Molecular Basis of Immunological Dysfunction in People Living with HIV and AIDS in Enugu, Nigeria

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ABSTRACT

Molecular basis of immunological dysfunction in people living with HIV and AIDS was studied among HIV-positive people attending clinics at the University of Nigeria Teaching Hospital Ituku-Ozalla, Annunciation Specialist Hospital Emene, Mother of Christ Specialist Hospital and Enugu State University Teaching Hospital, all in Enugu metropolis. A total of 90 subjects recruited for the study were divided into three groups: 30 diagnostically positive HIV subjects (A), 30 HIV-positive subjects on highly active antiretroviral therapy (HAART) (B) and 30 apparently healthy individuals with HIV seronegative status as control group (C). Blood samples (8ml from each subject) were collected for the estimation of IL-2 cytokines, malondialdehyde (MDA) and total antioxidant status (TAS) using ELISA method. CD4+ and CD8+ T-lymphocyte count, and expression of CD25 and CD38 were analyzed using Flow Cytometry. Also samples were tested for IL-2, Tim-3 and Fos gene expressions using standard gene extraction methods and real time polymerase chain reaction (RT-PCR) test. IL-2 and Fos genes were sequenced for single nucleotide polymorphisms (SNPs) using Sanger’s method with Big Dye Terminator chemistry. HIV viral load was estimated using RT-PCR method with TaqMan chemistry. The mean CD4 and CD8 T-cell count, percentage CD38 and CD4/CD8 ratio of group A subjects were statistically significantly lower (p<0.05) than those of group C. However, there was no statistically significant difference observed when the same variables in group A were compared with those of group B (p>0.05). The mean plasma IL-2 cytokines in group B was statistically significantly higher than that of group A (p<0.05) with corresponding statistically significant increase (p<0.05) in both IL-2 gene and Fos gene expressions. This may be as a result of statistically significant reduction in viral load (p<0.05), observed during antiretroviral therapy (B). Furthermore, the expression of IL-2, Tim-3 and Fos genes in group A were statistically significantly lower (p<0.05) than those of group B and C respectively. Also, the expression of Fos gene in group B was statistically significantly lower (p<0.05) than that of group C, while those of Tim-3 gene and IL-2 gene showed no statistically significant difference (p>0.05). On the other hand, the oxidative stress (MDA) in both A and B were statistically significantly higher (p<0.05) than that of group C while mean plasma concentration of TAS in group A was statistically significantly lower (p<0.05) than those of groups B and C. Finally, there was statistically significant difference in IL-2 gene SNPs among the three study groups (p<0.05) while that of Fos gene showed no statistically significant difference (p>0.05). The result of this study showed that HIV infection interferes with the activation of Fos gene which is a major regulatory factor for the
expression of IL-2 gene in T-helper cells, thereby down regulating the production of IL-2 cytokine during progressive HIV disease. The elevation of IL-2 cytokine secretion and reduction in viral burden during antiretroviral therapy does not show a corresponding increase in T-cell proliferation, indicating a qualitative defect in the IL-2 cytokines produced. The study also indicates that the expression of Tim-3 molecules on T-helper cells may be another mechanism for CD4+ T-cell depletion in HIV infection through Tim-3-galactin-9 ligation-induced cell death. On the other hand, oxidative stress may be associated with viral load, CD4+ T-cell depletion and total antioxidant capacity during HIV infection. The need for the initiation of drug intervention as soon as HIV diagnosis is established to enable drug and immune response act synergistically to prevent the observed qualitative and quantitative IL-2 cytokine defect after T-cell exhaustion is hereby suggested. Also, the use antioxidants should be included in the management of HIV and AIDS, while research should be designed to produce drugs which will be able to block Tim-3 signaling pathways to prevent Tim-3-galactin-9 ligation-induced T-cell death during HIV infection.