

Adherence to antiretroviral therapy among HIV-infected subjects in a resource - limited setting in the Niger Delta of Nigeria

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SUMMARY

Since the early days of antiretroviral therapy, adherence has emerged a milestone to success. The objective of this study was to evaluate the factors militating against adherence to antiretroviral therapy among HIV-infected individuals in the resource – limited setting of the Niger Delta of Nigeria. A structured interviewer- administered questionnaire from consecutively recruited 187 HIV-infected patients on combination antiretroviral therapy of two-nucleoside analogue; stavudine and lamivudine and one non-nucleoside (nevirapine) was used. Association between the independent variables and adherence were analyzed using chi square analysis. This study observed an adherence level of 49.2% and identified the following as factors associated with non-adherence: cost of antiretrovirals, educational status, medication adverse effect, occupational factors, and high pill burden of prescribed regimen ($p < 0.05$). There is an urgent need for universal access and sustainability of antiretroviral therapy particularly in resource – limited settings. There is need for supervised medication delivery. Efforts should be made towards simplifying the therapeutic regimen to reduce the pill burden and substitution with treatment combination and strategies that minimize negative adverse effects, coupled with the re-intensification of patient's education and counseling.

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Introduction

HIV/AIDS remains the greatest health crisis in the world today with an estimated 40 million people now living with HIV/AIDS, 95% of them in developing countries [1]. With the development and widespread use of antiretrovirals in the developed world, there has been a transformed perception of HIV/AIDS from a fatal incurable disease to a manageable chronic illness [2]. This treatment causes improvement in immunologic status and a reduction in the viral load [3, 4] thus reducing the incidence of hospitalization and mortality [5, 6]. Treatment effectiveness however requires a high level of adherence to medication regimen [7]. Missing of even a few doses of antiretroviral medication can lead to drug resistant strains of HIV [8]. Low adherence has been associated with detectable viral load (> 500 viral RNA copies/ ml of plasma) [9] and with cross-resistance to other antiretrovirals of the same class [10, 11].

Cross-resistance can potentially interfere with future therapeutic regimens for HIV-infected patients undergoing treatment and for those who subsequently become infected with resistant strains

of HIV. Low adherence can lead to devastating public health problems. An adherent patient is defined as one who takes $> 95\%$ of the prescribed doses [12]. However a significant proportion of HIV-infected patients do not reach high levels of adherence. In this study we aim to determine the level of adherence and evaluate factors responsible for non-adherence to antiretroviral therapy among HIV-infected Nigerians.

Materials and Methods

A total of 187 consecutively recruited HIV-infected were prescribed antiretroviral drugs from June 2002 to January 2005. They were made up of 82 males and 105 females and were aged between 19 to 68 years (mean age 35.54 ± 9.42 years). They were recruited into the Federal Government subsidized antiretroviral therapy programme and the hospital antiretroviral initiative at the University of Port Harcourt Teaching Hospital. These constituted the subjects of this study. The hospital is a large 500-bed teaching hospital in the cosmopolitan oil rich city of Port Harcourt in the heart of the oil and gas industry of the Niger Delta of Nigeria. Inclusion criteria included age ≥ 18 years, use of antiretroviral therapy for a minimum

of 6 months, HIV positivity and willingness to give informed consent. The patients had received a fixed HAART of stavudine (40mg) lamivudine (150mg) and nevirapine (250mg) twice daily for a minimum of 6 months. Reasons for non adherence were assessed using a structured interviewer-administered questionnaire which included socio-demographic data of age, sex as well as employment status, current income, highest level of education, perception to adverse events associated with medication, perception to high pill burden of prescribed regimen, perception of cost of laboratory test for monitoring treatment outcome and reasons for non-adherence to treatment. The interviewers were trained social workers and counselors attached to the antiretroviral clinic in the hospital. All eligible participants were offered pre-interview counseling. The interview was carried out in English language except for 20 participants who could not understand English language who had to be interviewed in their local languages through the help of an interviewer. Inclusion criteria included age > 18 years, HIV positivity, minimum of 6 months use of antiretroviral use prior to the time of interview and willingness to give informed consent after counseling.

Statistical analysis

Data was entered and analyzed using a statistical package (Version 9 SPSS). Statistical analysis included descriptive analysis of mean, standard deviation and chi square analysis. Predictions of non-adherence were assessed with multivariate logistic regression. A p-value of ≤ 0.05 was considered significant in all statistical analysis.

Results

One hundred and eighty-seven (187) eligible respondents made up of 105 females (56.2%) and 82 males (43.8%), aged 19 – 68 years (mean age 35.51 ± 9.42) constituted the subjects for this study. Monthly income ranged from #500 to #75,000 (mean income $9,127 \pm 11,376$) Naira. Majority of respondents 80 (42.8%) were on monthly income less than the national minimum wage of # 7,500 (about \$54). All patients have had more than 6 months of antiretroviral treatment. Antiretroviral therapy consisted of a fixed HAART combination therapy of stavudine (40 mg), lamivudine (150 mg) and nevirapine (250 mg) orally twice daily. All patients used 6 or more pills per day. Patients were in two treatment groups; the Federal government of Nigeria subsidized initiative 121 (64.7%) under which antiretroviral regimen were accessed at a subsidized rate of #1000 (about \$7) and the

Hospital initiative 66 (35.3%) where drugs are accessed at the rate of #7,000 (about \$50). Respondent's marital status included single 85 (45.3%); married 75 (40.1%) divorced 11 (5.9%) and widowed 17 (8.6%). Baseline characteristics of subjects are shown in **Table 1**. Of the 187 participants on antiretrovirals 92 (49.2%) were adherent while 95 (50.8%) were non-adherent. Adherence was higher among respondents on the Federal government antiretroviral initiative 66 (55.5%) compared to the Hospital initiative (33.3%). Reasons for non-adherence ranged from; cost constraints 53 (55.8%) unavailability of drugs 18 (18.9%), medication side effects 17 (17.9%), doctor's strike 3 (3.2%), pregnancy 1 (1.1%) and job related transfers 3 (3.2%) ($X^2 = 8.93, p=0.01$). Medication - associated adverse events included; nausea and vomiting 3(17.6%), Steven Johnson's syndrome 9(52.9%), jaundice 2(11.8%) and leg swelling 3(17.6%). History of non-adherence to therapy was compared based on educational status.

Non-adherence was relatively higher among less-educated respondents with non-formal education 30 (31.6%) and primary education 27 (21.1%) compared to better educated with secondary 20(21.1%) and tertiary education 18 (18.9%). This difference however was not statistically significant ($X^2 = 2.73, p = 0.32$). Non-adherence was compared based on occupational groups. Non-adherence was significantly higher among applicants 30 (31.6%) compared to other professional groups ($X^2 = 6.11, p = 0.01$). Of the 187 respondents, 23 (12.3%) claimed to have shared their medication with their HIV-infected spouses 19 (82.6%) and children 4 (17.4%) due to cost constraints. Respondent's perception to pill burden of prescribed regimen prescribed indicated that 139(74.3%) had a negative perception to a high pill burden and would prefer a regimen with a low pill burden while 48(25.7%) had a positive perception ($p = 0.001$). The reasons for non-adherence are shown in **Table 2**.

Unavailability of drugs was the observed reason for non-adherence to antiretroviral regimen among 18.9% of non-adherent respondents. Adverse events associated with medication were the cited reason for non-adherence in 17.9% of non-adherent respondents. Non-adherence was relatively higher among less- educated respondents without formal education (31.6%) and primary education (28.4%) compared to better-educated with secondary (21.1%) and tertiary education (18.9%). The level of adherence based on marital status, educational status and occupation is shown in **Table 3**.

Table 1: Baseline characteristics of respondents

| Characteristics | Adherent Respondents n (%) | Non-adherent Respondents n (%) | p- values |
|-------------------------------------|-------------------------------|-----------------------------------|-----------|
| Age | | | |
| Median (range) | 35.04 ± 8.06 | 34.21 ± 7.64 | 0.32 |
| Income | | | |
| Median (range) | 29,740 ± 8.93 | 7,624 ± 5.81 | 0.001 |
| Sex | | | |
| Males | 24 (26.1) | 58 (61.1) | 0.001 |
| Females | 66 (73.9) | 37 (38.9) | |
| Adherence based on treatment groups | | | |
| Hospital initiative | 22 (33.3) | 44 (66.7) | 0.001 |
| Federal government | 66 (55.5) | | |

Table 2: Reasons for non-adherence to therapy

| Reason for non-adherence | n | % | p-value |
|--------------------------|----|------|---------|
| Non-availability | 18 | 19.0 | 0.001 |
| Cost constraint | 53 | 55.8 | |
| Medication side effects | 17 | 17.9 | |
| Doctors strike | 3 | 3.2 | |
| Pregnancy | 1 | 1.1 | |
| Job-related | 3 | 3.2 | |

Discussion

Since the early days of antiretroviral therapy, adherence has emerged as a milestone to success and had remained the most potent predictor of effectiveness. We observed a low adherence rate of 49.2%. Our observed adherence rate is consistent with a 49% observed in a previous study [13]. It is however lower than that obtained in a similar study in which 69% of patients used 95% of prescribed medication [14]. The exorbitant cost of

antiretrovirals in Nigeria a country with a very low per capital income may have been responsible for the low adherence rate observed in this study. The experience in South Africa a country where reduction in the prices of antiretrovirals has greatly improved adherence brings to bear the potential benefits that prize reduction may have on adherence to therapy particularly in resource-poor settings in sub Saharan Africa.

Table 3: Adherence to therapy based on marital status, educational status and occupation.

| Variable | n (%) | n (%) | p-value |
|----------------------------|-----------|-----------|---------|
| Marital status | | | |
| Single | 47 (51.1) | 38 (40.0) | 0.004 |
| Married | 35 (38.0) | 40 (42.1) | |
| Divorced | 4 (4.3) | 7 (7.4) | |
| Widowed | 6 (6.5) | 10 (10.5) | |
| Educational status | | | |
| Non formal | 21 (22.8) | 30 (31.6) | 0.005 |
| Primary | 19 (20.7) | 27 (28.4) | |
| Secondary | 27 (29.3) | 20 (21.1) | |
| Tertiary | 25 (27.2) | 18 (18.9) | |
| Occupational groups | | | |
| Business | 5 (5.4) | 10(10.5) | 0.001 |
| Health care worker | 1 (1.1) | 1(1.1) | |
| Clergy | 1(1.1) | 2(2.1) | |
| Applicants | 19 (20.7) | 30(31.6) | |
| Armed forces | 4 (4.3) | 4(4.2) | |
| Artisan | 22 (23.9) | 14(14.7) | |
| Civil servant | 17 (18.5) | 12(12.6) | |
| Farmer | 1 (1.1) | 5(5.3) | |
| House wife | 6 (6.5) | 6(6.3) | |
| Students | 16 (17.4) | 11(11.5) | |

Non-adherence was significantly higher among unemployed respondents compared to other groups. Also the adherence was significantly higher in patients on the highly subsidized Federal government initiative compared to the more expensive hospital initiative. Cost constraints were the major reason for non-adherence in 55.8% of non-adherent patients. We observed a mean monthly income of # 9,127 ± 11,376 Naira (about \$ 65). There is need for reduction in the cost of antiretrovirals. High pricing of antiretrovirals and associated low monthly income are major factors associated with non-adherence to antiretroviral particularly in resource-limited settings [14, 15, 16]. Cost constraints have remained a limiting factor on adherence to antiretroviral agents. National government particularly those in sub-Saharan Africa have prolonged reluctance to provide the best possible treatment citing numerous concerns ranging from cost to the ability of patients to adhere to complex life long treatment.

South Africa a country with more than 5 million citizens living with HIV/AIDS has proved the pundits wrong. The prices of antiretrovirals having precipitously plummeted by more than 95% as a result of government developing the desired political will to take the challenge of universal access to treatment. This strategic and humanitarian obligation has resulted in an increase in adherence to a high level of more than 90%. The World Health Organization must remain resolute on their initiative to get 3 million people living with HIV/AIDS in resource-limited settings, on antiretroviral therapy by the end of 2005. This is likely to become a giant step toward achieving the goal of universal access particularly in resource – limited setting in sub-Saharan Africa where paradoxically the greatest disease burden exist but with less than 8% having access [1].

Unavailability of drugs was the observed reason for non-adherence to antiretroviral therapy among (18.9%) of non-adherent respondents. Evaluation of most antiretroviral initiative in resource-poor setting has shown that the purchase, supply and distribution of antiretrovirals are not properly coordinated. In most cases there is no adhoc plan and no commodity management plan. This has often led to stock out and expired drugs thus producing a negative effect on adherence to therapy [14].

Adverse events associated with medication were the cited reason for non-adherence in (17.9%) of non-adherent respondents. Antiretroviral associated adverse events can contribute a lot to the degeneration of HAART –related quality of life of HIV-infected [17]. It is unfortunate that up to 25% of HIV-infected patients discontinue their initial HAART regimen because of toxic effect of therapy [18]. There is need to find treatment combinations and strategies that minimize these negative effects.

Low adherence can result in cross-resistance to other antiretrovirals [18]. Cross-resistance can potentially interfere with future therapeutic option for those being treated and those who subsequently become infected with resistance virus.

Non-adherence was relatively higher among less educated respondents compared to better educated (secondary and tertiary). Speculatively better educated people generally have greater access to information and are more likely to make better-informed decisions. They generally have better jobs and greater access to money to regularly procure their drugs and support healthier and productive lives. Low adherence can have a devastating effect on the individual and can also pose an even greater problem for public health.

A significant majority of respondents indicated a negative perception to the high pill burden of antiretroviral regimen prescribed. Difficulty in taking large number of pills can negatively affect adherence to therapy [19]. Efforts should be made towards simplifying therapeutic regimen to reduce the number of daily doses. Increasing the simplicity of antiretrovirals promotes adherence and leads to extremely high therapeutic success in both developing and developed countries. A significant majority of respondents (94.1%) believed that the use of mechanical aids like pagers and pills boxes could improve adherence to therapy. Emphasis on instruction of patients to take medication is fundamental as well as patient's participation in treatment decisions is advocated [20]. It is also important to stimulate the patients to implement therapeutic regimen into their daily routine.

There is an urgent need for universal access and sustainability of antiretroviral therapy in resources – poor settings particularly in sub-Saharan Africa. Increasing the simplicity of antiretroviral regimens and substitution of regimens associated with significant adverse effects could potentially improve adherence to therapy. Provision of family and social support coupled with a re-intensified patient's education and counseling can potentially promote adherence, lead to high therapeutic success and reduce the incidence of drug resistance.

Conclusion

This study indicates a low level of adherence to antiretroviral therapy. There is an urgent need for universal access and sustainability of antiretroviral therapy particularly in resource – limited settings. There is need for supervised medication delivery. Efforts should be made towards simplifying the therapeutic regimen to reduce the pill burden and substitution with treatment combination and strategies that minimize negative adverse effects, coupled with the re-intensification of patient's education and counseling

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