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The Effects of HAART on the Renal Functions of HIV Positive Patients in Nsukka, South East Nigeria

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Short Research Article

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ABSTRACT

Background: Renal failure is highly prevalent among persons with Human Immuno Deficiency virus (HIV) infection and is linked to high morbidity and mortality rate.
Aim: The aim of this study was to determine the effect of HIV infection on $CD4^+$ cells, urea and creatinine of HIV patients that are being treated with Combivir N for a period of 8 months.
Study Design: Forty three male and female HIV positive subjects ready to be placed on Highly Active Antiretroviral Therapy (HAART) (Combivir N) and 20 non HIV positive subjects were randomly selected and $CD4^+$ cells, urea and creatinine levels of HIV positive subjects were determined before treatment, 4 months and 8 months into treatment.
Methodology: Flow cytometry using partec cyflow machine was used in analyzing the $CD4^+$ cells, serum urea was determined by Berthelot's method, while creatinine was measured by Bartels and Bohmer method.
Results: Mean cell level of $CD4^+$ count was higher in 8 months of treatment (319.02 ± 138.68) than before treatment and 4 months into treatment (246.51 ± 71.30 and 310.04 ± 106.60) but lower than control group (1023. 01 ± 203.03). Mean serum level of urea was higher in 4 months into treatment (35.51 ± 13.92) than before treatment and control group (27.14 ± 11.06 and 14.71 ± 3.80). Also mean serum level of creatinine was higher in 4 months into treatment (1.30 ± 0.53) than 8 months into treatment and control subjects (0.98 ± 0.31 and 0.93 ± 0.12). In this study serum levels of urea were significantly correlated with creatinine level ($p < .001$).

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Conclusion: The commencement of HAART for the study population led to an increase in their CD_4+ count. The levels of the renal markers creatinine and urea, showed a picture of an initial derangement but an attempt towards recovery by the system. These effects are indicative of a positive prognosis with regard to HIV/AIDS infection which resulted from the initiation of HAART (Combivir N).

Keywords: HIV/ AIDS; HAART; CD4+; creatinine; urea.

1. INTRODUCTION

The HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome) pandemic has undermined the health of so many people, consequently affecting adversely, the work force and the economic stability of so many countries all over the world. World Health Organization (WHO) and United Nations Programme on AIDS (UNAIDS) [1,2], estimated that about 33.4 million people worldwide were living with AIDS, with 2.7 million new infections per year. Some biochemical anormalies accompany infection with human immunodeficiency virus as a result of the complications of the disease itself, for example the body's normal response to infection depletes nutritional stores. Studies have shown that the antioxidant system of the body is adversely affected in HIV infection, and changes in the activities of its components have been documented by several workers [3,4]. Other studies have also stated that alanine transaminase (ALT) and aspartate transaminase (AST) activities usually increase in asymptomatic HIV sero-positive patients, signaling liver involvement in HIV infection. Patients especially at the final stage of AIDS may develop, HIV associated nephrophathy (HIVAN) which leads to an increase in their serum creatinine levels [5,6]. The current treatment for HIV infection consists of highly active anti retroviral therapy. These drugs which are classified into, Nucleoside Reverse Transcriptase Inhibitors (NRTI), Non nucleoside reverse transcriptase inhibitors (NNRTI), Protease inhibitors (PT), and Fusion inhibitors (FI) were introduced in 1996 to improve the patients' quality of life, reduce HIV viraemia, and possibly prolong the life of the patient. They do not cure the patient of HIV or prevent the return once treatment is stopped [7].

Since infection with HIV compromised the general well being of its patients, giving rise to many adverse biochemical changes, it became necessary that researchers direct their effort towards examining the biochemical effects of HAART (Highly active antiretroviral therapy) with a view to determining their exact effects on the parameters or systems under study, with respect to the population under consideration. A closer look at the, renal functions of these patients following treatment needed to be taken in order to appreciate the effects of these drugs as these have been observed to be severely affected by the infection. Hence the aim of the study is to examine the changes in the renal function markers (urea and creatinine) of HIV positive patients on HAART in Nsukka locality.

2. MATERIALS AND METHODS

The minimum sample size was calculated using the formular proposed by the creative research system (2012) with HIV prevalence in Nsukka being 1.8% (Sentinel group).

2.1 Sample Size

The minimum sample for this research was calculated using the formular proposed by Creative Research System, (2012) as follows:

$n = Zo^2 P (1-P) - d^2$

- n = Minimum Sample Size
- z = Constant (1.96 at 95% Confidence interval)
- p = Proportion of interest. In this case 1.8% (prevalence rate of HIV in Nsukka) (Sentinel group, 2008)
- d = Error margin; in this case 0.05 (95% confidence interval)

$n = (1.96^2)\ 0.018\ (1- 0.018) – 0.05^2 = 27.16$

2.2 Subjects

This included 43 (forty three) HIV/AIDS subjects, attending the AIDS clinic of Bishop Shanahan Hospital, Nsukka south east Nigeria and twenty (20) apparently healthy subjects who served as controls were recruited for the study. Informed consent was obtained from the participants and ethical clearance was sought for and obtained from Annunciation Hospital ethical clearance committee, Emene Enugu Nigeria. Venous blood, five mililitre (5 ml), was aseptically collected from each subject, three mililitre (3 ml) aliquot was allowed to clot and centrifuged at 3000 rpm for 5 minutes, to separate serum from

erythrocytes. The serum was pipetted into a clean serum bottle and either analyzed immediately or stored at -4℃ for a maximum of 48 hours. A two milliliters (2 ml) amount of the sample was emptied into a sodium EDTA container for $CD4^+$ count. Retroviral screening was done using the requisite methods. $CD4^+$ enumeration was done by the principle of flow cytometry using partec cyflow machine.

The results were presented as mean ± standard deviation. Differences between the results of the control subjects, and those of HIV positive subjects, before the commencement of HAART, 4 Months and 8 months into treatment, were analyzed using Student's t test. Effects of HAART on the biochemical parameters of HIV positive patients' were analyzed using ANOVA. Pearson correlation was employed in analyzing the relationship between $CD4^+$ count and the biochemical parameters.

2.2.1 Inclusion criteria

HIV positive patients not yet on antiretroviral therapy but are due to be placed on it by virtue of their $CD4^+$ counts (patients with $CD4^+$ count 500/mm^3 of blood and below were placed on HAART).

2.2.1.1 Design of the experiment

All subjects were tested at presentation (after being confirmed positive), 4 months after the initiation of the antiretroviral therapy (Combivir N is the HAART in use in Bishop Shanahan Hospital, it contains zidovudine, lamivudine and nevirapine) and 8 months after. Their $CD4^+$ counts were also estimated, at all the presentations. The subjects were divided into 4 groups as follows:

Group 1 (G1): HAART naïve subjects (forty three HIV positive individuals ripe for HAART initiation).
Group 2 (G2): The same HIV positive subjects four months into treatment with HAART.
Group 3 (G3): The same HIV positive subjects eight months into treatment
Group 4 (G4): Control (twenty apparently healthy individuals).

3. RESULTS AND DISCUSSION

Table 1 shows that mean ± SD of urea and creatinine levels for the control subjects (group 4) 14.71 mg/dl (SD= 3.80) and 0.93 mg/dl (SD=0.12) were lower than those of groups 1, 2 and 3 but while the differences were significant (P <.05) for urea, they were not significant (P > .05) for creatinine. The highest concentration of urea, was observed for (group 2) 35.5mg/dl (SD=13.92). The difference between urea concentrations for group 2, (35.51 mg/dl (SD= 13.92)) and 3 (27.86 mg/dl) (SD = 8.72)) were significant (P < .05).

However the differences between the groups for creatinine were not significant (P > .05). Group 1 showed the lowest $CD4^+$ count (246.51 cells/mm^3; SD=71.30) while group 4 showed the highest $CD4^+$ count (1023.01 cell/mm^3; SD = 203.03). Separate comparisons revealed that the differences between the $CD4^+$ count of group 1 (246.51 cells/mm^3; SD= 71.30) and 3 (319.02 cells/mm3; SD = 138.68) were significant (P < .05). However, the difference between the $CD4^+$counts for groups 2 and 3 was not significant (P >. 05).

According to Pearson Correlation, there was a positive and significant correlation of urea with creatinine (r= 0.481, p=.001). But there was a negative and non-significant correlation of CD4+ count with urea (r= -0.062, p=.488) and creatinine (r= -0.071, p=.427).

The results of the work showed that the use of highly active antiretroviral therapy (HAART) led to a steady increase in CD_4^+ count from the HAART naïve stage to eight months into treatment this agrees with the work of Ibe et al. [8]. This showed that the use of HAART reduces the replication of HIV, leading to the improvement of CD4+ count and ultimately the general well being of patients. The mean CD4+ count was significantly higher in controls than HIV treatment naïve patients and also HIV patients on HAART. The finding is in line with previous study done in Ethiopia [9] and Benin City Nigeria [10]. The level of the renal function marker, urea increased from the baseline (HAART naïve) stage**,** to the 4^{th} month of treatment, but reduced by the 8^{th} month to about the same level as the baseline value. On the other hand there was no appreciable change in the level of creatinine over the duration of the treatment.

The effect of HAART on the renal function markers of the subjects proved interesting, this is because after four months of initiation of HAART, urea increased showing a negative effect on renal function, but eight months into HAART, the

Table 1. Mean ± SD of CD4 + count, urea and creatinine

Groups	Urea (mg/dl)	Creatinine mg/dl	$CD4^+$ count cell/mm^3
G1(43)	27.14± 11.06	1.28± 0.19	246.51±71.30
G2 (43)	35.51± 13.92	1.30±0.53	310.04±106.60
G3(43)	27.86±8.72	0.98±0.31	319.02±138.68
G4(20)	14.71± 3.80	0.93±0.12	1023.01±203.03
F(p) value	17.29 (0.000)	2.33(0.077)	198.96(0.000)
G1 vs. G2	0.000	0.888	0.02*
G1 vs. G3	0.755	0.068	0.008*
G2 vs. G3	0.001*	0.05*	0.740
G1 vs. G4	0.000*	0.083	0.000*
G2 vs. G4	0.000*	0.065	0.000*
G3 vs. G4	0.000*	0.781	0.000*

F = F ratio
P = Probability value
* *Significant Probability value*

urea level dropped back to almost baseline. This means that the kidneys may have experienced an initial negative effect in reaction to the initiation of the drug, but recovered after sometime. On the other hand creatinine levels did not display any significant change.

This brief period of renal function alteration, may be attributed to the side effect of the drugs. HAART can cause renal injury through a variety of mechanisms: direct renal tabular toxicity (Fanconi-like syndrome and distal tubular acidosis), obstruction (Crystal deposition in the kidney) and glomerular lesions [11,12]. The work of Obirikorang et al. [13] also suggested that changes in renal function can also occur especially in severe HIV infection, involving HIV associated nephropathy. The good thing is that there seemed to be a recovery phase showing that there can be a resultant positive prognosis with the continued use of HAART as regards renal function. Typical examples are seen for creatinine levels, which became almost the same for the healthy control group and the HIV positive group, eight months into treatment. This disagrees with the work of Bigionisantos *et al* [14], which stated that HAART can cause renal failure through a variety mechanisms: direct renal tubular toxicity, obstruction and so on.

It is noteworthy that urea and creatinine, showed higher baseline levels and activities for HIV positive subject than was found in their apparently healthy counterparts. This can be attributed to the fact that the presence of the virus itself and its destructive activities can lead to damages in crucial organs like the kidneys and the liver leading to increases in the levels of the renal function markers, prior to the use of HAART. This is in consonant with the work of Biagionisantos et al. [11], which claimed that in patients with AIDS, kidney function can be compromised, due primarily to the infection itself or secondarily to the side effect of HAART.

4. CONCLUSION

The commencement of HAART for the study population led to an increase in their CD_4+ count. The levels of the renal markers creatinine and urea, showed a picture of an initial derangement but an attempt towards recovery by the system. These effects are indicative of a positive prognosis with regard to HIV/AIDS infection which resulted from the initiation of HAART.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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