The magnitude of intentional non-adherence to antiretroviral therapy among patients attending HIV care and treatment clinic at Muhimbili National Hospital, Dar es Salaam, Tanzania

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Abstract

Background: Suppression of viral replication is the goal of antiretroviral therapy. It is one of the most important factors influencing long-term prognosis of HIV infection. Non-adherence increases the risk of viral mutations which can result in cross-resistance and thus the risk for therapy failure.

Objectives: To determine the magnitude of intentional non-adherence to antiretroviral therapy among patients receiving antiretroviral therapy comprised of two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor at the HIV care and treatment clinic (CTC) of Muhimbili National Hospital (MNH) in Dar es Salaam, Tanzania.

Method: A total of 250 patients were recruited between July 2007 and January 2008 at the HIV CTC of MNH. A structured questionnaire was used for interviewing the patients in order to assess intentional non-adherence through recall, as well as the presence of solicited antiretroviral drugs (ARVs) related side effects during the past 3, 7 and 30 days respectively, since ARV initiation. In addition, clinical (weight changes and incident opportunistic illnesses) as well as immunological (CD4 count) progress in the past 2 years was ascertained through review of patients' clinical documents.

Results: About half (45.6%) of the patients reported to have experienced the side effects associated with ARVs. Most patients (70.1%) experienced peripheral neuropathy. Other side effects reported included; skin itching/rashes (19.6%), breast enlargement (10.3%), abdominal pain (7.5%), dizziness (5.6%), lipodystrophy (4.7%), vomiting (3.7%), poor vision (2.8%), nausea (1.9%), and headache (1.9%). A total of 18 (7.2 %) patients reported to have ever missed taking their medications. Four patients (1.6%) reported to have skipped their medication in the past 3 days; two (0.8%) in the past 7 days; and twelve (4.8%) in the past 30 days. Only 3 (1.2%) patients admitted to have intentionally skipped their doses due to the side effects they experienced while taking ARVs. The median CD4 count and mean body weight increased from 206 cells/µL and 62 kg to 311 cells/ µL and 65 kg, respectively, during a period of previous 24 months.

Conclusion: ARV related side effects were common among patients attending the MNH CTC, but these did not result into significant intentional non-adherence. It is however recommended that a more comprehensive study involving a larger number of patients at different ART providing sites in the country be conducted so as to make a more comprehensive conclusion on this subject. Studies involving self-reported adherence and plasma ARVs concentration measurement area are also necessary in order to make a good correlation of adherence self-reporting and the actual amount of the drug in the blood.

Key words: Intentional non-adherence, ARVs, CD4, Weight change, HIV, Antiretroviral therapy

Introduction

Lasting suppression of viral replication is the goal of antiretroviral therapy (ART) and one of the most important factors influencing long-term prognosis of HIV infection.[1,2] Factors associated with the failure of viral suppression and progression to AIDS or death are low CD4 cell counts and viremia at the start of ART, adverse drug reactions, and non-adherence to ART.[3-5] Non-adherence increases the risk of viral mutations, which can result in cross-resistance to other medications or transmission of multi-resistant virus strains, and thus the risk for initial therapy failure in subsequently infected individuals. Although preliminary evidence indicates that even high and sometimes complete adherence does not prevent accumulation of HIV drug resistance mutations, suboptimal adherence remains a critical issue in the development of resistance.[6]

As a result of a high and constant rate of replication and mutation of HIV, it has been suggested that a level of at least 95% adherence is required in order to maintain undetectable viral load.[7] Non-adherence is not only the most common cause of therapy failure, but it also represents one of the most important factors that health services can manage to reach a higher effectiveness of treatment. Thus patient adherence to and persistence with ART are crucial factors in achieving virological and immunological success and avoiding resistance.

Numerous studies have evaluated the reasons why patients "accidentally" miss doses of antiretroviral drugs (ARVs), but few have evaluated the reasons why patients `intentionally` skip doses.[8-10] Medication side effects are one of the main causes of people intentionally becoming non-adherent. Non-adherence because of side effects is a more complicated problem. Some side effects of ART are easier to manage than others. For example, if one is having diarrhea, one's health-care provider may be able to prescribe a medication that works very well against diarrhea. However, other side effects, such as the body changes that occur with lipodystrophy, are more difficult to manage and there is no standard way of approaching this problem. If the side effects are manageable then one should continue on the same regimen. If the side effects are not manageable or severe, then one should discuss the possibility of switching therapy with their health-care provider. Switching therapy because of unmanageable side effects may lead to a better outcome because the reason for the non-adherence has been addressed. The new regimen may have a different set of side effects, however, so a discussion with the health-care provider about these should take place prior to the switch.[8,9]

A recent survey conducted in some ART providing sites in Dar es Salaam indicated the lack of enough adherence strategies that have been put in place (unpublished data). Thus although ART is promising, the issue of adherence needs to be addressed critically so that the expected benefits of therapy are achieved. It is known that ARVs are associated with side/adverse effects which may greatly impair adherence. The aim of the present study was therefore to explore the magnitude of intentional non-adherence due to adverse effects by patients receiving ARVs at Muhimbili National Hospital (MNH) and the influence of such adverse effects on adherence.

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Methodology

Study design and area

This was a cross-sectional analytical study of a cohort of antiretroviral recipients who have been using ARVs for at least 6 months at the MNH ART clinic.

Methods

Responses from 250 patients were obtained through interviewing the patients at MNH ART care and treatment clinic (CTC) between July 2007 and January 2008. Structured questionnaire was used to gather the information. Prior to conducting the study, the questionnaire was pre-tested in 15 patients at MNH. Gaps were identified and the final version of the questionnaire was prepared and used for data collection. Interviews went hand in hand with recording patients' clinical and immunological progression over the last 2 years (past 24 months) in terms of weight changes and opportunistic infections as well as CD4 count profile from their files. The questionnaire contained questions regarding demographic information and 3-days, 7-days, and 30-days recall of adherence. Patients were asked if they have ever missed or skipped doses because of not feeling well or having adverse symptoms due to the effects of the drugs they are taking. Information pertinent to use of other non-ARV medications, side effects they experienced, eating habits, drinking and smoking were also captured.

Data analysis

The data collected was analyzed using the Statistical Package for Social Sciences (SPSS, version 10) computer programme. Summary statistics were employed to describe categorical data. The chi square and Fishers exact tests were used to compare proportions between females and males who were experiencing ARVs side effects. A p-value of less than 0.05 was regarded as significant.

Ethical Issues

The study received ethical permission from MUHAS Research and Publications Committee. Having been given the relevant information regarding the purposes of the study enrolled patients were also provided with written consent. Permission to conduct the study at MNH was obtained from the hospital management. All the information obtained was kept strictly confidential, and none of the patient's responses were recorded into their medical records. No names of the patients were recorded in the questionnaire and data were entered into the computer using only study code numbers.

Results

A total of 250 ARVs recipients attending the HIV and AIDS CTC at MNH were involved in this study. Table 1 shows the summary of socio-demographic characteristics of the 250 patients that were recruited for the study. The study population comprised of 61 (24.4%) males and 189 (75.6%) females. Eleven (4.4%) of these patients had no any formal education, 141 (56.4%) had acquired primary education, and 98 (39.2%) had Secondary to Tertiary education. Twenty six (10.4%) patients were 18-30 years of age, 137 (54.8%) were 30-44 years and 87 (34.8%) were above 45 years.

Table 1. Socio-demographic characteristics of the study participants

Socio-demographic characteristics	No.	Percent
Age (years)		
<30	26	10.4
30-44	137	54.8
45 and above	87	34.8
Sex		
Male	60	24.1
Female	189	75.9
Education		
None	11	4.5
Primary	138	55.9
Secondary and above	98	39.7

The drug regimen provided to patients included combinations of: Stavudine, Lamivudine, Nevirapine; Stavudine, Lamividine, Efavirenz; Zidovudine, Lamivudine, Nevirapine and Zidovudine, Lamivudine, Efavirenz. A total of 114 (45.6%) patients reported to have experienced side effects associated with ARVs. As shown in table 2, most patients (70.1%) experienced peripheral neuropathy.

Table 2. Type and frequency of side effects experienced by male and female patients using ARVs at Muhimbili National Hospital (n = 114).

Side effect	Total (107)		M (n = 24)		F (n = 83)		p-value
	No.	%	No.	%	No.	%	
Peripheral neuropathy	73	68.2	19	79.2	56	67.5	0.27
Skin itching/ rashes	21	19.6	6	25.0	15	18.1	0.56
Breast enlargement	11	10.3	1	4.2	10	12.0	0.45
Abdominal pain	8	7.5	0	0	8	9.6	0.19
Dizziness	6	5.6	2	8.3	4	4.8	0.61
Lipodystrophy	5	4.7	0	0	5	6.0	0.58
Vomiting	4	3.7	1	4.2	3	3.6	1.00
Poor vision	3	2.8	0	0	3	3.6	1.00
Nausea	2	1.9	1	4.2	1	1.2	0.40
Headache	2	1.9	1	4.2	1	1.2	4.40

There were multiple responses in which an individual indicated to have experienced more than one side effect. Table 2 further shows that no statistically significant differences were seen between males and females in terms of the proportion of experiencing the side effects (p> 0.05). Out of those who experienced the side effects, 53% mentioned that they informed their care providers. For those who informed their care providers about the side effects they were experiencing, 57.1% were told to continue with the medication, while 28.6% had their medications changed.

A total of 18 (7.2%) out of 250 patients reported to have ever missed taking their medications. Four subjects (1.6%) reported to have skipped their medication in the past 3 days, 2 (0.8%) in the past 7 days and 12 (4.8%) in the past 30 days. The days for recall of adherence were counted retrospectively from the date of interview. Only 3

(1.2%) of the 250 subjects admitted to have intentionally skipped their doses due to side effects they experienced when taking ARVs.

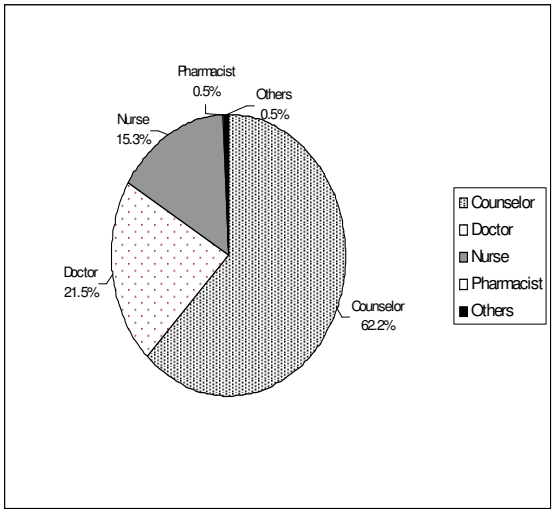

Figure 1. Health care providers who informed patients on the possible side effects of ARVs.

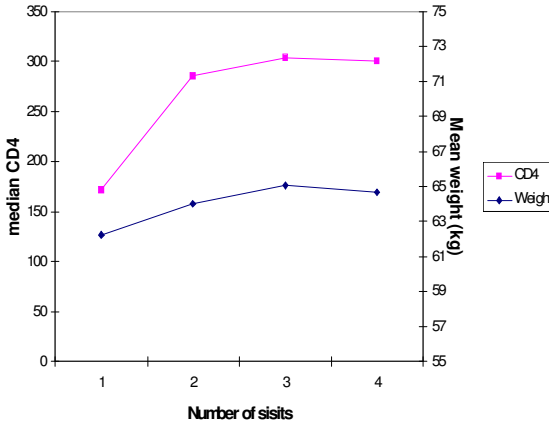

Figure 2. Profile of median CD4 count and mean weights of patients during two years follow up.

Majority of the patients (83.6%) indicated that they were given information and counseled on ARVs side effects prior to their commencement of treatment. Most of them (62.0%) received this information from their CTC counselors. The other care providers mentioned to have given drug information were Doctors and Pharmacists (Figure 1). Regarding advice on what to do in case side effects are experienced, majority (43.6%) were told to report to the hospital. Other advises given included; to see the Doctor (34.8%), to contact a Pharmacist (0.4%) or to continue with the drugs if side effects are not severe (1.2%).

A positive change in CD4 count and weight gain was observed during the previous 24 months. A progressive increase in median CD4 count and mean body weight of study subjects during treatment over the previous 24 months was noted as depicted in figure 2. Indeed the median CD4 count increased from 206 cells/μL to 311 cells/μL during this period. Similarly, the mean body weight increased from 62 kg to 65 kg. On the other hand, no severe opportunistic infections (defined as those that required hospitalization and/or discontinuation of medications) were recorded in these patients.

Discussion

Non-adherence to medication amongst patients treated for HIV and AIDS clearly exists and there is some evidence to suggest that differences exist between those who forget and those who choose not to adhere to medication because of several reasons. Some studies have shown that intentional non-adherence to antiretroviral therapy is common among persons experiencing therapy-related side effects.[8-10] Although the type and severity of adverse effects impact intentional non-adherence, this activity occurs in relation to symptoms regardless of their strict clinical relevance.[8]

The results of this study indicate that adverse drug effects were very common among ARVs users, since 45.6% of the study participants reported to have experienced one or more side effects during the past two years. Peripheral neuropathy was the commonest side effect with 70.1% of the patients reporting to have been experiencing this problem. This is not surprising since more than 95% of the assessed patients did indeed receive a stavudine containing regimen which is known to be associated with peripheral neuropathy.[11] However, despite experiencing the side effects majority of patients continued to use the medications. This is an indication that counselors at the care and treatment centre of MNH do play a significant great role in facilitating appropriate use of ARV therapy.

The degree of intentional non-adherence was found to be very low in this study. The proportion of patients who admitted to have intentionally skipped their doses due to side effects was found to be 1.2%. This is a low figure when compared to the findings of other similar studies that were conducted in Canada, Italy and France.[9,10] Furthermore, this proportion of intentional non-adherence is relatively low as compared to the results of the study conducted in British Columbia in which 11% of the study population admitted to have either selectively skipped their medications or to have taken a drug holiday in order to ameliorate symptoms due to their medications against their physicians' recommendations.[8] Also our results show a relatively small number of patients (7.2 %) who admitted to have ever missed taking their medications due to several reasons including forgetting to take the pills or taking them at the wrong time. The differences could be due to effectiveness of adherence given, or inherent in the characteristics of patients themselves.

The study conducted by Ammassari *et al* in 358 subjects receiving ARVs showed that 22% of the patients were found to be non-adherent.[9] In the latter study, the non-adherent group also had higher mean overall symptom score, indicating a possible association between their non-adherence and the symptoms they were experiencing. Our figures on non-adherence are also very low compared to those reported by Duran *et al* who assessed the impact of

side effects on adherence to Highly Antiretroviral Therapy (HAART) among 336 patients taking a triple-combination regimen (two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and one Protease Inhibitors (PI)).[12] In that study, 33% of the patients were unable to maintain complete adherence due to side effects. In the present study, the 3 patients out of the 250 patients who admitted to have intentionally skipped their doses due to side effects were all males in the age group of 30-44 years and all had acquired formal education. The findings by Heath *et al* showed that a high proportion of the non-adherent group had low level of education.[8] However, such a conclusion can not be made in our study due to a very small number of non-adherent patients.

The high rates of intentional non-adherence due to side effects in the studies by Heath *et al*[8], Ammassari *et al*[9] and Duran *et a*[1(10)] as compared to our results may be attributed by many factors. ARVs regimen used in the three studies[8-10] were HAART that includes a PI whereas in our study all of the patients were on the combination of two NRTI and one None-Nucleoside Reverse Transcriptase Inhibitor (NNRTI). The reported high rates of PI-induced side effects might partly explain the differences observed in these two sets of studies.[13]

Similar to other studies[8-10], the assessment of adherence in the present study was based on patient-self reporting. Although patients were sensitized on the objectives of the study, some patients might still not be willing to tell the truth if they have missed their doses fearing that revealing intentional non-adherence might impact negatively on their care and treatment at the hospital. However, the findings of this study indicate that patients at MNH are well counseled on the importance of strict adherence to ARVs. This is also supported by the improvement in CD4 count, weight change profile and disappearance of opportunistic infections during treatment. The immunological and clinical improvement of patients in this study is therefore in correlation with the patients' self-reported adherence.

Conclusion and Recommendations

ARV related side effects were common among patients attending the MNH CTC, but these did not result into significant intentional non-adherence. It is however recommended that a more comprehensive study involving a larger number of patients at different ART providing sites in the country is conducted so as to make a more comprehensive conclusion on this subject. In addition, studies involving self-reported adherence and plasma ARVs concentration measurement are necessary so as to make a good correlation of adherence self-reporting and the actual amount of the drug in the blood.[12]

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