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EFFECT OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY ON CD4 COUNT AND WEIGHT IN AIDS PATIENTS SEEN AT THE UITH, ILORIN

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ABSTRACT
Objective: To determine the response on treatment-naïve HIV/AIDS patients to the Highly Active Antiretroviral Therapy (HAART) in terms of CD4 Count and Weight gain over a period of 2½ years.

Methods: Patients with Acquired Immunodeficiency Syndrome (AIDS) were recruited under the Federal Government Highly Active Antiretroviral Therapy (HAART) programme at the University of Ilorin Teaching Hospital. The treatment regimen included Lamivudine, Starvudine and Nevirapine. The patients' responses were evaluated with respect to CD4 count and weight over the period of treatment. The diagnosis of HIV/AIDS was made on the basis of reactivity with two different ELISA reagents, and CD4 count was done with Dynal T4 Quant method. The weights (kg.) of the patients were taken at monthly visit.

Results: The duration of treatment for the patients analysed ranged from 1 month to 14 months. Analysis of CD4 count was possible in 105 patients. The mean post treatment CD4 count and weight were significantly higher than the pre-treatment values ($p < 0.001$ and $p < 1.01$) respectively. There were significant positive correlations ($p < 0.05$ and $p < 0.001$) between increases in CD4 count and weight respectively, and duration of treatment. In eight (8) patients, CD4 Count reduced or remained the same in spite of treatment.

Conclusion: The HAART regime is associated with increase in CD4 Count and weight gain. While increases in CD4 Count and weight correlated with duration of therapy, there was no correlation between CD4 Count increase and weight gain.

Key Words: HIV/AIDS Antiretroviral Therapy CD4 Weight. *(Accepted 18 June 2007)*

INTRODUCTION

Highly Active Antiretroviral Therapy (HAART) refers to a category of treatment regimen usually comprising of 3 or more antiretroviral drugs that are expected to reduce plasma viral levels below the limits of detection (500 copies/mL). Most HAART regimens include drugs from at least 2 of the 3 classes of antiretroviral therapeutic drugs referred to as Nucleoside Reverse Transcriptase Inhibitor (NRTI), Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), and Protease Inhibitors (PI)[1]. Potent combination regimens offer the greatest likelihood of reducing the replication of Human Immunodeficiency Virus (HIV); facilitating CD4 T cell expansion and delaying progression into Acquired Immune Deficiency Syndrome (AIDS)[2]. Although it is well established that treatment with HAART can lead to CD4 cell gain, full immune recovery is often incomplete[3].

Some Physicians tend to delay the use of HAART until CD4 cell count falls to 200 in order to reduce the associated adverse effect, since it has been observed that this does not increase the mortality rate in HIV patients with good compliance[4]. Mortality rate increases if HAART is initiated below CD4 cell count of 200. Also, non-adherent patients have higher mortality rates than those who are adherent with similar CD4 cell count. Above the CD4 cell count of 200, medication adherence is the critical determinant of survival, and not the CD4 Cell count at which HAART is begun. Treatment delay however, has been found to cause impaired functional immune reconstruction[3]. It has been observed that after the initiation of HAART, there is usually a rapid increase in CD4 cell count, and on the other hand, there is an early fall in the count after interrupting therapy[5]. HAART also has a positive effect on CD4 cell count in children with HIV infection[6]. These changes may however be affected by the co-infection with Tuberculosis, which has been shown by Salami et al to be associated with a lower CD4 cell count.[7]

Involuntary weight loss or wasting is one of the most common manifestations of HIV infection. It can occur at any stage of infection, regardless of HAART and indicates disease progression[8]. HAART has

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been observed to reduce the impact of HIV disease on body weight, in addition to the direct effect on appetite, body composition, and body fat redistribution[9].

Studies have established the positive impact of HAART especially in patients with serious weight loss of greater than 10%[10]. Other studies have however shown that the weight gain of HIV patients on HAART is primarily fat with no changes in lean body mass[11]. Changes in body weight and Body Mass Index (BMI) have also been found not to correlate with changes in CD4 or plasma HIV RNA. Patients with good CD4 and RNA response to HAART were as likely to experience increase in weight and BMI as patients with lesser response to HAART[12]. The aim of this review is therefore to examine: i. the response of HIV/AIDS patients to HAART in terms of CD4 Count and weight, ii. the relationship between increases in CD4 Count and weight, and iii. any correlation between increase in CD4 Count and increase in weight.

MATERIALS AND METHODS

The University of Ilorin Teaching Hospital is one of the centres approved by the Federal Government for its programme on the Highly Active Antiretroviral Therapy (HAART) for HIV/AIDS patients. Patients had pre- and post-test counseling and were recruited from February, 2002 based on reactivity of sera with two different ELISA methods. Each patient was then examined clinically and weights were taken before commencement of the antiretroviral therapy. The CD4 Cell Count was determined using the Dynal T4 Quant by Dynal Biotech ASA, Oslo, Norway. Patients were recruited if CD4 cell count was 200 cells/l and below with or without AIDS-defining clinical features, if they had Stage III disease with CD4 cell count less than 350 cell/l, or Stage IV disease regardless of CD4 cell count values, in line with Nigeria's Guideline on the Antiretroviral therapy[13]. Treatment was done with three drug regimen comprising Starvudine, 40mg. twice daily, Lamivudine 150mg. twice daily, and Nevirapine, 200mg. twice daily, all taken orally. While on treatment, patients had their CD4 Cell Count and body weight among other parameters, monitored and recorded at three monthly intervals. Prophylactic antibiotics were not offered to the patients except those with evidence of bacterial infections.[14]

Analysis of patients' responses in terms of increase or otherwise of CD4 Cell Count and body weight was carried out in 185 patients two years after commencement of the programme. The pretreatment CD4 Count and weight were compared to those at the point of analysis using the Students' t test while the association between outcome measurements and duration of treatment was examined using regression analysis.

RESULTS

Patients were recruited at different times during the treatment period. One hundred and eighty-five patients, 91 male and 94 females aged 15 to 66 years, were analysed at the end of two years of the HAART programme. Due to the combination of patients defaulting and financial incapacity, only 105 and 149 patients respectively had pre and post treatment CD4 Count and weight recorded along with period of therapy. The period of treatment ranged from 1 to 14 months with a mean of 5 months.

The mean pre-treatment and post-treatment CD4 Counts were 218±133 and 370±180 cells/cu. mm. respectively. The difference is statistically significant (p = 0.000). The mean pre-treatment and post-treatment weights were 52.1±10.6 and 59±10.5 kg. respectively, and the difference was statistically significant (p = 0.000) as shown in Table 1. There was a significant positive correlation between duration of treatment and increase in CD4 Count (r = 0.24, p = 0.013). There was a significant positive correlation between the increase in weight and duration of treatment (r = 0.458, p = 0.000), see Table 2. There was no correlation between increase in CD4 cell count and increase in weight (r = 0.0), see Table 2 and Figure 1. In eight patients the CD4 Count remained the same or reduced in spite of the retroviral therapy.

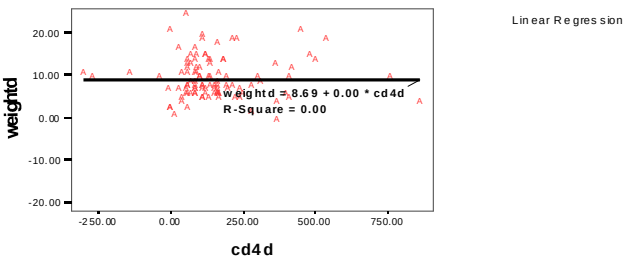
Table 1: **Comparison between Pre-Treatment and Post-Treatment CD4 Cell Count and Weight**

Parameter	Pre-treatment	Post-treatment	n	p value
CD4 cell count/cu. mm.	218±133	370±180	105	0.000
Weight (kg)	52.1±10.6	59±10.5	145	0.013

Table 2: **Correlation of Increase in CD4 Cell Count and Weight with Duration of Treatment**

Parameters Correlated	Correlation Coefficient	p value
Increase in CD4 count vs. Treatment duration	0.24	0.013
Increase in Weight vs. Treatment duration	0.458	0.000
Increase in weight vs. Increase in CD4 cell count	0.00	0.997

Figure 1: Regression of increase in CD4 (cd4d) count versus increase in weight (weightd) in HIV/AIDS patients on HAART.



DISCUSSION

The treatment of HIV/AIDS has changed considerably over the last 20 years as knowledge and treatment options have increased. HAART was introduced in 1996 in the industrialized countries and its effects have been established in those countries[1,2,8]. Reports since 1999 in the United States of America and the Netherlands have associated the use of HAART with reduction in viral load and increase in weight[1,8].

Not much work has been done in this part of the world on this subject before now because the drugs were very expensive and unaffordable to many patients until recently when it was subsidized by the Federal Government. Consequently, many more patients can now afford to buy the drugs and this development has made this study possible.

Analysis of the CD4 Cell Count was possible only on 105 patients because the CD4 Cell Count is even more expensive than the drugs and some patients could not afford to pay. The mean post-treatment CD4 Cell Count was significantly higher than the pre-treatment one and there was a significant positive correlation between the post-treatment CD4 count and the duration of treatment. This is in keeping with work done in the industrialized countries state above[1,8]. Those with relatively lower CD4 Cell count pre-therapy had a more dramatic increase in CD4 Count than those with relatively higher CD4 Count pre-therapy. This may be the reason for physicians' preference for delaying the use of HAART until the CD4 Cell Count falls to 200 cell/cu. mm. to avoid the adverse effects of the drugs and moreso when such delay does not increase the mortality rate[4]. These physicians however believe that mortality may increase if treatment is started at CD4 Cell Count below 200. In our study however, patients with CD4 Cell Counts below 200 cells/cu. mm. did well on the HAART regimen, especially those who complied well with the drugs. Antibiotics were given only to patients with clinical, radiological, and laboratory evidence of bacterial or mycobacterial infections, since we have previously reported them to be associated with relatively lower CD4 cell count and reduced survival. [7,13]

The mean post-treatment weight of those patients was significantly higher than the pre-treatment weight, and there was significant positive correlation between the weight gain and duration of treatment. The weight gain can be attributed to improvement in the clinical condition of the patients, reduction in psychological stress as well as a direct effect of the drug on the appetite. However, it is interesting to note that, in line with the finding of Verweel et al[6] among children, there was no correlation between increase in CD4 cell count and increase in weight. This implies that weight may not be useful as surrogate for CD4 cell count or An index in the assessment of response to antiretroviral therapy.

Only 8 patients experienced no improvement in CD4 count in spite of treatment. This could be due to inadequate compliance to therapy, lack of response, or very low pre-treatment CD4 count. The kind of diet that these patients were able to afford is another factor that should be considered.

In conclusion, this study has shown that the HAART regimen conferred clinical improvement on patients involved as the CD4 count and weight gain represent good indices of response to therapy. Government and NGOs should therefore proceed quickly with the planned scaling up of the programme to make the drugs available to more patients. The treatment of infected children and prevention of mother to child transmission should be given the same coverage as for the HAART programme.

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