT were measured by commercially available kits.

Results: Pearson correlation test was used to establish the relationship between caffeine clearance and AST/ALT ratio. A definite negative association was found.

Conclusion: Caffeine clearance test may be used to measure the functional capacity of liver in patients of liver cirrhosis.

Key words: Caffeine clearance, AST/ALT ratio, liver cirrhosis.

Introduction

Cirrhosis refers to a disorder of the liver in which normal cells are permanently damaged and replaced by scar tissue. This causes distortion of the normal structure of liver and blocking of normal blood flow through the organ resulting in the failure of the liver to perform many of its usual functions.¹ It is an irreversible sequel to a number of disorders like vascular, metabolic, autoimmune, viral hepatitis, drugs and toxins, excessive ethanol consumption and crypto-genic.² Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) are hepatic intracellular enzymes. Serum elevation of both of these enzymes reflects leakage from injured hepatocyte and consider to be a sensitive indicator of liver injury.³ The AST/ ALT ratio is more frequently 1 or higher in cirrhotic patients. Progressive liver functional impairment is reflected by an increase in the AST/ALT ratio.⁴

In addition to the conventional liver function test another biochemical approach to assess liver function is to monitor its clearance capacity.⁵ A substance is injected or ingested orally and its clearance from the blood is measured after specified intervals. The key determinant which allows hepatic clearance is a functional portion of hepatocytes and

blood hepatic exchange which is significantly reduced in cirrhosis.^{6,7} Data from the past few years have shown that as caffeine metabolizes solely in the liver, caffeine clearance test may serve as a dynamic assessment of liver function.⁸⁻¹⁰

The object of this study was to find a correlation between caffeine clearance and AST/ALT ratio in patients of liver cirrhosis. So that caffeine clearance might be used to measure the liver function quantitatively.

Materials and Methods

Forty hospitalized, prediagnosed patients of liver cirrhosis were included in the study from the Services Hospital, Lahore. Baseline blood sample was drawn after an overnight fast. The patients were informed to abstain from caffeine containing drinks, food and medicines during the experiment. A capsule containing 200mg caffeine powder was administered orally just after taking the baseline sample. Three more samples were drawn after 3 hours, 6 hours, and 9 hours intervals. Serum ALT and serum AST were measured by Randox Kit (Cat No. 485) and Cat No. AS 483 through UV method according to the recommendation of the Deutsche Gesellschaft for klinische chemie.

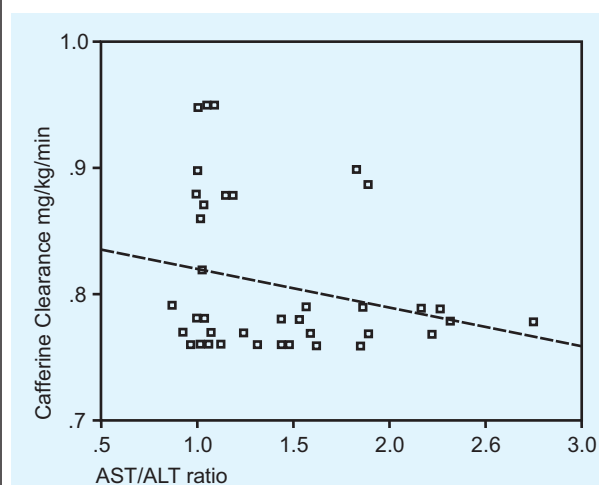


Fig. 1: A graph between caffeine clearance and AST/ALT ratio in patients of liver cirrhosis.

reverse phase chromatography on Sykam HPLC-Pump 1122. Chromatogram was obtained on LC-6A chromatograph by UV method.

Results

The mean value of AST/ALT ratio was found to be 1.40 ± 0.47 U/L whereas mean caffeine clearance was 0.81 ± 0.06 ml/kg/min. By the application of Pearson correlation test a definite negative association was found between the two values ($r = -0.226$, $p = 0.08$) which is significant at 90% confidence limit though not significant or near to significant at 95% confidence limit. It is suggested that more studies should be conducted to narrow down the likely range of values of the correlation. The graph (Fig-1) between the two values clearly shows that the caffeine clearance decreases with increasing AST/ALT ratio. This is a clear indication that with increasing fibrosis the clearance capacity of liver decreases.

Discussion

When necrosis of hepatic cells occurs, considerable amount of mitochondrial AST is also released and the AST/ALT ratio which normally is less than unity becomes equal to or more than one.¹¹ The mean AST/ALT ratio in cirrhotic patients was seen to be significantly higher than non cirrhotic patients ($p < 0.001$) and a ratio of >1 had 100% specificity and positive predictive value in distinguishing cirrhotics from non cirrhotic patients.¹² AST/ALT ratio >1 was seen to be the first manifestation of cirrhosis.¹³ It was also mentioned that AST/ALT ratio increased with increasing score of cirrhosis. This appeared to be due to reduction of ALT production with increasing damage to the liver.¹⁴

The present study has shown an inverse relationship between AST/ALT ratio and caffeine clearance in cirrhotic patients which indicates that liver clearance decreases with increasing degree of fibrosis. So the caffeine clearance test may be used to measure the metabolizing capacity of the liver quantitatively.

It was demonstrated in a number of studies that there is an inverse relationship between caffeine clearance and the degree of fibrosis in liver cirrhosis.¹⁵⁻¹⁶

Conclusion

Caffeine clearance measures the functional capacity of liver because it decreases with increasing ratio of AST/ALT, and indicator of hepatic fibrosis. So caffeine clearance test may be used as a quantitative test for the measurement of liver function in liver cirrhosis.

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Picture Quiz

What is the Diagnosis?



Answer on page 30