ejpmr, 2018,5(9), 383-386

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SUPEROXIDE DISMUTASE AND CORTISOL LEVELS IN HIV-1 PATIENTS IN PORT HARCOURT, NIGERIA

[1]*Elechi-Amadi Kemzi Nosike and [1]Briggs Ojoye Ngoye

Department of Medical Laboratory Science, Rivers State University, Port Harcourt.

***Corresponding Author: Elechi-Amadi Kemzi Nosike**

Department of Medical Laboratory Science, Rivers State University, Port Harcourt.

Article Received on 24/06/2018 **Article Revised on 13/07/2018** **Article Accepted on 03/08/2018**

ABSTRACT

HIV infection is one of the most prevalent infections in Nigeria, and has negative effects on the human immune system. This study evaluated the levels of superoxide dismutase (SOD) and cortisol in HIV positive subjects. A total of 173 subjects of age 20 to 70 years were involved in this study, comprising 60 HIV positive patients receiving HAART (Highly Active Antiretroviral Therapy), 57 HAART-naïve HIV positive subjects and 56 apparently healthy control subjects. Individuals who had tuberculosis, diabetes and malaria were excluded from the study, as well as female subjects who were pregnant. The sample obtained were analysed for CD4 count using Fluorescent Activated Cell Sorter (FACSCount) automation, while superoxide dismutase (SOD) and cortisol were determined using enzyme-linked immunosorbent assay (ELISA) technique. It was observed that HIV patients had significantly reduced level of SOD and higher level of cortisol than control subjects. Those who were on HAART had lower levels of SOD and higher levels of cortisol than those who were not on HAART. The results are indicative of impaired immune function and greater oxidative stress in HIV patients. Incorporation of antioxidant therapy in the treatment regimen for HIV infection may lead to better management of the condition.

KEYWORDS: HIV, Superoxide dismutase, Cortisol, HAART, Nigeria.

INTRODUCTION

The Human Immunodeficiency Virus (HIV) is a retro-virus that affects the $CD4^{+}$T-Cells in humans, leading to a decline in immune response. The virus is a type of human T-cell leukaemia – lymphoma virus (HTLV). When HIV attaches to a host cell, the RNA is converted to DNA with the aid of the enzyme, Reverse Transcriptase, and there is a replication of the viral particle in the host cell. As a result of this, there is immunosuppression in HIV patients, leading to a diminished response to infection and tumours (Rote, 2002; Mohan, 2010).

Reactive oxygen species (ROS) are produced during normal cellular metabolism and have beneficial physiological functions, through cellular responses and immune function at low concentrations. However, at high concentrations they cause adverse modifications to cellular components (Birben *et al*., 2012, Kabel, 2014). There are three major ROS that are of physiological importance in the human system. They include superoxide ion (O_2^-), hydroxyl radical (OH^-) and hydrogen peroxide (H_2O_2).

HIV-infected patients have oxidative imbalance early in the disease, and there is generation of ROS (Friis-Moller *et al*., 2007). Thus, HIV infection increases oxidative stress which may result to oxidative damage of cellular components (Stephensen *et al*., 2007). ROS generated may enhance viral replication by activating nuclear transcription factors, which ultimately lead to an increased rate of viral gene expression (Sundaram *et al*., 2008). HIV patients are under chronic oxidative stress (Gwarzo & Muhammad, 2010) probably because HIV induces oxidative stress by disturbing cellular antioxidant defence and initiating oxidative reactions (Pasupathi *et al*., 2009). Enhanced oxidative stress also plays a pathogenic role in HIV infection (Hensley *et al*., 2000).

Highly Active Antiretroviral Therapy (HAARTs) have the potential of increasing toxicities and metabolic changes if used long term (Sundaram *et al*., 2008). The toxicities in HIV patients on anti-retroviral therapy include metabolic, hepatic, neurological and cardiovascular complications (Morse *et al*., 2006). HAART therefore may increase chemically reactive species in circulation (Awodele *et al*., 2012).

Cortisol is a hormone that is secreted in the adrenal gland. Its secretion is usually in response to the adrenocorticotropic hormone (ACTH) released from the pituitary gland. ACTH is secreted in response to several factors, one of which is corticotrophin-releasing hormone (CRH), which is synthesized and released from the hypothalamus (Guber & Farag, 2011). Another factor

that increases cortisol levels is stress, and it has been reported that HIV patients are under oxidative stress. Other factors that can increase ACTH level, and therefore cortisol, are pro-inflammatory cytokines, especially interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNFα) (Stewart, 2003). There exists a complex interaction between the immune system and the HPA axis (Mastorakos *et al*., 2006). Abnormalities in adrenal function have been reported to be more common in HIV patients than in the general population (Lo & Grinspoon, 2010), and it has also been reported that HIV envelop protein gp120 can stimulate the release of corticotrophin-releasing hormone (Costa *et al*., 2000).

The human body has a complex system of antioxidants that work together to protect the cells of the body against the dangerous effects of oxidants. Antioxidants are compounds that inhibit or delay the oxidation of other molecules by inhibiting the initiation or propagation of oxidative chain reactions. The antioxidant system consists of both enzymatic and non-enzymatic systems (Panda, 2012). SOD is the first antioxidant enzyme in the line of antioxidant defence, and is reportedly altered in a number of human diseases like diabetes mellitus (Briggs *et al*., 2016).

This work seeks to evaluate the levels of superoxide dismutase and cortisol in patients with HIV in Port Harcourt, Nigeria.

METHODOLOGY

This work was carried out on a total of one hundred and seventy three (173) subjects between the ages of 20 to 70 years. One hundred and seventeen (117) subjects were HIV positive, of which sixty (60) were receiving antiretroviral therapy and fifty-seven (57) were not on antiretroviral therapy. Fifty six (56) apparently healthy subjects, who were not HIV positive were used as controls. The bio-data and medical history of the subjects were obtained using an interviewer- based questionnaire. Ethical approval was obtained from local authorities and informed consent gotten from the subjects involved. Pregnant females, persons with tuberculosis, diabetes and malaria were excluded from the study.

Five millilitres (5ml) of blood was collected from each subject after overnight fast. Two millilitres (2ml) were put in a sample bottle containing ethylene diamine tetraacetic acid (EDTA), for the assay of CD4 count, while three millilitres (3ml) were put in plain bottle for the assay of Superoxide dismutase (SOD) and Cortisol.

The blood samples were centrifuged at 3,000rpm for 10 minutes and the plasma separated and put in a plain bottle. The plasma samples were then preserved at -20^{o}C in the refrigerator prior to analysis. Analysis of the samples for superoxide dismutase and cortisol was done using ELISA technique while Fluorescent Activated Cell Sorter (FACSCount) automation was used for CD4 count. The data generated was analysed using SPSS version 22. $P \leq 0.05$ were considered statistically significant.

RESULTS

Table 4.1: Mean ± SD of parameters for Study Subjects.

	CD4/ml	***SOD(pg/ml)***	***Cortisol(ng/ml)***
HAART-naive (A) n=57	310± 69	66.11 ± 13.04	60.80 ± 10.36
HAART (B) n= 60	414± 87	39.50 ± 12.17	83.98 ± 13.83
Control (C) n=56	858± 38	73.93 ± 13.38	42.83 ± 11.87
p-values	<0.0001	<0.0001	<0.0001
Post Hoc (Tukey)			
A vs B	S	S	S
A vs C	S	S	S
B vs C	S	S	S

DISCUSSION

SOD is the first antioxidant enzyme to act on ROS, acting as both antioxidant and anti-inflammatory agent in the body (Mgbekem *et al*., 2011). The results of this study indicate that there were differences in the levels of antioxidant enzyme, SOD in HIV patients compared to the control subjects. The level of SOD was significantly reduced in HIV patients than in control subjects. During HIV infection, there is enhanced oxidative stress due to activation of the immune system, which increases the generation of free radicals. These ROS deplete the levels of the antioxidant enzymes as they are consumed in the process of protecting cells against oxidative damage (Suresh *et al*., 2009). Therefore, HIV infection leads to a reduction in the levels antioxidant enzymes.

Also, the levels of the antioxidant enzyme, SOD, were lower in HIV patients on HAART than in HIV patients who are not on antiretroviral therapy. HAART has been reported to increase chemically reactive species in

humans (Awodele *et al*., 2012), and has also been associated with increased oxidative stress (Ngondi *et al*., 2006). Antiretroviral therapy therefore exerts a negative effect on the activities of antioxidant enzymes.

Plasma cortisol level was also performed in order to assess the effects of oxidative stress due to HIV infection and HAART administration on the immune system in the study subjects. From the result obtained the level of cortisol differed significantly among the study groups. HIV patients had significantly higher levels of cortisol than control subjects. Cortisol is synthesized by the HPA axis in response to stress. The elevated cortisol levels may be due to stress-related shift of steroid production from adrenal androgens towards cortisol or the increase in the concentration of cortisol-binding globulin (CBG) observed with the disease progression (Zapanti *et al*., 2008). Also, impaired adrenal function can result from direct infection of the adrenal gland by HIV, as well as many of the drugs that are used in the treatment of HIV (Zapanti *et al*., 2008).

The level of cortisol in HIV subjects on HAART was significantly higher than that of HAART-naïve HIV subjects. Collazos *et al*., (2003) had earlier reported a similar result in their work. HAART has been reported to increase cortisol level (Ebuehi *et al*., 2015), and has also been associated with increased oxidative stress (Ngondi *et al*., 2006). This state of increased oxidative stress causes a marked increase in the level of cortisol.

CONCLUSION

HIV patients are constantly under oxidative stress, evidenced by the low levels of SOD and increased levels of cortisol. Also, treatment with HAART seems to worsen the oxidative status as SOD levels were further reduced and cortisol increased significantly. Therefore, there is a need for additional modalities in the treatment of HIV infection and improving their oxidative status.

REFERENCES

1. Mohan, H. (2010). Textbook of pathology (6th Ed). USA. Jaypee Brothers Ltd.
2. Rote, N.S. (2002). *Infection and alterations in immunity and inflammation* in McCance, K.L. and Huether, S.E.(Eds). Pathophysiology. St Louis. Mosby Inc.
3. Birben, E., Sahiner, U.M., Sackesen, C., Erzurum, S., & Kalayi, O. (2012). Oxidative stress and antioxidant defence. *World Allergy Organization Journal*, 5(1): 9-19.
4. Kabel, A.M. (2014). Free Radicals and antioxidants: role of enzymes and nutrition. *World Journal of Nutrition and Health*, 2(3): 35-38.
5. Friis-Moller, N., Reiss, P., & Sabin, C.A. (2007). Class of anti-retroviral drugs and the risk of myocardial infarction. *New England Journal of Medicine*, 356: 1723-1735.
6. Stephensen, C.B., Marquis, G.S., Douglas, S.D., Kruzich, L.A., & Wilson, C.M. (2007). Glutathione, glutathione peroxidase, and selenium status in HIV-positive and HIV-negative adolescents and young adults. *American Journal of Clinical Nutrition*, 85: 173-181.
7. Sundaram, M., Saghayam, S., Priya, B., Venkatesh, K.K., Balakrishnan, P., Shankar, E., Murugavel, K.G., Solomon, S., & Kumarasamy, N. (2008). Changes in antioxidant profile among HIV-infected individuals on generic highly antiretroviral therapy in Southern India. *International Journal of Infectious Diseases*, 12(6): 61-66.
8. Gwarzo, M.Y., & Muhammad, S.A. (2010). Extracellular superoxide dismutase activity and plasma malondialdehyde in human immunodeficiency virus subjects of Kano as surrogate markers of CD4 status, *International Journal of Biomedical Science*, 6(4): 294-300.
9. Pasupathi, P., Ramchandran, T., Sindhu, P.J., Saranavan, G., & Bakthavathsalam, G. (2009). Enhanced oxidative stress markers and antioxidant imbalance in HIV infection and AIDs patients. *Journal of Scientific Research*, 1(2): 370-380.
10. Hensley, K., Robinson K.A., Gabbita, S.P., Alsman, S., & Floyd, R.A. (2000). Reactive oxygen species, cell signalling and cell injury. *Free Radical Biology and Medicine*, 28: 1456-1462.
11. Morse, C.G., & Kovacs, J.A. (2006). Metabolic and Skeletal complications of HIV infection: the price of success. *Journal of the American Medical Association*, 296: 844-854.
12. Awodele, O., Olayemi, S.O., Nwite, J.A., & Adeyemo, T.A. (2012). Investigation of the levels of oxidative stress parameters in HIV and HIV-TB co-infected patients. *Journal of Infection in Developing Countries*, 6(1): 79-85.
13. Guber, H.A., & Farag, A.F. (2011). *Evaluation of endocrine function*, in McPherson, R.A & Pincus, M.R. (Eds). Henry's clinical diagnosis and management by laboratory methods. Philadelphia. Elsevier Saunders.
14. Stewart, P.M. (2003). *The adrenal cortex*, in Larsen, P.R. Kroneberg, H.M, Melmed, S., & Polonsky, K.S. (Eds). Williams Textbook of endocrinology. Philadelphia. Saunders.
15. Mastorakos, G., Karoutsou, E.I., & Mizamtsidi, M. (2006). Corticotropin-releasing hormone and the immune/ inflammatory response. *European Journal of Endocrinology*, 155(1): 77-84.
16. Lo, J., & Grinspoon, S.K. (2010). Adrenal function in HIV infection. *Current Opinion in Endocrinology, Diabetes and Obesity*, 17(3): 205-209.
17. Costa, A., Nappi, R.E., Polatti, F., Poma, A., Grossman, A.B., & Nappi, G. (2000). Stimulating effect of HIV-1 coat protein gp120 on corticotrophin-releasing hormone and arginine vasopressin in the rat hypothalamus: involvement of nitric oxide. *Experimental Neurology*, 166: 376-384.
18. Panda, S.K. (2012). *Assay-guided comparism for enzymatic and non-enzymatic antioxidant activities*

with special reference to medicinal plants in El-Missiry, M.A. (Ed.). Antioxidant Enzyme. Croatia. In Tech.

19. Mgbekem, M.A., John, M.C., Umoh, I.B., Eyong, E.U., Ukam, N., & Omotola, B.D. (2011). Plasma antioxidant micronutrients and oxidative stress in people living with HIV. *Pakistan Journal of Nutrition*, 10(3): 214-219.
20. Suresh, D.R., Annam, V., Pratibha, K., & Prasad, B.V.M. (2009). Total antioxidant capacity-a novel early biochemical marker of oxidative stress in HIV infected individuals. *Journal of Biomedical Science*, 16(61): 186-196.
21. Kostyushov, V.V., Bokal, I.I., & Petrov, S.A. (2011). The study of activity of blood antioxidant enzymes in HIV infection. *Biochemistry (Moscow). Supplement series B: Biomedical chemistry*, 5(2): 193-196.
22. Ngondi, J.L., Oben, J., Forkah, D.M., Etame, L.H. & Mbanya, D. (2006). The effect of different combination therapies on oxidative stress markers in HIV infected patients in Cameroon. *AIDS Research and Therapy*, 3: 19.
23. Sinha, U., Sengupta, N., Mukhopadhyay, P., & Roy, K.S. (2011). Human immunodeficiency virus endocrinopathy. *Indian Journal of Endocrinology and Metabolism*, 15(4): 251-260.
24. Zapanti, E., Terzidis, K., & Chrousous, G. (2008). Dysfunction of the hypothalamic-pituitary-adrenal axis in HIV infection and disease. *Hormones*, 7(3): 205-216.
25. Collazos, J., Ibarra, S., & Mayo, J. (2003). Thyroid hormones in HIV-infected patients in HAART Era. *AIDS*, 17: 763-765.
26. Ebuehi, O.A.T., Awolola, A., & Akanmu, A. (2015). Changes in serum cortisol, thyroid hormones and lipid profiles in Nigerian men and women on first and second line antiretroviral therapy for 52 weeks. *International Journal of Virology and Molecular Biology*, 4(1): 12-18.
27. Briggs, O.N., Brown, H., Elechi-Amadi, K., Ezeiruaku, F. & Nduka, N. (2016). Superoxide Dismutase and Glutathione Peroxidase Levels in Patients with Long Standing Type 2 Diabetes in Port Harcourt, Rivers State, Nigeria. *International Journal of Science and Research*, 5(3): 1282-1288.