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Research article

ANTIOXIDANT STATUS AND LIPID PROFILE IN PATIENTS INFECTED WITH HUMAN IMMUNE DEFICIENCY VIRUS

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ABSTRACT: Antiretroviral therapy has been associated with the development of 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 their development is not well established. It was the aim of this study to assess the incidence of oxidative stress and dislipemia in HIV-infected patients who began highly active antiretroviral therapy (HAART). 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 .Biochemical parameters such as Ascorbic acid (Vit C), Cholesterol and Triglyceride were monitored. Seventy five (75) patients were used in this study comprising, 50 HIV positive individuals taking relevant antiretroviral therapy at least for three months. Thirteen HIV positive persons that have just received their sero status from voluntary counseling and testing center (VCT) and are yet to start drug and 12 apparent healthy HIV seronegative individuals served as control. The blood collected from the patients was centrifuged and serum used for the determination of cholesterol, triglyceride. Though serum for vitamin C determination was deproteinized and 2, 4- dinitrophenylhydrazine used for its determination. Results obtained were subjected to statistical analysis using student's test. Reduced concentrations of anti-oxidant vitamin C was found to be significantly decreased in HIV patients not on drugs when compared to control group, but level of triglyceride was drastically increased in HIV patients on drugs compared to HIV infected patients not on drugs($P<0.05$). In addition, the level of cholesterol was increased in the body of people with HIV not on drugs (178.38 mg/dl) when compared to the HIV positive patients on drugs (163.28 mg/dl) and control subjects (169.67 mg/dl). This was statistically significant ($P<0.05$). The study has shown that in HIV patient's free radical activity is relatively high hence the low level of vitamin C obtained in this study. Though, this was more pronounced in HIV patients on drugs. Furthermore hyperlipidemia (increased triglyceride level) was equally observed as a result of dual effect of HIV infection and antiretroviral drugs in HIV patients on antiretroviral drugs. Change in oxidative status was also associated with alteration in lipid profile. Incidentally lipid profiles are now mostly affected by use of antiretroviral therapy. The study has revealed that lipid profile parameters are slightly altered in HIV individuals taking antiretroviral drugs. Even though slight, this alteration may cause cardiovascular complication with time and need to be monitored regularly.

Key words: Lipid, antioxidant status, HIV, Ascorbic acid, Cholesterol and Triglyceride.

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INTRODUCTION

Africa is said to be the global epicenter of AIDS (Ellen and Elizabeth; 2002).According to UNAIDS 1999 report an estimated 83% of all the world AIDS death, since the time of the epidemic occurred in Africa and to the end of 1998 at least 34 million people living in Sub Saharan Africa had become infected with HIV, out of which 11.5 million have died already. In 1998 about 2 million Africans died from HIV/AIDS (Allen and Elizabeth; 2002). It is currently estimated that there are between 3.2 and 3.8 million persons living with HIV/AIDS in Nigeria and about 55-65% of which are females(Allen and Elizabeth;2002). HIV infection result in the release of pro-oxidant cytokines and other reactive oxygen species which lead to increase in utilization of 'Antoxidant' Vitamins such as C, E and A (Allen and Elizabeth; 2002) .Incidentally, Vitamin C increases the body's resistance to infection and acts as an antioxidant during stressful conditions (Baum et al, 1995, Lacey et al, 1996, Allen and Elizabeth; 2002). HIV infection affects the production of hormones such as Glucagon, epinephrine and cortisol, ultimately are involved in metabolism of carbohydrates', proteins and lipids. Elevation of these hormones contributes in weight loss and lipodystrophy (Allen and Elizabeth; 2002). The depletion of $CD4^+$ T–cells after HIV infection is due to cytopathic effect of the virus resulting from production of viral particles as well as death of infected cells which ultimately leads to AIDS(Baker and Wood ,1992 ,Treitinger; et al, 2000 , Andrea and Angela; 2006). HIV infection has much effect on the immune system. Once person is infected the immune system is stimulated. The stimulation of the immune system causes an increase in free radical production, as a result of increase in phagocytosis. Antioxidants neutralize the free radicals. Constant stimulation of the immune system can upset the balance between free radicals and antioxidants. Immune cells produce superoxide radicals and mobilize other reactive oxygen species (ROS) to destroy bacteria, viruses and other foreign matter. On the surface of phagocytes is a dormant enzyme that produces O_2• (superoxide radical) once phagocytosis occurs. The phagocyte consumes a lot of oxygen in a "respiratory burst" that precedes the O_2• production. Antioxidants protect the body from the damaging effects of free radicals. There are two types of antioxidants: antioxidant enzymes and nonenzymatic dietary antioxidants. Superoxide dismutase (SOD) is an enzyme able to convert superoxide radicals into the less-toxic hydrogen peroxide. SOD requires mineral cofactors to function; either manganese or copper and zinc. Other enzymes catalase and glutathione peroxidase—then convert the hydrogen peroxide into oxygen and water. Catalase is a heme-requiring enzyme; glutathione peroxidase is a selenium-containing enzyme that requires glutamine or glutamate to produce glutathione. The ability of these enzymes to work depends upon the availability of the minerals needed as cofactors: manganese, selenium, zinc, copper and iron. However, iron and copper have a dual role in the production and destruction of ROS. While both are necessary for protective enzymes, they can, in the presence of hydrogen peroxide, cause the production of the toxic hydroxyl radical (Delmas, et al, 1996). Therefore, the body will bind and sequester these metals to protein carriers, such as transferrin and ceruloplasmin, to make them unavailable for conversion to ROS. Nonenzymatic antioxidants are the other line of defense against ROS and include vitamins E and C, carotenes, glutathione, uric acid, taurine and phytochemicals. All these antioxidants work by intercepting and stabilizing the ROS. This is known as "scavenging." Disease may be viewed as an imbalance of free radicals and antioxidants the production of free radicals may increase without a corresponding increase in antioxidants. Without protection from antioxidants, the free radicals damage cells. Over time, accumulated cellular damage leads to disease. Conversely, the amount of free radicals may not change, but intake of antioxidants may be insufficient to neutralize the free radicals being produced by the body. This imbalance of free radicals and antioxidants is now known as "oxidative stress" Numerous studies have shown that antiretroviral drugs are linked with metabolic side effects including hyperlipidemia in HIV patients .This is of concern since blood lipid abnormalities are associated with increased risk of cardiovascular disease(Joly; et al, 2003,and Tassiopoulos et all;2008). With these information on the importance of antioxidants and how hyperlipidemia is observed under stressful conditions in HIV patients .We decided to assess the antioxidant status of HIV infected patients to ascertain whether HIV infection was associated with lower plasma concentrations of a key antioxidant vitamin C, Secondly to relate our observation to any upset in lipid level.

MATERIAL AND METHODS

Lipid and antioxidant status in Patients Infected with Human Immune Deficiency Virus was evaluated using biochemical parameters such as Ascorbic acid (Vit C), Cholesterol and Triglyceride. Seventy five (75) patients were used in this study comprising, 50 HIV positive individuals taking relevant antiretroviral therapy at least for three months.

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Thirteen HIV positive persons that have just received their sero status from voluntary counseling and testing center (VCT) in Aba Abia State of Nigeria and are yet to start drug and 12 apparent healthy HIV seronegative individuals served as control. 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 blood collected from the patients was centrifuged and serum used for the determination of cholesterol, triglyceride. Though serum for vitamin C determination was deproteinized and 2,4- dinitrophenylhydrazine used for its determination.(Omage,1979). Results obtained were subjected to statistical analysis using student't' test.

RESULT AND DISCUSSION

Reduced concentration of anti-oxidant vitamin C was found to be significantly decreased in HIV patients on drugs when compared to control group, but level of triglyceride was drastically increased in HIV patients on drugs compared to HIV infected patients not on drugs($P<0.05$) (Table). In addition, the level of cholesterol was increased in the body of people with HIV not on drugs (178.38 mg/dl) when compared to the HIV positive patients on drugs (163.28 mg/dl) and control subjects (169.67 mg/dl) (Table-1). This was statistically significant ($P<0.05$).

Table-1: Ascorbic Acid (Vit C), Cholesterol and Triglyceride Levels in Patients Infected with Human Immune Deficiency Virus.

Parameters	Ascorbic Acid (mg/dl)	Triglyceride (mg/dl)	Cholesterol (mg/dl)
HIV Negative Subject (control)	0.88 ± 0.47	184.83. +32.97	169.67 ± 13.50
HIV Positive Subjects not On drugs	0.75 ± 0.34	157.38. ±19.37	178.38 ± 20.38*
HIV Positive Subjects on drugs	0.50 ± 0.25*	284.80. ±42.71*	163.28± 12.4

*Significant difference ($P<0.05$).

The study has shown that in HIV patient's free radical activity is relatively high hence the low level of vitamin C obtained in this study. Though, this was more pronounced in HIV patients on drugs .Furthermore hyperlipidemia (increased triglyceride level) was equally observed as a result of dual effect of HIV infection and antiretroviral drugs in HIV patients on antiretroviral drugs. An increase in the pro-inflammatory cytokines and an increase in ROS and oxidative stress resulted to the depletion of anti-oxidant (vitamin C) as observed in this study with HIV patients, more so in those on antiretroviral drugs. The results obtained in this study were consistent with other findings (Ellen and Elizabeth; 2002, Cyril; 2006; Aruna and Bina; 2008) .Also in people with HIV and AIDS, decreased levels of antioxidants and increased oxidative stress have been documented (Allard and Aghdassi, 1998). As oxidative stress increases so does viral replication which precedes increase in the destruction of CD4+ T cells and the progression of the disease (Cole and Langkamp-Henken, 2005). It was equally suggested that decrease in Vitamin C level is due to its role in preventing oxidative injury in the mitochondria. The mitochondria contribute markedly to the intracellular burden of c reactive oxygen species'. Vitamin C enters the mitochondria via glucose transport 1(GLUT 1) and therefore protect the mitochondria from oxidative injury. Results obtained from serum fasting cholesterol and triglyceride levels equally follow the pattern observed in other studies (Carr et al, 1998, Joly et al,; 2003 and Khiagte et al, 2007). Hypertriglyceride in late stage of HIV infection are due to cytokine effects on lipid metabolism and equally due to antiretroviral effects. (Kereveur et al, 2001 .Numerous studies have shown that antiretroviral drugs are linked with metabolic side effects including hyperlipidemia in HIV patients .This is of concern since blood lipid abnormalities are associated with increased risk of cardiovascular disease(Joly; et al, 2003 , and Tassiopoulos et all;2008). The study has revealed first that Vitamin C was depleted in HIV patients and in those on antiretroviral drug .Secondly that lipid profile parameters are slightly altered in HIV individuals taking antiretroviral drugs. Even though slight, this alteration may cause cardiovascular complication with time and need to be monitored regularly.

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