

Synergistic effect of alcohol and antiretroviral drugs on hepatic function

N.M. IGBOH¹, D. ONWUBIKO¹, E.N. AGOMUO²,
I. ONYESOM⁴, C.A. MADUAGWUNAL³ and U.E. UZUEGBU⁴

¹College of Medicine and Health Sciences, Abia State University, Uturu (Nigeria).

²Department of Biochemistry, Faculty of Science, Imo State University, Owerri (Nigeria).

³Department of Pharmacology, College of Medicine, Abia State University, Uturu (Nigeria).

⁴Department of Medical Biochemistry, Delta State University, Abraka (Nigeria).

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ABSTRACT

No doubt, the introduction of highly active antiretroviral therapy (HAART) has led to a substantial reduction in morbidity in HIV/AIDS patients. Possible alcohol use by HIV-infected persons is not uncommon. This may lead to decreased antiretroviral adherence and increased susceptibility to liver disease. At present there is little information on the interactions between alcohol and antiretroviral drugs in HIV-infected patients and their impact on the liver in our locality. The aim of this study was to determine the effects of alcohol and retroviral drugs on the liver, by assessing the activities of serum enzymes and bilirubin level in HIV patients on high active antiretroviral therapy. Those on highly active antiretroviral therapy were placed in group I, while those who are on (HAART) and could not however stop their drinking habit and probably, take between 37 to 74 grams (< 40%) alcohol per day, were placed in group II. Blood samples were obtained from these HIV patients thirty HIV negative patients who served as control individuals. The biochemical parameters monitored were serum enzymes: aspartate transaminase (AST), Alanine transaminase (ALT), gamma glutamyl transferase (GGT), and alkaline phosphatase (ALP). Total bilirubin was also determined. The result showed a significant increase ($p < 0.05$) in the activity of AST among the group II patients (HIV patients on antiretroviral drugs and still take alcohol). The Activity of ALT and GGT were also high ($p < 0.05$) in this same group of patients when compared with those on antiretroviral alone (group I) or control group. However, serum total bilirubin level was in significantly highest in group II. Alcohol appears to worsen the degree of liver dysfunction induced by HAART. HIV/AIDS patients on antiretroviral drugs should be advised to discontinue the intake of alcohol.

Key words: Liver enzymes, Total bilirubin, HIV, AIDS, High active antiretroviral drugs.

INTRODUCTION

Reasonably, the introduction of highly active antiretroviral therapy (HAART) has led to a substantial reduction in morbidity in HIV/AIDS patients. The benefits of antiretroviral therapy for HIV infected people clearly outweigh the risks for not taking the drugs. Growing experience in the treatment of HIV/AIDS has led to the recognition that antiviral therapy may be lifelong, thus raising

concerns about side effects and long term safety. Antiretroviral hepatotoxicity may include lactic acidosis, hepatic steatosis and lipodystrophy. Should severe hepatotoxicity arise this may require interruption of therapy, thereby increasing the risk of viral breakthrough, (Igboh, 2005, Mbanaso and Akubugwo, 2007).

Mitochondrial toxicity is a serious side effect of nucleoside reverse transcriptase inhibitors

(NRTIs), the cornerstone of HAART. NRTIs can cause severe macrosteatosis, lactic acidosis, hepatic steatosis, and acute liver failure in HIV patients by impairing mitochondrial functions. NRTI mitochondrial toxicity manifests as mtDNA replication defects, mtDNA mutation and dysfunction. Oxidative stress (caused by increases in reactive oxygen species (ROS) consequent to HIV infection and NRTIs is another source of mitochondrial toxicity (Igboh, 2005).

Possible alcohol use by HIV-infected persons is not uncommon, and this may lead to decreased antiretroviral adherence, increased susceptibility to liver disease. Unfortunately, alcoholic liver disease (ALD), is a major complication of heavy alcohol consumption, and is characterized by earlier stages of fatty liver (steatosis) with variable rates of progression to fibrosis, cirrhosis, and end stage liver disease (Igboh and Braide, 2003, Igboh, *et al.*, 2006a, Igboh *et al.*, 2006b).

Alcohol is metabolized in the liver by cytochrome P450 enzyme. Metabolism of alcohol increases reactive oxygen species (ROS) production in mitochondria through complex of the electron transport chain leading to oxidative stress. Also, acute and chronic alcohol intake can affect the structure and function of mitochondria in humans or in animal. The increased ROS associated with alcohol metabolism may contribute to mitochondria dysfunction by modification of the mitochondrial DNA and proteins (Davies, 1995; Hensley *et al.*, 2000; Hemnani *et al.*, 1998).

At present there is little information on the interactions between alcohol and NRTIs in HIV-infected patients and their impact on the liver in our locality. It is in recognition of this fact that this study was conducted.

MATERIAL AND METHODS

Subjects and Collection of Blood Specimens: Fifty HIV-infected patients on highly active antiretroviral therapy (HAART) and those on highly active antiretroviral therapy (HAART) and alcohol 37-74g (<40%) alcohol/day were used for the study and they were placed on group I and II, respectively. Blood samples were obtained from the

HIV-infected patients in both groups, and HIV negative individuals (n=30) who served as control, individuals.

Assay Methods

Serum activities of AST and ALT were determined by enzymatic-colorimetric method (Reitmen and Frankel, 1956). ALP and GGT activities were respectively assayed by spectrophotometric methods previously described (Klein *et al.*, 1960; Teitz 1987). Total bilirubin was determined using diazo method described by Mac Donald (1965).

Statistical Method

The statistical analysis used was the one-way analysis of variance (ANOVA) and the degree of significance was set at 5% probability level.

RESULTS AND DISCUSSION

The results obtained from the investigation into the synergistic effect of HAART and alcohol in HIV seropositive patients are recorded on Table 1. The results showed significant increase ($P < 0.05$) in the activities of AST, ALT and GGT in HIV patients on HAART + alcohol when compared with those on HAART alone (group I) or control group. ALP activity was slightly reduced among group II patients (HAART alcohol) when compared with group I patients (HAART alone) but both were significantly different from control value ($P < 0.05$). The total bilirubin for the two groups of patients were significantly higher ($p < 0.05$) when compared with control level.

Marked elevation in these serum enzymes and bilirubin are indicative of liver disease. From this study, it can be observed that ALT was elevated. Elevation of ALT appears to reflect hepatic disease and it is more specific for hepatic disease than AST, because of the biochemical location of the enzymes. Though the activity of any of the enzymes (ALT or AST) may be elevated in extra hepatic disease. However, the elevation of AST and ALT along with the elevation of ALP activity may reflect some inflammatory disease or injury to the liver (Ayalogu *et al.*, 2001). In this study the maximum activity of ALP obtained was high. Thus, suggesting the possibility of hepatocellular damage. Similarly, the

Table 1: Changes in serum liver enzymes induced by HAART and alcohol in HIV positive patients.

	Changes in serum liver enzymes (U/L)				Total bilirubin (mg/dL)
	ALT	AST	ALP	GGT	
HIV negative individuals (control: n=30)	20.6±2.2	4.0.0±1.4	64.8±2.9	34.6±2.8	0.22±0.04
HIV positive patients	48.8 ± 9.8*	46.2±15.9*	94.4±1.6*	62.4±3.6*	0.29±0.06*
HIV positive patients (on HAART and alcohol: n=50)	70. 0 ± 2.8*	84.6±2.5*	90.8±1.4*	82.8±4.8	0.27±0.01*

* Significantly different ($P < 0.05$) when compared with control value HAART - Highly active antiretroviral therapy

high activity of GGT in patients on highly active antiretroviral therapy (HAART) and alcohol is not surprising considering that alcohol induces the enzyme resulting in high activity of the enzyme. Conversely, any damage to the hepatocytes cause the liver enzymes to be discharged into the serum. This will then manifest as increase in activities of such enzymes, as observed in patients particularly on highly active antiretroviral therapy (HAART) and alcohol. The present study agrees with the findings reported by Argiris, *et al.* (1999); Rodriguez-Rosado, *et al.* (1998); Hill *et al.* (2001).

Alcohol intake by HIV patients on HAART could potentiate the liver damage associated with HAART. HIV patients on HAART should be carefully monitored for signs and symptoms of hepatotoxicity and alcohol consumption by HIV patients on HAART should be strongly discouraged.

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