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HAART and Lipid Metabolism in a Resource Poor West African Setting

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ABSTRACT

Highly active antiretroviral therapy (HAART) confers several benefits, including reduction in viral load and longevity in HIV positive patients. However, Metabolic and morphological complications have been increasingly reported among patients in the advanced industrialized countries receiving chronic HAART up to 10-20years. We report occurrence of hyperlipidaemia in subjects on HAART in a West African Community. The CD4+ cell count and fasting lipid profile were estimated in One hundred and ten (110) HIV positive patients attending the HIV clinic of Obafemi Awolowo College of Health Sciences, Sagamu. Fifty five subjects served as the study subjects and were selected randomly from the patients on triple combination therapy of ARV medication for a minimum of 3 years and matched for age and sex with the control group (55) of those who were not on ARV medication. All the subjects were symptomatic grade 3 or 4 WHO classification. The CD4 count of the study was $355.11\text{cells}/\text{mm}^3 \pm 185.0$ and was statistically significantly higher than the CD4 count of the control subjects which was $177.95\text{cells}/\text{mm}^3 \pm 59.1$ ($P < 0.05$). The mean values for VLDL, LDL, Cholesterol, and triglyceride concentrations were $32.9\text{mg}/\text{dl} \pm 8.9$, $75.9\text{mg}/\text{dl} \pm 45.8$, $142.3\text{mg}/\text{dl} \pm 48.6$, $163.6\text{mg}/\text{dl} \pm 44.5$ in study group respectively and were statistically significantly higher than $30.3\text{mg}/\text{dl} \pm 1.2$, $48.9\text{mg}/\text{dl} \pm 34.4$, $114.6\text{mg}/\text{dl} \pm 35.8$, $150.5\text{mg}/\text{dl} \pm 37$ in the control group. ($P < 0.05$) The mean concentration of HDL of $36.0\text{mg}/\text{dl} \pm 13$ in the control subjects was significantly higher than $29.7\text{mg}/\text{dl} \pm 8.9$ in the study ($P > 0.05$). The prevalence of hypertriglyceridemia ($>200\text{mg}/\text{dl}$) was 15%.in the study group and 2.5%.in the control. (*Afr. J. Biomed. Res. 11: 27 -31*)

Key words: dyslipidaemia, limited resource settings, hypertriglyceremia, hypercholesteremia, HAART, lipid concentration

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INTRODUCTION

The benefits of antiretroviral therapy can be striking when compared with the HIV epidemic in the nineteen nineties. HAART confer several benefits, such as virological, immunological, clinical, and survival, to HIV positive patients. (Schapiro and Collier 1996, Palella 1998.) As a result of antiretroviral therapy, HIV-infected persons can expect a prolonged and perhaps even normal survival duration. (Dominc *et al* 2006)

However, many unrelated clinical management challenges still exist.

One of such challenges is the decision to start therapy. (Riddler *et al* 2003) This is largely because the effectiveness of treatment must be balanced against the possibility of toxicity. For many patients and providers, concern about long-term toxicity weighs most heavily in the decision to defer or delay initiation of antiretroviral therapy. The side effects that cause most concern are morphological and metabolic complications. (Carr 2000.). Metabolic complications include dyslipidaemia, hyperinsulinemia, hyperglycemia, insulin resistance, lactic acidosis, osteonecrosis and osteoporosis.(Carr 1998, 1999, & 2000, Behrens and Schmidt 2005) These conditions vary from patient to patient and the pathophysiology of the occurrence of these metabolic alterations is not well understood. (Massip 1999, Behrens and Schmidt 2005).Several possible factors have been identified as effecting the development of these metabolic complications. White race, age of patient, and affluence are some of the factors that have been suggested by several groups as playing a role in determining the metabolic changes .(Kotler 1999b,Boyle 2002) Therefore, an understanding of how a resource limited population is affected by HAART will have a profound effect on treatment decisions.

MATERIALS AND METHODS

Free antiretroviral drug programme for HIV/AIDS patients started in July 2000 at the centre for special studies (CSS) Sagamu, Ogun state Nigeria. The centre is currently located at the infectious disease clinic of the department of Community

Medicine and Primary Care of Olabisi Onabanjo University Teaching Hospital Sagamu, Nigeria.

The CD4 and fasting lipid profile was estimated in one hundred and ten HIV positive patients attending the HIV clinic. Fifty five subjects who served as the study subjects were picked randomly from the patients on free triple combination therapy of ARV medication for a minimum of 3 years and matched for age and sex in the control group (55) of those who are not on ARV medication. All the subjects are AIDS or symptomatic HIV patients mainly in Group 3 and 4 of WHO classification. They presented with thrush, cough, rashes, unexplained fever for more than two weeks, and other opportunistic infections. In addition the patients had a CD4 count of below 200mm^3 and a viral load of more than $20,000\text{mm}^3$.The subjects receiving HAART medication were managed with combination of at least 3 antiretroviral drugs from 2 of the 3 groups of antiretroviral drug. Viz: The protease inhibitors (PI), The Nucleoside Reverse Transcriptase Inhibitors (NRTI), and the Non Nucleoside Reverse Transcriptase Inhibitors. (NNRTI) The two arm of drugs given to the patients were combined thus

ARM 1 = 1PI + 2NRTI

Or

ARM 2 = 1NNRTI + 2NRTI.

Laboratory methods

The CD4 – T cells: were determined by the Dynal beads manual method. Concentrations of total cholesterol, High density lipoprotein cholesterol(HDL-C) and triglycerides were measured using enzymatic assays.

Triglycerides: Triglyceride estimation was made by the enzymatic colorimetric test of glycerol phosphate oxidase method. (Tietz, 1999)

High density lipoprotein-cholesterol: Low density lipoproteins (LDL and VLDL) and chylomicron fractions were precipitated quantitatively by the action of phosphotungstic

acid in the presence of magnesium ions. After centrifugation, the cholesterol concentration in the HDL fraction which remains was determined by the enzymatic colorimetric method. (Tetz, 1999)

Total Cholesterol: This was carried out by the enzymatic colorimetric method.(Clinical laboratory Diagnostics 1998)

Low density lipoprotein cholesterol levels: were calculated from total cholesterol, HDL-C, and triglyceride by the Friedewald equation (Friedewald *et al* 1972)

Quality control: control samples were assayed along with the test samples and assay batches with controls values that fall outside the established laboratory values were repeated.

RESULTS

The study populations were mainly adults with the mean age of 40.4 ± 10.9 in the HAART group and 36.9 ± 9.3 in the control group.(Table 1) There were improvements in the weight and consequently in the body mass index of the two groups after the initiation of HAART in the study group and the treatment of opportunistic infection in the control group.(Table 2) However the weight increase in the study group on HAART were statistically significantly higher than in the control.

The CD4 cell count and absolute lymphocyte count in the HAART group was significantly different from the control group, thus showing the effects of HAART in improving the immunological properties of the subjects. Similarly the concentrations of the lipid concentration in the HAART group was significantly elevated than in the control. (Table 3).

The prevalence of hypertryglycaeraemia and hypercholesteronaemia was 23.1% in the ARM one group which contains one protease inhibitor. The prevalence of hypertryglyceridemia (>200mg/dl) was 15% in the study subjects and 2.5%.in the control. The prevalence of hypercholesterolemia (> 210mg/dl) was 12.5 in the study subjects and 0% in the control.

Table 1

Mean Age, weight, and Body mass index of subjects.

	HAART	NO HAART	P value
Mean Age (years)	40.4 ± 10.9	36.9 ± 9.3	P>0.05
Weight before treatment (Kg)	55.2 ± 10.6	53.6 ± 9.7	P>0.05
Weight during treatment (Kg)	63.0 ± 12.4	56.8 ± 10.7	P<0.001
Body mass index	23.8 ± 4.2	21.0 ± 3.3	P<0.001

Table 2

Mean concentration of CD4 and Absolute lymphocyte count of subjects

	HAART	NO HAART	P value
CD4 count (cell/mm ³)	344.1 ± 171.5	179.9 ± 64.2	P < 0.0001
Absolute lymphocyte count (cell/mm ³)	529 ± 156.7	399.3 ± 104.5	P < 0.0001

Table 3

Mean concentration of LIPID Profile of subjects

	HAART (mg/dl)	NO HAART(mg/dl)	P VALUE
VLDLC	32.9 ± 8.9	30.34 ± 1.2	P < 0.05
HDLC	29.7 ± 9.3	35.9 ± 13.0	P < 0.05
LDLC	75.9 ± 45.8	48.9 ± 34.4	P < 0.0001
Total cholesterol	142.3 ± 48.6	114.6 ± 35.8	P < 0.0001
Tryglyceride	163.6 ± 44.5	150.5 ± 37.0	P < 0.05

Table 4

Effect of arm of drug used on cholesterol level of subjects on HAART

	ARM 1	ARM 2	
Abnormal Cholesterol mg/dl	23.1 %	4.5 %	P< 0.05 Significant
Normal Cholesterol mg/dl	76.9 %	95.5 %	

The cut off point of > 200mg/dl for hypertryglyceridemia and > 210mg/dl for

hypercholesterolemia were based on reference values of National Cholesterol Education Program (NCEP, 1993) as determined by the expert Panel on the detection, evaluation, and treatment of high blood cholesterol in adults. Generally the Trglyceride concentration in both groups are however higher than the reference value of 150mg/dl in this environment.

Table 5

Effect of arm of drug used on Tryglyceride level of subjects on HAART

Tryglyceride mg/dl	ARM 1	ARM 2	P < 0.05 significant
Abnormal	23.1 %	9.1%	
Normal	76.9 %	90.9 %	

DISCUSSIONS

Metabolic derangements associated with the use of HAART calls for clinical concerns about their use. Some of these metabolic disorders like Dyslipidemia(abnormally elevated triglycerides and cholesterol) could lead to heart disease. Debate continues about whether these outcomes are a direct result of the drugs alone or whether the disorders are primarily from the course of HIV disease or from some combination of HIV disease progression plus anti- HIV drug effects. Other factors which have been identified as effecting the development of these metabolic complications includes, white race, age of patient, and affluence are some of the factors that has been suggested by several groups as playing a role in determining the metabolic changes .(Kotler 1999b, Boyle 2002).

Hyperlipidaemia defined as an increase in triglyceride and cholesterol levels has been reported in several studies. In one study, Bernasconi reported that 66% of the patients on HAART had an increase in triglyceride levels. In addition, 54% of the patients on protease inhibitors had hypercholesterolemia compared to 19% of the patients on non-protease inhibitor regimes (Bernasconi 1998).The result of this study shows that dyslipidaemia is mainly due to the use of the HAART, especially the Protease Inhibitors.

However, the prevalence of dyslipidaemia in this study is less than what has been reported by Bernasconi in the developed country. (Bernasconi 1998) Patients who demonstrate elevated total cholesterol and/or triglyceride levels should be treated appropriately to prevent the development and progression of atherosclerotic heart disease, stroke, and pancreatitis. Appropriate dietary and exercise measures remain the foundation of treatment for hyperlipidaemia. Nutritionist, dietician should therefore be fully involved in the treatment and care of these patients. Patients with hyperlipidaemia, and smoke should be counseled on the importance of smoke cessation, since smoking is a modifiable cardiac risk factor.

The drug combinations that have protease inhibitors had more effect on the concentration of the lipids. A number of studies have been performed that evaluate indirect markers of atherosclerosis. (Kuritzkes and Currier 2003) All such studies have been small and in conclusive. The most conclusive of these studies is the Data collection on Adverse Events of Anti-HIV Drugs (DAD) study. (Friis *et al* 2003) shows that many well-recognized factors were associated with myocardial infarction. These include old age, current or former smoking, previous cardiovascular disease, male sex, higher total serum cholesterol level, higher triglyceride level, and the presence of diabetes. There is hyperlipidaemia in the patients on HAART therapy in poor resource limited settings. Although the values observed are not as high as what is observed in the developed countries.

It is important that physicians, nurses, AIDS service providers, and other health care professionals understand the potential liabilities and limitations of these drugs. Armed with these limitations, HIV caregivers will be in a position to more ably assist patients and clients in confronting the challenges posed by these drugs adverse effects. As a result, people living with HIV infection will enjoy an improved standard of care characterized by improved clinical outcomes and a higher quality of life.

Baseline lipid profile and lipid profile monitoring during therapy especially in the patients with preexisting cardiac risk factors is

recommended in limited resource countries.

In conclusion, Dyslipidemia is present in HIV/AIDS patients on HAART in black population of West Africa, although the level of dyslipidaemia is not as high as the observed in developed, industrialised countries.

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