Self-reported adverse effects as barriers to adherence to antiretroviral therapy in HIV-infected patients in Pretoria

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Abstract

Background: Adherence is the key to the effectiveness of antiretroviral therapy. However, many factors have been identified as facilitating or hampering adherence. The aim of this study was to determine barriers and facilitators of adherence with particular emphasis on adverse effects.

Methods: A survey of patients, who started antiretroviral treatment between July 2004 and August 2005, was conducted by means of a semi-structured questionnaire. Those who consented to participate were interviewed for the collection of information on sociodemographic characteristics and clinical and other data.

Results: The 180 patients who participated had a mean age of 36.7 ($\pm$8.1); 68.8% were female, 86.7% unemployed, 73.9% had a high school level of education, and 77.8% were single. Some 8.9% of the respondents used at least one non-prescribed medicine, while 34.4% received disability grants. Overall, 94% of the respondents reported at least one side effect; the mean number of self-reported side effects was 2.6 ($\pm$ 1.4). With regard to adherence, the mean number of doses missed during the last seven days prior to the interview was 2.7 ($\pm$3.9), ranging from 0 to 18. The mean adherence level was 92.3%, ranging from 48.6% to 100.0%; overall, only 57.2% reported taking at least or over 95% of their prescribed doses. The two most common reasons for missing doses were forgetting (26.6%) followed by being away from home (15.6%). In the bivariate analysis, the only facilitator or factor that was significantly associated with at least or over 95% self-reported adherence was eating well (80.6% vs 64.5%; p = 0.025), whereas barriers or factors more likely and significantly associated with with self-reported adherence of at least or over 95% included having used non-prescribed medicines (15.6% vs 3.9%; p = 0.008), having suffered from headaches (28.6 vs 14.6%; p = 0.026) and reported symptoms such as insomnia (27.3% vs 12.6%; p = 0.013) and abdominal pain (20.8% vs 9.7%; p = 0.037). In the multivariate analysis, the facilitators or factors that were significantly associated with self-reported adherence of at least or over 95% were having an initial bodyweight of less than 50 kg (p = 0.026) and viral load of >33 000 copies /ml (p = 0.047).

Conclusions: In conclusion, self-reported barriers to optimal adherence included the use of non-prescribed drugs, and the presence of side effects such as insomnia, headaches and abdominal pain; while eating well was a facilitator. These findings emphasise the need for better communication between patients and clinicians, and the need for integrating pharmacovigilance concepts in clinical practice.

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Introduction

Conceptually, complete adherence implies that a patient takes 100% of all doses of each prescribed medicine according to instructions he or she received from the prescribing doctor and/or dispensing pharmacist. The instructions refer to the taking of medicines in terms of the frequency and interval between doses, the need to take the medicines with or without foods, as well as other precautions.[1] Adherence is the key to the effectiveness of the antiretroviral therapy because, in order to ensure that the viral load in a patient is kept at undetectable levels, high levels of adherence (about 100%) are required.[2] However, in the case of antiretroviral therapy (ART), it is estimated that the average rate of adherence is approximately 70%, well in the same order as with other chronic conditions.[3] Studies from Canada, Latin America and elsewhere demonstrate similar rates of suboptimal adherence.[4,5] In general, 10% of patients report missing at least one antiretroviral dose on any given day and 33% report missing at least one dose within the past month.[6] In South Africa, in a 48-week study involving 289 patients attending a public hospital, HIV clinic and receiving ART through Phase III studies, the mean adherence as measured by clinic-based pill counts and pharmacy refill data was 87.2%.[7] Although many factors have been identified as being associated with less optimal adherence, the types of adverse effects involved with such level of adherence is still less established in South Africa. The objectives of this study were to determine the level of self-reported adherence, the reasons given for missing doses, the adverse effects self-reported, and to assess the association between adverse effects and adherence.

Methods

A survey was conducted of HIV-infected patients, who started ART between July 2004 and August 2005 at the Dr George Mukhari Hospital in Pretoria. The population of the study comprised patients treated at the antiretroviral treatment clinic within the hospital. Recruitment into the study was processed during a seven-week period from July to August 2005. The recruitment was conducted during the morning 8:30 to 12:00 and the afternoon sessions 13:00 to 16:00. All consecutive patients, both males and females, were approached and requested to be interviewed. Only patients who were actually on ART and who consented to participate in the study were immediately interviewed. Patients who were unable to respond to an interview were also excluded. Using a pre-tested semi-structured questionnaire, data was collected by two trained interviewers on sociodemographic characteristics, clinical data, experienced side effects and non-prescribed medicines as reported elsewhere.[8] In this study, adherence was assessed in terms of dose taking, the prescribed number of tablets to be taken for each day. Bivariate and multivariate analyses of relationships between self-reported adherence with explanatory variables were performed using logistic regression. The findings presented here are a component of a study that was approved by the Ethics Committee of the Faculty of Medicine at the University of Limpopo.

Results

From 285 patients who were approached, a response rate of 63.2% was achieved. The 180 patients who consented to be interviewed had a mean age of 36.7 (±8.1) years, ranging from 19 to 63 years (see Figure 1); 68.8% were female, 86.7% unemployed, 73.9% had a high school level of education, and 77.8% were single. Some 8.9% of respondents used at least one non-prescribed medicine, while 34.4% received disability grants. Overall, 73.9% reported eating daily balanced diets including fruits and vegetables. The most prescribed regimen comprised stavudine, lamivudine and efavirenz (Table I)
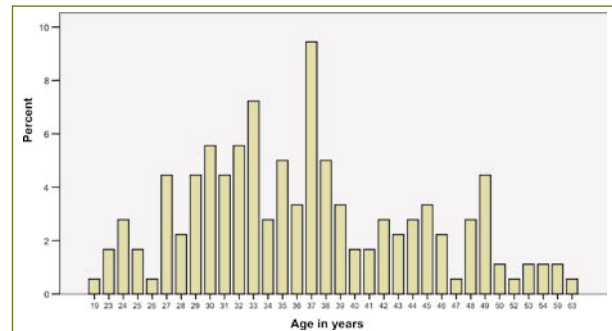
Figure 1: Age characteristics of respondents

Table I: Regimens prescribed to respondents (n = 180)

| Regimen prescribed	Composition	Frequency	Percent
Regimen 1a	Stavudine, lamivudine, efavirenz	169	93.8
Regimen 1b	Stavudine, lamivudine, nevirapine	9	5
Regimen 2	Didanosine, lamivudine, efavirenz	1	0.6
Regimen 3	Zidovudine, lamivudine, efavirenz	1	0.6

With regard to self-reported adverse effects, overall 94% of respondents reported at least one side effect. Respondents reported 19 different side effects (see Table II). The side effects or symptoms reported by at least 10% of respondents were, in descending order, sexual problems, depression, forgetfulness, muscle pains, insomnia, fever, suicide ideation, abdominal pain, nightmares and loss of appetite. The average number of side effects reported was 2.6 (±1.4).

Table II: Adverse effects self-reported (n = 180)

Adverse effects	Frequency	Percent
Sexual problems (decreased libido, satisfaction)		40.0
Depression (feeling sad, down)		37.2
Forgetfulness		37.2
Joint/muscle pain		19.4
Insomnia		18.9
Fever		15.6
Suicide (thoughts of, desire for, feeling of)		15.6
Abdominal discomfort		14.4
Nightmares		14.4
Appetite loss		11.1
Peripheral neuropathy		8.3
Fatigue		6.7
Vomiting		5.6
Hair loss		4.4
Diarrhoea		3.3
Body changes (fat deposit)		2.2
Dizziness		1.7
Skin rashes		1.7
Chest pain		1.1

With regard to adherence, overall only 57.2% reported taking ≥ 95% of their prescribed doses. The mean number of doses missed during the last seven days prior to the interview was 2.7 (±3.9), ranging from 0 to 18. Although 50.6% reported not missing any dose, 8.9%, 35.6% and 5% reported missing one to two doses, three to ten doses, and more than ten doses, respectively. The mean adherence was 92.3%, ranging from 48.6% to 100.0%; overall, only 57.2% reported taking ≥ 95% of their prescribed doses. As shown in Figure 2, the most common reasons for missing doses were forgetting and being away from home.

Figure 2: Reasons for missing doses (n = 180)
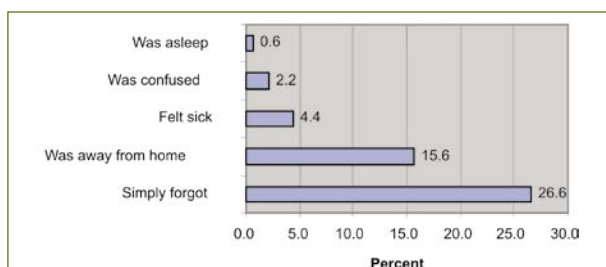
In the bivariate analysis, the only facilitator or factor that was significantly associated with ≥ 95% self-reported adherence was eating well (80.6% vs 64.5%; p = 0.025), whereas barriers or factors more likely and significantly associated with < 95% adherence included having used non-prescribed medicines (15.6% vs 3.9%; p = 0.008), having suffered from headaches (28.6 vs 14.6%; p = 0.03), and reported symptoms such as insomnia (27.3% vs 12.6%; p = 0.013) and abdominal pain (20.8% vs 9.7%; p = 0.037).

In the multivariate analysis, the facilitators or factors that were significantly associated with a self- reported adherence level of ≥ 95% were having initial bodyweight of less than 50 kg (p = 0.026) and viral load of > 33 000 copies/ml (p = 0.047). Other factors that were more likely but not significantly associated with ≥ 95% adherence included having a tertiary education and good working relationship with clinic staff, being employed and receiving a disability grant. Barriers or factors that were likely and significantly associated with less than optimal self-reported adherence were having used non-prescribed medicines (p = 0.01) and having reported insomnia (p = 0.01).

Discussion

Overall only 57.2% reported taking ≥ 95% of their prescribed doses, while the mean number of doses missed was 2.7 (±3.9). In previous South African studies, the level of adherence reported by other investigators was higher than in this study.[7,9] The level of self-reported adherence found in our study is a cause for concern because it points out to a possible threat of antiretroviral drug resistance.[10] It is established that drug resistance strives well when HIV replication is incompletely suppressed and may reach as high as 50% against non-reverse transcriptase inhibitors.[11] The implication of this finding is that the necessary investment to ensure an effective scale-up of ART must be made available in terms of human resources, finances, procedures and policies, buy-in from communities and public health interventions.[12,13]

The use of non-prescribed medicines was significantly associated with a self-reported adherence level of less than 95% in the bivariate and multivariate analysis. This finding suggests that when patients have obtained medicines by their own initiative from other sources,

they value them more and most probably take them while neglecting what was prescribed for them.[14] The implication of this is that clinicians should regularly find out from patients whether they are taking any non-prescribed medicines.

The majority of respondents reported at least one side or adverse effect. Self-reported adverse effects such as insomnia were significantly associated with an adherence level of less than 95% in the bivariate and multivariate analysis; while complaints of headaches and abdominal pain were significantly associated with a similar level of adherence in the bivariate analysis. This finding confirms what is well established from the literature, namely that side effects affect adherence negatively. Nevertheless, our findings differ from reports by Johnson and colleagues with regard to the types of side effects implicated. In this study it was insomnia, headaches and abdominal pain; while in theirs it was nausea, vomiting and skin rashes.[15]

With regard to reasons cited for missing doses, the findings from this study concur with reports from the literature that forgetting and being away from home were the most common.[16] Limitations of this study included that causal relationships could not be determined due to the design of the study, and the fact the response rate was low, probably because of the fact that this was an exit interview – some interviewees just wanting to go back to their homes.

In conclusion, self-reported barriers to optimal adherence included the use of non-prescribed drugs, and the presence of side effects such as insomnia, headaches and abdominal pain, while eating well was a facilitator. These findings emphasised the need for better communication between patients and clinicians, and the need for integrating pharmacovigilance concepts in clinical practice.

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