American Journal of Pharmacy and Pharmacology
2014; 1(3): 23-27
Published online August 20, 2014 (http://www.aascit.org/journal/ajpp)

AASCIT American Association for Science and Technology

Keywords
HIV,
HAART,
Renal Function,
Liver Function

Received: July 30, 2014
Revised: August 14, 2014
Accepted: August 15, 2014

Effect of Highly Active Antiretroviral Therapy (HAART) on renal functions among persons living with HIV and AIDS (PLWHA) in Sokoto, North Western Nigeria

Mainasara A. S.[1, *], Isah B. A.[2], Ahmed A. Y.[1], Erhabor O.[1]

[1]Faculty of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto, Sokoto State, Nigeria
[2]Department of Community Health, College of Health Sciences Usmanu Danfodiyo University, Sokoto, Sokoto State, Nigeria

Email address
asnasara@hotmail.com (Mainasara A. S.)

Citation
Mainasara A. S., Isah B. A., Ahmed A. Y., Erhabor O.. Effect of Highly Active Antiretroviral Therapy (HAART) on Renal Functions among Persons Living with HIV and AIDS (PLWHA) in Sokoto, North Western Nigeria. *American Journal of Pharmacy and Pharmacology.* Vol. 1, No. 3, 2014, pp. 23-27.

Abstract
HIV/AIDS is a global public health problem. As of 2012, approximately 35.3 million people were living with HIV/AIDS worldwide. The aim of this descriptive comparative was to determine the effect Highly Active Antiretroviral Therapy (HAART) of Stavudine, Lamivudine and Nevirapine on renal function of Persons Living with HIV and AIDS (PLWHA) accessing care at Usmanu Danfodiyo University Teaching Hospital Sokoto, North Western Nigeria. The level of total protein, albumin and creatinine were determined in 90 HIV-infected subjects aged 20-50 years. Thirty HIV-seronegative, age and gender-matched individuals were monitored as controls. Seventy of the HIV/AIDS infected patients were on HAART while 20 of the patients were yet to commence HAART. The level of the serum total protein and albumin observed among HIV infected subjects (on HAART and those not on HAART) and HIV negative controls were not significant ($p > 0.05$). Significant difference was observed in serum creatinine of HIV infected subjects on HAART and those not on HAART ($p = 0.02$). The results show that HAART of Stavudine, Lamivudine and Nevirapine improves renal creatinine clearance functions among the HIV positive clients but have no effect on levels of total protein and albumin.

1. Introduction

Human Immunodeficiency Virus (HIV) is of retrovirus family that can lead to Acquired Immunodeficiency Syndrome (AIDS), a condition in humans in which the immune system begins to fail leading to life threatening opportunistic infections such as tuberculosis, pneumonia, diarrhoea, meningitis and tumors (1). The illness was first described in 1981 and HIV- 1 was isolated by the end of 1983 (2). Since then, AIDS has become a worldwide epidemic, expanding in scope and magnitude as HIV infections have affected many populations' across

the globe. Millions are now infected worldwide and once infected, individuals remain infected for life. Within a decade, if left untreated, the vast majority of HIV-infected individuals will develop fatal opportunistic infections as a result of HIV-induced deficiencies in the immune system. AIDS is one of the most important public health problems worldwide at the start of the 21st century (2).

HIV-associated nephropathy (HIVAN) is an important cause of renal failure in HIV-1 seropositive patients (3). Incidence of human immunodeficiency virus-1-associated nephropathy (HIVAN) is high among HIV-infected individuals (4-5). HIVAN can be the initial presentation of HIV-1 infection and can also develop late in the course of HIV-1 infection following the development of AIDS (6).

Antiretroviral drugs are medications for the treatment of infection by retroviruses, primarily HIV. The use of an approach involving a combination antiretroviral therapeutic agents is known as Highly Active Antiretroviral Therapy (HAART). The American National Institute of Health and other organizations recommend the offering of antiretroviral treatment to all patients with AIDS (7). The complexity of selecting and following a regimen, the severity of the side effects and the importance of compliance to prevent viral resistance led to the emphasis on the need to involve patients in therapy choices, timing, recommendation of the need to analyze the risks and the potential benefits to patients including those without symptoms (7-9).

Serum proteins are proteins found in blood plasma. Serum total protein in blood is about 7g/dl. The reference range of serum total protein in area of the study is 6-8g/dl. About 60% of the plasma proteins are made up mainly of the albumin, which is a major contributor of osmotic pressure of plasma and assist in the transport of lipids and steroid hormones. Globulins makes up 35% of plasma protein, 4% is fibrinogen and less than 1% of plasma proteins are in the form of enzymes, proenzymes and hormones (10). Creatinine is a breakdown product of creatine phosphate which is an important part of muscle. Creatinine is removed from the body entirely by the kidneys. If the kidney function is abnormal, creatinine levels will increase in the blood.

Highly active antiretroviral therapy involves the use of a combination of antiretroviral drugs in the effective management of HIV/AIDS. The current standard of care for people with HIV/AIDS indicated for treatment worldwide, is a combination of three or more antiretroviral drugs taken every day for life, known as Highly Active Antiretroviral Treatment (HAART). The introduction of highly active antiretroviral therapy (HAART) in 1996 led to a dramatic and sustained decrease in HIV-related morbidity and mortality (11). However, issues on adherence and adverse effects have become evident as limiting effect in a substantial proportion of individuals (12-13).The advantage of HAART over monotherapy is a significant reduction in the risk of development of resistant strains commonly seen with monotherapy. In this present study we investigated the effect of HAART made up of 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (stavudine and lamivudine) and one Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) (Nevirapine). There is paucity of data on the effect of HAART on the level of total protein, albumin and creatinine of PLWHA. The potential effect of HAART of stavudine, lamivudine and nevirapine on the renal function of HIV-infected Nigerians is unknown. The aim of this present descriptive comparative study was to determine the effect HAART on Persons Living with HIV and AIDS (PLWHA) accessing care at Usmanu Danfodiyo University Teaching Hospital Sokoto, North Western Nigeria.

2. Methodology

The study is descriptive comparative type comparing the liver and renal functions of the Patients that are HIV positive and on HAART to those that are not on HAART and HIV negative controls. The study was carried out in a tertiary medical facility in Sokoto, North Western Nigeria. The participants were recruited from the clients that were accessing care in the institution at the ART centre and controls from other speciality clinics not related to kidney or liver problems. The sample were collected and processed under appropriate and standard laboratory techniques.

2.1. Study Site

This present study was carried out at Usmanu Danfodiyo University Teaching Hospital (UDUTH) in Sokoto Nigeria. The hospital is a tertiary health institution located in Sokoto metropolis committed to the provision of quality tertiary healthcare services to the entire North-western region and neighboring border country - Niger Republic. The state is located between longitudes 11° 30□ to 13° 50□ East and latitude 4° to 6° North. It has a land area of about 28,232.37sq kilometer and stands at an altitude of 272 m above sea level near to the confluence of the Sokoto River and the Rima River. Sokoto state is at the extreme Northwest of Nigeria forming a border with Niger Republic. The state is in the dry Sahel surrounded by sandy terrain and isolated hills with an average annual temperature of 28.3°C (82.9°F). The weather is characterized by two seasons the wet and dry seasons. Rainfall (wet season) starts late around June and ends in September sometimes extending into October. The average annual rainfall is 550 mm with peak rainfall usually recorded in the month of August. The highest temperatures of 45°C during the hot season are experienced in the months of March and April. Harmattan, a dry cold and dusty condition is experienced between the months of November and February. Sokoto state had a population of 4.2million as at the 2006 census. The metropolis is estimated to have a population of 427,760 people (14)

made up of Hausa and Fulani majority and a minority of Zabarmawa and Tuareg and other non- indigenous settlers. The two major languages in the state is Hausa and Fulfulde is spoken among the Fulani. The main occupation of the people is grain production and animal husbandry. Majority of the indigenous people practice agriculture. Crops produced include commercial crops like millet, sorghum, beans, rice and maize. Other occupations commonly practiced are dying, blacksmithing, weaving, carving, trading, and cobbling. Sokoto ranks second in livestock production in Nigeria. Modern Sokoto city is a major commercial center in leather crafts and agricultural products. Occupation of city inhabitants also include trading, commerce, with a reasonable proportion of the population working in private and public sectors. Socio cultural characteristics is homogenous as majority of its indigenes and inhabitants are Muslims, therefore the doctrines of Islam provides the singular code of conduct and behavioral characteristics generally accepted across the State. Common practices are early marriage, polygamy, consanguity and multiple births.

2.2. Statistical Analysis

The data was entered into a preformed template of an SPSS computer statistical software version 17 and was analyzed accordingly. The results of this study (data) were analyzed using independent student t-test and the results were expressed as mean ± standard deviation. A p-value less than < 0.05 was considered as statistically significant.

3. Results

The level of total protein, albumin and creatinine were determined in 90 HIV- infected subjects aged 20-50 years. Thirty HIV-seronegative, age and gender matched individuals were monitored as controls. Seventy of the HIV/AIDS infected patients were on HAART while 20 of the patients were yet to commence HAART. The level of the serum total protein and albumin observed among HIV infected subjects (on HAART and those not on HAART) and HIV negative controls were not significant ($p > 0.05$). Table1 show the comparison of serum total protein and albumin (g/dl) among HIV –infected and HIV -negative controls. Significant difference was observed between serum creatinine of HIV infected subjects on HAART and those not on HAART ($p = 0.02$). Table 2 show the comparison between the serum creatinine (mg/dl) levels of HIV –infected subjects and HIV -negative controls.

Table 1. *Comparison for serum total protein and Albumin (g/dl) among HIV –infected and HIV -negative controls.*

Participant group	Number	Mean	Standard deviation	t-value	p-value
Total Protein					
HIV-infected on HAART [(a)]	70	7.16	0.73	0.52 [a,b]	
HIV-infected not on HAART [(b)]	20	7.06	0.94	1.73 [a,c]	>0.05
HIV- negative controls [(c)]	30	6.86	0.90	0.28 [b,c]	
Serum albumin					
HIV-infected on HAART [(a)]	70	3.77	0.88	1.71	
HIV-infected not on HAART [(b)]	20	3.43	0.76	0.14	> 0.05
HIV- negative controls [(c)]	30	3.79	0.61	1.89	

Key
a, b = Comparisms between subjects on HAART and those not on HAART
a, c = Comparisms between subjects on HAART and HIV-negative controls
b, c = Comparisms between subjects not on HAART and HIV-negative controls

Table 2. *Comparison for serum creatinine (mg/dl) among HIV –infected and HIV -negative controls.*

Participant group	Number	Mean	Standard deviation	t-value	p-value
Serum Creatinine					
HIV-infected on HAART [(a)]	70	0.96	0.30	2.30 [a,b]	0.02 [a,b]
HIV-infected not on HAART [(b)]	20	0.79	0.24	0.19 [a,c]	0.84 [a,c]
HIV- negative controls [(c)]	30	0.95	0.22	2.39 [b,c]	0.02 [b,c]

Key
a, b = Comparisms between subjects on HAART and those not on HAART
a, c = Comparisms between subjects on HAART and HIV-negative controls
b, c = Comparisms between subjects not on HAART and HIV-negative controls

4. Discussion

We compared the serum total protein of HIV-positive patient not on HAART with those on HAART and control (HIV negative). We observed that there was no significant difference ($p > 0.05$). This finding was in agreement with the previous report of Ogundahunsi and colleagues (15). There was also no significant difference when the level of albumin of HIV-positive patients on HAART were compared with Controls (HIV negative). There was also a non-significant difference when the albumin results of HIV-positive subjects not on HAART was compared with controls (HIV negative). This result is in agreement with the previous report by Ugwuja and co-workers (16). Our finding is however in contrast to previous report by Olawumi and Olatunji (14) who observed a significant

difference between pre-treatment and post- treatment serum albumin level among the patient on HAART.

There was a statistically significant increase in the level of creatinine among HIV-positive subjects on HAART compared with HIV-positive subjects not on HAART. This result was in agreement with previous reports (15, 16, and 18). This study has shown that renal dysfunction exists in HIV infected patient, the dysfunction was more evident in patient not on HAART compared to those receiving HAART. The results also shows that there is no statistically significant different in creatinine clearance between patients on HAART and HIV negative controls. This may be an indication that HAART may have protective effect on the renal functions of PLWHA. Many PLWHA particularly in Sub-Saharan Africa (SSA) present late for treatment majorly due to unaffordability and treatment-related stigma issues. Incidence of renal impairment is present in as high as 40% of PLWHA particularly in SSA (19). There is compelling evidence that highly active antiretroviral therapy (HAART) is effective in preventing end-stage renal disease in patients affected with HIVAN (3). Similarly, previous report by Levin and colleagues (20), indicated that HAART is associated with improved kidney functions among patients with baseline kidney problems. Similarly, a previous report by Lucas and colleagues (21) investigated the effect of HAART on human immunodeficiency virus-1-associated nephropathy (HIVAN) and observed that HAART was associated with a substantial reduction in HIVAN incidence. Our finding is however at variance with previous report which indicated that exposure to mono antiretroviral therapy involving Tenofovir (TDF) was associated with renal dysfunction *(22-23)*.Our finding highlights the therapeutic advantage of HAART over monotherapy.

5. Conclusion

The findings shows that there is no significant difference in serum total protein and albumin among the patient on HAART, patients not on HAART and HIV- negative controls. There is a statistically significant difference in renal creatinine between PLWHA on HAART, those not on HAART and HIV-negative controls. This study indicates that HAART of stavudine, lamivudine and nevirapine can potentially reverse the HIV/AIDS-related impairment in renal functions.

References

[1] Greener R. AIDS & Macroeconomics Impact" in S. Forsyth (ed.) States of the Art: AIDS and Economics IAEN 2002: 49-55.

[2] Brooks G.F, Carnoll K.C, Janet. S Butel, Morse S.A, Mietne T.A. "Jawetz, Melnick S. Adelberg's Medical Microbiology" McGraw-Hill Companies North American. 25th Edition 2010: 406-407.

[3] Lu TC, Ross M. HIV-associated nephropathy: a brief review. Mt Sinai J Med 2005; 72(3):193-199.

[4] Post FA, Campbell LJ, Hamzah L, Collins L, Jones R, Siwani R, Johnson L, Fisher M, Holt SG, Bhagani S, et al. Predictors of renal outcome in HIV-associated nephropathy. Clin Infect Dis 2008; 46(8):1282-1289.

[5] Szczech LA, Gupta SK, Habash R, Guasch A, Kalayjian R, Appel R, Fields TA, Svetkey LP, Flanagan KH, Klotman PE, et al . The clinical epidemiology and course of the spectrum of renal diseases associated with HIV infection. Kidney Int 2004; 66(3):1145-1152.

[6] Winston JA, Klotman ME, Klotman PE. HIV-associated nephropathy is a late, not early, manifestation of HIV-1 infection. Kidney Int 1999; 55(3):1036-1040.

[7] Dybul M, Fauci AS, Bartlett JG, Kaplan JE, Pau AK. Panel on Clinical Practices for Treatment of HIV "Ann. Intern. Med 2002; 137: 381–433.

[8] Holkmann Olsen C, Mocroft A, Kirk O, Vella S, Blaxhult A, Clumeck N, Fisher M, Katlama C, Phillips AN, Lundgren JD, et al. Interruption of combination antiretroviral therapy and risk of clinical disease progression to AIDS or death. HIV Med 2007; 8(2):96-104.

[9] When To Start Consortium, Sterne JA, May M, Costagliola D, de Wolf F, Phillips AN, Harris R, Funk MJ, Geskus RB, Gill J, et al. Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: a collaborative analysis of 18 HIV cohort studies. *Lancet 2009; 373(9672):1352-1363.*

[10] Anderson NL and Anderson NG. High Resolution Two Dimensional Electrophoresis of Human plasma proteins" Proceeding of the National Academy of Sciences 1977; 74(12): 5421-5425.

[11] Fauci AS, Lane HC. Human immunodeficiency virus Disease; AIDS and related Disorders. In: Kasper DL, Fauci AS, *et al.* editors. Harrison's Principle of Internal Medicine. 16th ed. New York: McGraw-Hill Co; 2005:1076-1079.

[12] Qurishi N, Kreuzberg C, Luchters G, Effenberger W, Kupfer B, Sauerbruch P. Effects of antiretroviral therapy on liver-related mortality in patients with HIV and hepatitis C virus co-infection. Lancet 2003;362:1708-1713

[13] Chijioke A. Nwauche, Osaro Erhabor, Oseikhuemen A Ejele, Chris I Akani. Adherence to antiretroviral therapy among HIV-infected subjects in a resource - limited setting in the Niger Delta of Nigeria. African Journal of Health Sciences 2006;13 (3-4):13-17.

[14] NPC/FRN (2006). Nigeria Population Commission, Federal Republic of Nigeria. Special FGN. Gazette number 23 on the 2006 Population Census.

[15] Ogundahunsi, O. A, Akinyele, Oyegunle, V. A, Ambali, A. A, Mbacham, W. The prevalence of renal disorder in HIV/AIDs patients on HAART. Int J Biomed & Health. Sci 2008; 4 (1): 1-4.

[16] Ugwuja EI. An assessment of renal functions in HIV-seropositive patients at Ebonyi State University Teaching Hospital, Abakaliki, South Eastern Nigeria. International Journal of Biomedical and Health Sciences 2010; 210-213.

[17] Olawumi HO and Olatunji PO. The value of serum albumin in pre-treatment assessment and monitoring of therapy in HIV/AIDS patients. British HIV Association, HIV Medicine 2006; 72006: 351–355.

[18] Emem P, Arogunde F, Sanusi A, Adelusola K, Wokoma F and Akinsola A. Renal disease in HIV seropositive patients in Nigeria: an assessment of prevalence, clinical features and risk factors. Nephro Dialysis transplantation 2008; 23 (2): 741-746.

[19] Isaac M K, Loren M D, and Judith A.H. Late disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in sub-Saharan Africa. Journal of immune deficiency syndrome 1999; 52(2): 280.

[20] Levin J, Kalayjian R, Machekano R, Crane H, Kitahata M, Multani A, Salata R, Willig J, Kestanbaum B, Krishasami Z, and Rodriguez B. HAART is associated with improved kidney function in patients with impaired kidney function at baseline but was associated with slight worsening of kidney function in patients with normal baseline kidney function. Conference on Retroviruses and Opportunistic Infections San Francisco CA February 2010: 16-19.

[21] Lucas GM, Eustace JA, Sozio S, Mentari EK, Appiah KA, Moore *RD* . Highly active antiretroviral therapy and the incidence of HIV-1-associated nephropathy: a 12-year cohort study. *AIDS 2004; 18(3):541-546.*

[22] Chaisiri K, Bowonwatanuwong C, Kasettratat N, Kiertiburanakul S. Incidence and risk factors for tenofovir-associated renal function decline among Thai HIV-infected patients with low-body weight. Curr HIV Res 2010; 8(7):504-509.

[23] Côté HC, Magil AB, Harris M, Scarth BJ, Gadawski I, Wang N, Yu E, Yip B, Zalunardo N, Werb R, et al. Exploring mitochondrial nephrotoxicity as a potential mechanism of kidney dysfunction among HIV-infected patients on highly active antiretroviral therapy. Antivir Ther 2006; 11(1):79-86.