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Original Article

Assessment of the therapeutic success of antiretroviral combinations used in a HIV treatment center, Jos, Nigeria

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ABSTRACT

HIV/AIDS pandemic has been a health challenge worldwide. Antiretroviral therapy (ART) has been used to reduce viral load to an undetectable level. The study was aimed at evaluating the effectiveness of antiretroviral combinations used in a HIV treatment center, Jos, Nigeria. A retrospective cohort study of 321 adult HIV patients' folders was carried out from January 2010 to December 2010. A stratified data extraction form was used to extract relevant information from the patient's folders. Data analysis was done using SPSS software version 16, Chicago Illinois. The mean household size was 6.06, the number of HIV infected individuals per household was 1.41 and 0.94 persons per households had died of HIV/AIDS. There was a significant increase ($P < 0.05; P < 0.01$) in the CD_4 cell counts of the groups in combinations A (Truvada+ Nevirapine), B (Truvada + Efavirenz), E (Truvada+ Aluvia) and J (Lamivudine + Starvudine + Nevirapine) regimens. There was a significant increase ($P < 0.05; P < 0.01$) in the body weights of all the combinations except H (Combivir + Aluvia), I (Combivir + Nevirapine) and L (Lamivudine + Starvudine + Effavirenz). Drug combinations A (Truvada+ Nevirapine), B (Truvada + Efavirenz), E (Truvada+ Aluvia) and J (Lamivudine + Starvudine + Nevirapine) demonstrated an appreciable therapeutic success.

Keywords: Antiretroviral, Adherence, Opportunistic Infection, HIV/AIDS, HAART

INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is a disease (or syndrome) caused by a retrovirus called Human Immunodeficiency Virus (HIV) and characterized by profound immune system depression that leads to opportunistic infections, secondary neoplasm and neurological defect [1,2].
HIV is an RNA retrovirus that attacks CD_4 lymphocytes, macrophages and dendrite cells causing loss of body immunity and ultimately the clinical condition called AIDS. As a retrovirus, it is characterized by the possession of the reverse transcriptase enzyme which allows viral RNA to be transcribed into DNA and subsequently incorporated into the host cell genome [2]. The level of CD_4 cell counts and viral load among others determine the progression of HIV infection. The viral load increases while the CD_4 cell counts fall as HIV infection progresses to AIDS [3].

Social, cultural and political factors has influenced the transmission of HIV/AIDS within different regions of the world. Despite the fact that HIV can be isolated from a wide range of body fluids and tissues, the majority of infections are transmitted via semen, cervical secretions, breast milk, blood and blood products. The major routes of transmission include sexual intercourse, parenteral inoculation and mother to child transmission [3].

Progression from HIV infection to AIDS is often insidious, but once sufficient immunologic damage and immunosuppression have occurred, different signs and symptoms appeared, depending on the clinical severity and pathology of the disease. The common symptoms of HIV/AIDS, among others, include severe weight loss, chronic diarrhoea, persistent fever, oral candidiasis, pulmonary tuberculosis, pneumocystic pneumonia, ulcerative stomatitis and gingivitis. These symptoms are classified by WHO into clinical stages 1- 4 according to its severity [3].

The impact of HIV/AIDS worldwide has led to a unified approach in the management of the disease.

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Cheap and effective medications are needed for the treatment of HIV infected patients to reduce morbidity and mortality, improve quality of life and increase societal productivity. More than a decade has passed since highly active antiretroviral therapy (HAART) was first used for the treatment of HIV/AIDS [4]. Widespread use of HAART among patients with HIV in industrialized countries has resulted in significant reductions in morbidity and mortality [5]. Unfortunately only less than 10 % of those infected with HIV in Sub-Saharan Africa have access to these drugs. Barriers to their introduction have included competing health care needs, high cost and lack of proper testing and monitoring facilities for clinical outcomes. In recent years, production of inexpensive generic antiretroviral drugs, amplification of guidelines for HAART usage and increased global financial support such as PEPFAR (President's Emergency Plan For AIDS Relief), APIN (AIDS Prevention Initiative in Nigeria) for HIV/AIDS has led to successful drug treatment programs in Sub-Saharan Africa and Asia [4].

In 2001, the Federal Government of Nigeria initiated a national antiretroviral treatment program as part of an expanded response of care and support for People Living with HIV/AIDS (PLWHAs). Since 2004, Nigerian Government has received funding through the US President's Emergency Plan for AIDS Relief (PEPFAR) to scale up HIV care and treatment activities in multi-treatment centers throughout Nigeria [4].

HAART consists of triple drug therapy, where two nucleoside reverse transcriptase inhibitors are combined with one non-nucleoside reverse transcriptase inhibitor or with one protease inhibitor. For example, one such HAART consists of zidovudine (AZT), lamivudine (3TC), both nucleoside analog reverse transcriptase inhibitors, and indinavir (IDV), a protease inhibitor (AZT+ 3TC+IDV). Another triple drug combination consists of two nucleoside analog reverse transcriptase inhibitors (tenofovir and emtricitabine) plus a non-nucleoside inhibitor of reverse transcriptase. It was hoped that HAART treatment would lead to the possibility of purging the patient of the virus [4, 6].

Despite the spectacular results achieved using HAART, these combination therapies are not without side effects. The protease inhibitors, for example, can lead to abnormal redistribution of body fat, called lipodystrophy which may be quite disfiguring. Lipodystrophy results in loss of sub-cutaneous fat. There is enlargement of the dorsocervical fat pad ("buffalo hump"), enlargement of the breasts and fat accumulation around various organs (visceral fat). Some protease inhibitors also lead to red blood cell destruction (hemolytic anemia) and hemorrhage [6].

Success in HIV therapy is largely dependent on adherence, which is the patient's ability to follow a treatment plan, take medications at prescribed times and frequencies, and follow restrictions regarding food and other medications [3]. If the treatment instructions are not followed, it is likely that there will be treatment failure. This can have serious short and long-term consequences, such as an increase in viral load and a greater risk of developing drug resistance.

The Impact of Antiretroviral Protocols on the Dynamics of AIDS Progression in 240 vertically infected children was investigated and the results showed better clinical outcomes in the groups on HAART regimen [7]. Similarly the Effectiveness of Dual Antiretroviral Therapy in the Treatment of HIV Infection in 101 Children showed that, triple therapy was more efficient for a longer period and showed better virologic response than dual therapy [8].

The objective of this study was to obtain and compare information on the effectiveness of the different antiretroviral drug combinations using changes in major indicators such as CD_4 cells counts, weight of patients, opportunistic infections and adverse drug reactions.

METHODS

Study setting: The study was carried out at Faith Alive Foundation Hospital Jos, Plateau State. Nigeria, which is a Nongovernmental health care facility that offers humanistic, holistic services to about 10,000 people living with HIV/AIDS monthly.

Study design: The assessment was based on the retrospective cohort study of 321 adult HIV positive patients carried out from January 2010 to December 2010. A pre-tested stratified data extraction form was designed and used to extract relevant information from the patient's folder. The CD4+ cell counts and weight of the patients attending clinics were recorded every three months for each of the different drug combinations and for a period of twelve months. The different ARV combinations used were grouped as follows; A = TVD+ NVP (Truvada + Nevirapine), B = TVD/ EFV (Truvada + Efavirenz), C = 650 FDC (Lamivudine + Zidovudine + Nevirapine), D = (Combivir + Efavirenz), E = (Truvada + Aluvia), F = (Tenofovir + Lamivudine + Nevirapine), G = (Tenofovir + Lamivudine + Efavirenz), H =

(Combivir + Aluvia) I = (Combivir + Nevirapine), J = 3TC + D4T + NVP (Lamivudine + Stavudine + Nevirapine), K = 3TC + AZT + EFV (Lamivudine + Zidovudine + Efavirenz), L = 3TC +D4T + EFV (Lamivudine + Stavudine + Effavirenz). Truvada contains Emtricitabine and Tenofovir disoproxil fumerate, Aluvia contains Lopinavir and Ritonavir while Combivir contains Lamivudine and Zidovudine.

Inclusion /Exclusion criteria: All adult HIV positive patients who were enrolled before January 2010 and were regularly keeping their clinic appointments and filling their prescription at the pharmacy were included. Exclusion criteria included pregnant HIV positive women and HIV positive patients of less than 15 years of age or HIV patients who were not regularly keeping their clinic appointments.

Ethical consideration: Application was made to the Research and Ethics Committee of the hospital and ethical clearance was obtained from the Committee of the hospital before the commencement of the study.

Statistical analysis: Data collected were entered into the Statistical Package for Social Sciences (SPSS) for windows version 16.0 (SPSS Inc, Chicago IL) for analysis. CD_4 cell counts and weight of patients, before and after treatment were analyzed using paired samples t-test. The chi-square test was carried out to establish associations between variables.

RESULTS

The mean household size was 6.06 while the average number of HIV infected individuals per household was 1.41 and about 0.94 persons per households had died of HIV/AIDS. Unemployment accounted for 41.4% of the patients (table 1). The data revealed influence of education on HIV infection 28.7% and 27.7% for secondary and tertiary levels of education respectively.

The mean CD_4 cell counts at the beginning of ARV therapy was 205.52±22.16. There were more patients (48.9%) on ARV combination A (Truvada+ Nevirapine) and the different combinations maintained appreciable CD_4 cells counts during the course of the therapy. There was a significant increase ($P < 0.05; P < 0.01$) in the CD_4 cell counts of the groups in combinations B (Truvada + Efavirenz), E (Truvada and Aluvia) and J (3TC + D4T + NVP (Lamivudine + Stavudine + Nevirapine) regimens (table 2). The mean body weight at the beginning of ARV therapy was 60.46±1.6. There was a significant increase ($P < 0.05; P < 0.01$) in the body weight of all the combinations except H, I and L (table 3). There were 28.7 % adverse drug reactions and 42.1% opportunistic infections among the patients under study (table 4). Treatment failure was 5.0 %, drug resistance was 1.6 % while adherence to therapy was 92.8 % of the total study group (table 4). Available data revealed that 35.3 % of patients suffered from malaria, 24.6 % had urinary tract infections (table 5) and 90.5 % of patients slept under long lasting treated mosquito net obtained from the hospital. Opportunistic infections were 80 % with drug combination L. Adverse drug reactions was high with combinations J and L. Those on antiretroviral regimen H however had neither adverse drug reaction nor opportunistic infections (table 6).

DISCUSSION

The demographic characteristics of the patients showed that the female HIV infected population (72.9 %) was more than twice that of the male population (27.1 %). This is in agreement with UNAIDS report on the global AIDS epidemic 2010 that more than half of all people living with HIV were women and girls [9]. The physiology of the female sex organ provides a more conducive environment for HIV transmission in addition to increased cases of sex abuse in Nigeria which might be responsible for this number. Effects of lamivudine, nevirapine and starvudine were investigated on 37 HIV infected patients in University of Benin Teaching Hospital the results showed that more females (56.7 %) than males (43.2 %) were HIV positive [10]. Also males rarely avail themselves for voluntary testing and counseling unlike the females who can easily be diagnosed during routine visits to antenatal clinics. The youths (aged 25 – 34 years) had higher prevalence of HIV infection as majority of them may have had sexual contacts between the ages of 15 – 24 years. This result is in agreement with other findings that 40.3 % of youths between the ages of 26-35 years were HIV positive [11]. 51.4 % of the population under study were married and involved in active sex compared with 53.1 % reported by Kenneth and his team [11]. The data also revealed that majority of HIV patients were married and came from polygamous homes and as such may have had multiple sex partners which is one of the indicators for the spread of HIV. There was a high prevalence of HIV infection (28.7 %) among patients with secondary level of education. While out of school at such an early and active age commonly found in the country results in redundancy, the fact that most of them can communicate in English and can travel freely to mix with opposite sex may be responsible for the

higher incidence. Unemployment is a major factor in the spread of HIV as this population may have had more time and traveled more in search of jobs. Although poverty has been shown to be responsible for higher prevalence of HIV in Sub-Saharan Africa, sexual and physical violence is also a key determinant of HIV prevalence.

The study revealed that more patients (48.9 %) were on drug combination A (truvada + nevirapine) and maintained an average CD_4 cell counts of about 520 cell/mm^3 throughout the 12 months of study. Increased mean CD_4 cell counts and body weight gain have been shown to be good indicators of immune response in patients receiving antiretroviral drugs [12]. There was a significant increase ($P<0.05$) in the mean CD_4 cell counts of the group receiving the drug combination B (truvada + efavirenz). There was consistent significant increase ($P< 0.05$, $P< 0.01$) in the mean CD_4 cell counts of the group receiving antiretroviral drug combination J (lamivudine + stavudine + nevirapine) consisting of two nucleoside reverse transcriptase inhibitors (NRTI) and one non-nucleoside reverse transcriptase inhibitors (NNRTI). A marked increase (86.48 %) in CD_4 cell counts of HIV infected patients on lamivudine + stavudine + nevirapine combinations has been reported. This is also in agreement with the findings that there is a steady increase in the mean CD_4 cell counts and body weight of patients on ART within the study period [11, 12].

There was a significant ($P< 0.05$, $P< 0.01$) increase in body weight of the patients receiving ARV combinations A, B, D, E and J respectively within the twelve months study period. Increased body weight is a prognostic indicator of HAART and it is an evidence of optimum body metabolism and utility of nutrients. It has been similarly reported that there was a significant increase in both the mean CD_4 cell counts and body weight of patients receiving HAART [12].

There were 92 (28.7 %) cases of adverse drug reactions (ADRs) out of which 80 % the highest case was associated with drug combination L (lamivudine+ stavudine + efavirenz). It has been reported that 15.7 % of patients initiated with stavudine and efavirenz based regimen had their drug switched because of either drug toxicity, intolerance or pregnancy [11]. There was no case of ADR associated with drug combination H (combivir + aluvia).

This study was limited by the exclusion of pregnant women and children. It was a retrospective study hence study design was based on available information.

CONCLUSION

The study demonstrated significant increase in CD4 cell counts of patients on antiretroviral regimen A (travuda+ nevirapine), B (Travuda + Efavirenz), E (truvada+ aluvia) and J (lamivudine + stavudine + nevirapine). There was also a significant increase in body weight of all the patients on different ARV regimen except combinations I (combivir + nevirapine), K (lamivudine + zidovudine + effavirenz) and L (lamivudine + stavudine + effavirenz). There were more incidences of opportunistic infection associated with drug combinations A, E, J and L. Adverse drug reactions were common in patients on drug regimen J and L.

Based on this study, drug combinations A, B, E and J have demonstrated a comparative therapeutic success throughout the period of study and are therefore recommended for prescribers using HAART programme.

Since choice of appropriate ARV combinations showed improved therapeutic outcomes in the study group, more research into the specific factors responsible for the effectiveness of these combinations should be done to achieve better treatment outcomes.

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Table 1: Demographic characteristics of patients

Variable	Frequency	Percentage (%)
Gender		
Male	87	27.1
Female	234	72.9
Age		
15-24	19	5.9
25-34	140	43.6
35-44	111	34.6
45-54	40	12.5
55-64	8	2.5
≥ 65	3	0.9
Marital status		
Single	82	25.5
Married	165	51.4
Divorced	7	2.2
Widowed	58	18.1
Widower	9	2.8
Educational status		
No education	30	9.3
Primary	70	21.8
Secondary	92	28.7
Tertiary	89	27.7
Not indicated	40	12.5
Occupation		
Unemployed	133	41.4
Employed	106	33.0
Self-employed	56	17.4
Students	17	5.3
Not indicated	9	2.8

N=321

Table 2: Mean CD_4 cell counts of different antiretroviral combination

ARV	N	0 month	3 months	6 months	12 Months
A	157	521.32 ± 20.61	527.90 ± 20.73	529.56 ± 18.08	539.50 ± 18.99
B	72	421.36 ± 29.15	463.40 ± 25.12	461.63 ± 24.26	465.21 ± 24.51*
D	12	493.33 ± 61.85	530.33 ± 59.43	490.17 ± 52.94	518.23 ± 52.91
E	15	369.33 ± 54.64	456.27 ± 45.51*	426.53 ± 43.18	435.53 ± 47.48
H	4	205.00 ± 12.06	235.50 ± 44.79	220.25 ± 34.26	265.50 ± 47.36
I	20	504.70 ± 46.27	508.15 ± 40.56	516.60 ± 37.29	528.75 ± 37.26
J	34	308.12 ± 36.90	417.47 ± 40.34**	404.82 ± 41.58*	436.71 ± 43.78**
K	2	233.50 ± 23.50	222.50 ± 34.50	272.50 ± 111.50	268.00 ± 107.00
L	5	483.20 ± 86.75	508.20 ± 113.57	497.20 ± 117.89	497.20 ± 117.88

** P < 0.05; **P < 0.01*

Table 3: Mean body weights of patients receiving different antiretroviral combinations

ARV	N	Body weight at 0 month	Body weight at 3 months	Body weight at 6 months	Body weight at 12 Months
A	157	62.48 ± 0.97	63.16 ± 0.99*	63.99 ± 1.00**	64.50 ± 1.07**
B	72	62.54 ± 1.28	63.76 ± 1.26*	64.17 ± 1.27**	64.94 ± 1.24**
D	12	68.62 ± 2.93	69.25 ± 2.59	70.17 ± 2.66	70.75 ± 3.15*
E	15	71.97 ± 4.04	73.07 ± 4.12	74.27 ± 4.02*	74.73 ± 4.23*
H	4	66.75 ± 6.07	64.50 ± 7.10	65.00 ± 6.56	65.25 ± 6.50
I	20	64.10 ± 2.33	64.40 ± 2.47	64.05 ± 2.28	64.68 ± 2.41
J	34	64.56 ± 2.47	66.26 ± 2.39	67.12 ± 2.43*	67.50 ± 2.41**
K	2	67.50 ± 4.50	67.25 ± 4.25	69.25 ± 4.25	69.25 ± 69.25
L	5	59.80 ± 11.10	58.80 ± 11.12	57.40 ± 9.75	58.40 ± 9.89

** P < 0.05; **P < 0.01*

Table 4: Occurrence of other indicators of therapy

Variable	Frequency	Percentage
Adverse drug reaction		
Yes	92	28.7
No	229	71.3
Opportunistic infections		
Present	135	42.1
Absent	186	57.9
Treatment failure		
Yes	16	5.0
No	305	95.0
Drug resistance		
Yes	5	1.6
No	316	98.4
Adherence		
Yes	298	92.8
No	23	7.2

Table 5: Prevalence of opportunistic infections amongst the population of HIV positive patients

Opportunistic Infection	Frequency (N=187)*	Percentage (%)
UTI	46	24.6
Malaria	66	35.3
Tuberculosis	5	2.7
Diarrhoea	28	15.0
Pneumonia	16	8.6
Typhoid	11	6.0

Herpes Zooster	3	1.6
Otitis media	1	0.5
Skin infection	6	3.2
Helminthiasis	1	0.5
Oral thrush	1	0.5
Sore throat	1	0.5
Others	2	1.0

*N > 135 (as some patients presented with more than one opportunistic infection)

Table 6: Relationship between ARV regimen, presentation of opportunistic Infections (OIs) and adverse drug reactions (ADRs)

ARV regimen	Number affected	OIs % of n	ADRs % of n
A	157	72 (45.9)	34 (21.7)
B	72	25 (34.7)	19 (26.4)
D	12	3 (25.0)	12 (41.7)
E	15	9 (60.0)	4 (26.7)
H	4	0 (0)	0 (0)
I	20	3 (15.0)	4 (20.0)
J	34	18 (52.9)	21 (61.8)**
K	2	1 (50.0)	1 (50.0)
L	5	4 (80.0)	4 (80.0)*

* *P < 0.05; **P < 0.01;* N = 321

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