Research Article

Hepatic Dysfunction in Patients Infected with Human Immune Deficiency Virus

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ABSTRACT

To determine the incidence of hepatotoxicity in HIV sero positive and to investigate whether antiretroviral drugs could predispose HIV sero positive patients on antiretroviral drugs to hepatotoxicity.HIV patients were on antiretroviral drugs (triviro-LNS-Lamivudine, Nevirapine and Starvudine) 1-2 pills daily depending on the CD4 count. Moreso, have been on the drug for the duration of 2- 3 years. Blood samples were collected for the determination of clinical chemistry parameters such as liver enzymes (Les)-Lactate Dehydrogenase (LDH), Aspartate and Alanine Transaminases (AST and ALT) and Albumin (ALB). Sixty subjects were randomly selected and placed in three groups comprising 20 HIV infected patients who are not receiving antiretroviral drugs and group two twenty receiving antiretroviral drugs. Another twenty healthy non infected patients made up group 3 and these groups served as control, the patients are within Aba metro. The patients' blood was collected and the serum separated. It was subsequently used for the analysis. All analysis was based on colorimetric method.The results obtained were subjected to statistical analysis using one-way analysis of variance. The result of the study showed that those patients on antiretroviral drugs had remarkable increase in LDH and AST levels compared to those not on the antiretroviral drugs and HIV negative patients (control (U/L) LDH 184.00± 5.75 VS 546 ± 25.60. AST control (U/L) 24.7.± 4.6 VS 67.95 ± 10.5. P<0.05).

Key words: AIDS, albumin, aspartate transaminase, HIV, lactate dehydrogenase

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INTRODUCTION

Since AIDS was first recognized in 1981, it has led to nearly 30 million deaths as of 2009 [1]. Around half of people infected with HIV will develop AIDS within ten years if not treated. There is currently no cure or effective HIV vaccine. Treatment consists of high active antiretroviral therapy (HAART) which slows progression of the disease and as of 2010 more than 6.6 million people were taking them in low and middle income countries. Today, with high active anti-retroviral therapy (HAART). HIV is possibly turning to what could be a manageable chronic illness not a death sentence [2].

However, Antiretroviral therapy has been associated with the development of morphologic body-shape changes and metabolic abnormalities, including dislipemia, insulin resistance, and hyperlactatemia. Mitochondrial damage secondary to the use of nucleoside analogue reverse transcriptase inhibitors (NRTIs) has been related to some of these complications, although the role of different NRTIs in the development of complications

is not well established [3]. Other common symptoms include: diarrhea, and increased risk of cardiovascular disease [3-5].

Incidentally, the liver is the site where most drugs and other ingested substances are metabolized and detoxified [6]. Impairment of liver function usually results in decrease in albumin level. Measurement of so-called "liver enzymes" and albumin are utilized to distinguish the primary pathology in liver diseases. Blood plasma Aspartate transaminase (AST) is a sensitive but non-specific marker of hepatocyte leakage .Plasma alanine transaminase (ALT) is a fairly specific but less sensitive marker of hepatocyte leakage [6].

Also, lactate dehydrogenase (LDH) enzyme can be increased in liver disease, heart attack, anemia, muscle trauma, bone fractures, cancers, and infections such as meningitis, encephalitis. Many patients with infection by the HIV show an increase in the levels of the lactate dehydrogenase (LDH) enzyme. In most of these cases, such increase has been associated to the presence of pneumonia by Pneumocystis carinii [7, 8].

Hepatic events have emerged as a key issue in the management of HIV infected patients .At the beginning of the AIDS era, liver dysfunction in HIV infected patients only correspond with opportunistic infections [9]. The risk of developing hepatotoxicity involves a complex interplay between the chemical properties of the drug, environmental factors, like alcohol, age, sex, disease and genetic factors. The most extensively documented risk factors are concomitant drug use and disease like HIV [10, 11]. There is recent evidence for an increase in drug –induced liver disease among patients with HIV Hepatitis B Virus (HBV) and Hepatitis C Virus HBV (HCV) infection.HBV or HCV co-infection is frequent in HIV –infected patients because of similar routes of transmission [12]. Co-infection with viral hepatitis and or antiretroviral drugs used in the treatment of HIV infection has been associated with asymptomic elevations of AST and or ALT levels.

The diagnostic or management of these hepatitis may be difficult because of their intricacies of the pathogenic mechanism involved [9, 13].

Although, several studies have shown that liver mortality now represents 30-55% of all deaths in patients with HIV. Hepatotoxicity associated with drugs is part of this spectrum of liver disease and has the potential to affect the lives of individuals with HIV. This may suggest that HIV alone may not induce hepatotoxicity. However the use of antiretroviral drugs or co-infection with HBV or HCV may result in hepatotoxicity [3, 14, 15].

In order to assess the state of the liver in HIV infected patients and those on antiretroviral drugs, we measured the activity of the serum enzymes, Aspartate Transminase (AST), Alanine transaminase (ALT).Equally monitored were lactate dehydrogenase (LDH) and Albumin.

MATERIALS AND METHODS

The effect of HIV infection and antiretroviral drugs on Lactate Dehydrogenase (LDH), Aspartate Transminase (AST), Alanine transaminase (ALT) and Albumin Levels were assessed. Sixty subjects were randomly selected and placed in three groups comprising 20 HIV infected patients who are not on antiretroviral drugs and group 2, twenty receiving antiretroviral drugs .Another twenty healthy non infected patients made up group 3 and this served as control all within Aba in Abia State. HIV patients were on antiretroviral drugs (triviro-LNS-Lamivudine, Nevirapine and Starvudine) 1-2 pills daily depending on the CD4 count. Moreso, have been on the drug for the duration of 2- 3 years.

The patients' blood was collected and serum separated and used for the analysis. The Lactate Dehydrogenase, Aspartate and Alanine Transaminases Levels were determined using [16, 17] respectively. Albumin level was determined using Randox kit. All was based on colorimetric method. The results obtained were subjected to statistical analysis using one-way analysis of variance ANOVA [18].

RESULTS AND DISCUSSION

Table 1: Lactate Dehydrogenase, Aspartate and Alanine Transaminases and Albumin Levels in Patients Infected with Human Immune Deficiency Virus

Parameters	LDH(U/L)	AST(U/L)	ALT(U/L)	Albumin (g/l).
HIV Negative Subjects (control)	184.00 ± 5.75	24.70 +4.6	16.35 + 3.2	25± 9.0 5
HIV Positive Subjects not On drugs	530 ± 20.50*	45.10. ±6.3*	28.20 + 4.8*	10 ± 5.40*
HIV Positive Subjects On drugs	546 ± 25.60**	67.95. ±10.5**	42.35 + 5.2**	15 ± 6.60**

*Significant difference P <0.05.

The result of the study showed that those patients on antiretroviral drugs had remarkable increase in LDH, ALT and AST levels compared to those not on the antiretroviral drugs and HIV negative patients (control (U/L) LDH 184.00± 5.75 VS 546 ± 25.60. AST control (U/L) 24.7.± 4.6 VS 67.95 ± 10.5.
(P<0.05) (Table).However, there was a great reduction in albumin level in patients not on antiretroviral drugs. (Control (g/L) 25± 9.0 5 VS 10 ± 5.40. P<0.05)
In this study, the increase of these serum enzymes LDH, ALT and AST in HIV positive patients on antiretroviral therapy may be attributed to the effect of the drugs which is also in conformity with other studies [19, 20]. Equally, most of the antiretroviral therapy has been associated with mitochondrial damage. [3]. Also, It has been suggested that HIV patients have an increased lactate dehydrogenase (LDH) levels .However, in most of these cases, such increase has been associated to the presence of pneumonia by Pneumocystis carinii . The Lactate Dehydrogenase level may also increase in other lung infections and in a variety of extrapulmonary disorders [7,8].
Consersely, lactate dehydrogenase being an enzyme found in blood cells, destruction of the blood cells will cause its elevation.Again any effect on the hepatocytes will cause increase in the activity of the enzyme lactate dehydrogenase.

The reduction in albumin level in patients on and not on antiretroviral drugs could either be as a result of decrease in the synthetic function of the liver due to the effect of the antiretroviral drug or due to its utilization in the multiplication of the viral particles. Again, it could also be attributed to an increase in the production of pro-inflammatory cytokines — IL-1, IL-6, IL-8. These cytokines, are part of the innate immune response, which initiate the acute-phase response, leading to decrease in production of albumin .With result of this study, careful monitoring for signs and symptoms of hepatotoxicity is important in patients on antiretroviral drugs.

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REFERENCES

1. UNAIDS 'UNAIDS report on the global AIDS epidemic 2010.
2. Coovadia, H. "Antiretroviral agents—how best to protect infants from HIV and save their mothers from AIDS". N. Engl. J. Med. 2004. 351 (3): 289-292. PubMed.
3. Blanco F, García-Benayas T, José de la Cruz J, González-Lahoz J, Soriano V First-line therapy and mitochondrial damage: different nucleosides, different findings.HIV Clin Trials. 2003 Jan-Feb; 4(1):11-9.
4. Laeyendecker O, Li X, Arroyo M et al, The Effect of HIV Subtype on Rapid Disease Progression in Rakai, Uganda" 13th Conference on Retroviruses and

Opportunistic Infections (abstract no. 44LB). 2006.
5. Montessori, V., Press, N., Harris, M., Akagi, L., Montaner, J. S. "Adverse effects of antiretroviral therapy for HIV infection." CMAJ, 2004: 170 (2): 229-238. PubMed.
6. Ayalogu, E.O.; Igboh, N.M; Dede, E.B. Biochemical changes in the serum and liver of albino rats exposed to petroleum sample (gasoline, kerosene and petroleum) J. Apple.Sci. Environ. Mgt.: 2001. vol. 5(1) 97-100.
7. Quist; A. Ross Hill, Serum Lactate Dehydrogenase (LDH) in *Pneumocystis carinii* Pneumonia, Tuberculosis, and Bacterial Pneumonia Free *CHEST*.August; 1995; 108(2):415-.418. doi:10.1378/chest.108.2.415.
8. Valencia ME, Laguna F, Camacho J, Castejón A, Soriano V, Adrados M, González Lahoz J..Serum activity of the lactate dehydrogenase enzyme in patients with human immunodeficiency virus infection]. An Med Interna. 1994 Dec; 11(12):580-3.
9. Pol, S HIV infection and Hepatic enzyme abnormalities 2004: 565-572.
10. Deleve, L., and Kaplowitz, N. Prevention and therapy of drug induced hepatic injury. In: Wolfe.M. (ed)Philadephia WB Saunders, Harcourt Brace 2000: 334-348.
11. Zimmerman H.J. The spectrum of Hepatotoxicity in Zimmerman H.J ed .Hepatotoxicity 2nd ed Baltimore, M .D; Lippincott, Williams & W ilkins 1999: 128-130.
12. Denis F, Adide, C.C .Rogez S. et al, Seroprevalence of HBC, HCV, and HDV marker in 500 patients infected with the Human Immunodeficiency Virus.Pathol.Biol. 1997: 45:701-70.
13. Sulkwoski M.S, Thomas D.L, Chiasson, R.E.et al, Hepatotoxicity associated with antiretroviral therapy in adults infected with Human Immunodeficiency Virus and the role of Hepatitis C or B Virus infection JAMA 2000: 283:74-80.
14. Bica,I, McGovern,B ,Dhar,R . et al Increasing mortality due to endstage liver disease in patients with Human immunodeficiency Virus infection. Clin. Infect.Dis 2001: 32:492-497.
15. Davenport Dealing with drug side effects Project inform 2000: 4-5.
16. Henry, cannon and winkelman, Estimation of lactate Dehydrogenase .Clin.Chem. 1974.
17. Reitmen, S. and Frankel, S. Colormetic assay of Alanine and Aspartate aminotransferase. Amer J. Clin. Path 1956. 28, 56.
18. Obi, I. U.,.Statistical methods of detecting differences between treatments. Snapp press (Nig) Ltd. Enugu.: 1986; 2 – 45.
19. ..Argiris A., Mathur-Wagh U., Wilets I., Mildvan D. Abnormalities of serum amylase and lipase in HIV-positive patients. Am J. Gastroenterol 1999. 94:1248-52.
20. Rodriguez-Rosado R., Garcia-Samaniego J., Soriano V. Hepatotoxicity after introduction of highly active antiretroviral therapy. AIDS; 1998; 12:1256.