

**WHEN “ACCESS TO ANTIRETROVIRAL
TREATMENT FOR ALL” IS NOT ENOUGH**

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ABSTRACT

Objective: To evaluate the effect of active case management and incentives on compliance with scheduled study visits as compared to compliance with visits to monitor antiretroviral therapy (ART) and viral control for 6 months in a cohort of 144 HIV-drug users on ART in Miami.

Methods: A prospective 6-month study to compare participant compliance with research visits using active case management, incentives, and close follow-up, versus their compliance with routine healthcare visits to monitor ART and viral load during the same time period. Attendance at research visits and routine healthcare visits was recorded, and CD4 cell count and viral load were measured at baseline and 6-months. Active case management included monthly scheduled visits to assess compliance with nutritional supplementation study protocol, follow-up of participants missing visits, and incentives for attendance at all visits. Descriptive statistics and Student's t-test for proportions was used in the analyses.

Results: Compliance with study visits in which active case management was used was 86% compared to 17.4% with routine self-directed healthcare ART monitoring visits. Only 29.8% of those receiving ART achieved viral suppression (<400 copies/mL).

Conclusions: In patients who are at high risk for non-adherence, active case management and incentives need to be implemented to achieve compliance with treatment in order to control the HIV epidemic more effectively.

INTRODUCTION

Florida ranked second in the nation in the number of AIDS cases with most cases being reported from Miami-Dade County in 2004 (DHHS: CDC, 2007). The majority of new cases of HIV in Miami-Dade County are among those who live at the fringes of society and are members of hard-to-reach populations (Miami-Dade Health Department, 2007; Inciardi et al., 2006), many of whom suffer from homelessness, mental health and substance abuse problems (Devieux et al., 2007; McCoy et al., 2004; Schultz et al., 1999). As a consequence of these characteristics, cases of HIV-infection are underreported and the available HIV-services are grossly underutilized (Barash et al., 2007). In addition to underutilization of HIV services among HIV-positive drug users, the socio-demographic and behavioral characteristics of this group increase the risk for low adherence and compliance with antiretroviral therapy (Kleeberger et al., 2001; 2004).

The degree to which individuals enact the instructions of their caregivers is especially important in delivering HIV care, and high levels of adherence and compliance are needed in order for antiretroviral treatment (ART) to be effective (Ickovics et al., 2002). Adherence, the degree to which the patient follows the caregiver's specific instruction (i.e. how to take the ART pills), needs to be greater than 95% to be effective and to prevent resistance to the medication (Ickovics et al., 2002).

Compliance, regular visits to the caregiver for updates on the condition of the patient, is critical for the continuous evaluation of treatment efficacy and the emergence of resistance to a given regimen (Vanhove et al., 1996; Montaner et al., 1998).

Direct Observed Therapy (DOT) was originally developed to address issues of adherence and compliance in tuberculosis patients through the direct observation of patients taking their tuberculosis medication (Massachusetts, 2001). DOT has been successfully applied for this purpose in different settings, and further modified to offer more freedom to patients while maintaining compliance (Farmer & Nardell, 1998). In a systematic review of reports of DOT programs, Volmink and colleagues (Volmink et al. 2000) attributed the effectiveness of DOT to a variety of additional strategies beyond the direct observation that were used to promote compliance such as phone and mail reminders, financial incentives, and active case management. Our experience in Miami with a modified Direct Observed Therapy Program for antiretroviral therapy demonstrated that with adequate case management patients at risk for non-adherence can become compliant with treatment (Jayaweera et al., 2004).

In a cohort of HIV+ drug users participating in a double-blind placebo-controlled trial of nutritional supplementation in Miami, we have observed a significant disparity between participants' viral load control and their self-report of receiving antiretroviral therapy (Campa et al., 2005). The effectiveness of ART may be diminished when strategies to assure adherence and compliance are not applied in a manner specific to the social, economic, and cultural realities of the population (Lane et al., 2004; Berkman et al., 2000).

The objective of our current study was to evaluate the effect of compliance strategies targeted for a largely

homeless, drug-using population on compliance with study visits. We conducted a six-month study in a cohort of 144 HIV+ drug users on ART in Miami to evaluate the effect of active case management with financial incentives and monthly reminders on compliance with scheduled study visits. The results of this study to promote compliance were compared to the participants' self-directed compliance with HIV-treatment visits to monitor ART and viral control during the same period.

METHODS

A community-based cohort of HIV infected drug users was recruited from the Camillus House, a non-profit organization that provides humanitarian services to the poor and homeless of South Florida, and other shelters and agencies for the poor and under-insured in Miami, Florida, between March 2002 and December 2006. Participants were eligible if they were HIV-seropositive, 18 years of age or older, active drug users (determined by urine toxicology), and living in Miami-Dade County. After the screening visit, 231 participants were enrolled in a nutritional study, of which 144 reported being prescribed ART as part of their regular HIV clinical care. The Florida International University Internal Review Board reviewed and approved this study.

At the baseline and 6-month visits, participants were given a physical examination that included medical and treatment history. A questionnaire on self-reported compliance with routine health-care visits to monitor ART was administered. Those who attended ≥ 2 clinic visits during the 6-month follow-up were considered compliant, as the standard of care for those on ART requires visits every 3-4 months to monitor viral control, disease progression, and to make changes in therapy and prescribe

medications as needed (DHHS Panel, 2006; Barlett and Gallant, 2005; Aberg et al., 2004).

Demographic information and anthropometrics were obtained to characterize the population. Drug use history which included prescribed medications, alcohol, tobacco and recreational drugs was collected, and blood was drawn for CD4 cell count, viral load, CBC, and blood chemistry. With the participant's written permission, critical values, including CD4 cell counts and viral load results, were sent to their Primary Care Physician.

Participants were seen monthly for study supplement dispensation, pill counts of returned bottles, reports of adverse events, and update of their contact information. At each monthly visit, the participants received a \$10.00 reimbursement for transportation expenses, and as an incentive for continual participation.

Participants were followed by monthly mail or phone reminders of the approaching study appointment visits. Referrals to detoxification and treatment programs were given as necessary. For those who missed more than 2 monthly study visits, additional efforts were made by the outreach worker to contact the participants, including personal visits to their last known address, and communication with known associates and acquaintances regarding the whereabouts of the participant. If the person was not located, periodic checks in the Miami-Dade County Correctional System and the Vital Statistics Bureau were conducted with permission from the Miami-Dade Correction and Rehabilitation Department. Participants who were incarcerated were visited in jail for dispensation of study pills and assessments.

Participants were considered compliant with routine healthcare visits if they reported attending ≥ 2 routine ART monitoring visits in the past 6 months, and compliant with research study visits if they attended all 6 of the scheduled monthly visits. This information was used to compare the

participants' compliance with the incentive-managed monthly study visits to the compliance with their ART monitoring routine medical visits during the same period of time.

Descriptive statistics were used to characterize the population and the compliance with the incentive-managed monthly study visits and pills compared to ART monitoring routine medical visits. Differences in characteristics between participants on ART with viral control compared to those on ART without viral control were evaluated using the Student's t-test for proportions

RESULTS

Of the 231 HIV-seropositive participants in our cohort, 62.3% (144/231) were receiving ART (Table 1). These participants on ART (N=144) had a mean age of 43.6 ± 7.0 years, were 78.5% male, 78.5% black, 45.8% homeless, and had a mean monthly income of $\$329.6 \pm 394$. Their mean CD4 cell count was 334 ± 263 cells/mm³ and mean log viral load was 3.8 ± 1.1 copies/mL.

Only 29.8% (46/144) of those on ART achieved consistent viral suppression (<400 copies/mL) at both baseline and 6-month visits, indicating that 70.2% of those who reported receiving ART either lacked adherence to treatment or were in treatment failure. Those who did not achieve viral suppression were more advanced in their disease (272 ± 219 CD4 cells/mm³, $p=0.001$) than those who had undetectable viral load (478 ± 300 CD4 cells/mm³). A significantly larger proportion of women, did not achieve viral load control. Those who did not achieve viral control were also significantly younger, and consumed more crack/cocaine than those who did (Table 1).

Of those on ART, only 17.4% reported attending ≥ 2 routine healthcare clinic visits for monitoring ART treatment in the past 6 months. These same research

participants, however, demonstrated an 86.1% (125/144) compliance with their monthly scheduled research study visits during the same 6 month period.

Table 1

Characteristics of HIV+ Drug Users Receiving ART Who Achieved or Did Not Achieved Viral Control

Variables	Viral control (<400 cp/mL) N=43	No viral control (≥400 cp/mL) N=101	p-value
Age	45.9 ± 7.1	42.7± 6.7	0.01
Gender			
Female	4 (9.3%)	27(26.7%)	0.026
Male	39 (90.7%)	74(73.3%)	
CD4 count	478 ± 300	272± 219	<0.001
Crack Cocaine	16(37.2%)	56(55.5%)	0.045

DISCUSSION

The provision of active case management, incentives and follow-up in this study effectively increased compliance with monthly study visits when compared to the participants' compliance with their ART monitoring visits. In a previous study conducted by Jayaweera and colleagues (Jayaweera et al., 2004) Direct Observed Therapy, was reported to effectively increase adherence to HIV treatment in a hard-to-reach population. We have demonstrated in our cohort of HIV-positive drug users, of whom approximately half were homeless, that active case management strategies and incentives increased compliance with study visits 5-fold over the participants' self-directed compliance with ART monitoring visits.

The active case management strategies included referrals to detoxification and treatment programs, update of contact information at each visit, monthly phone or mail

reminders for research appointments, and monthly dispensation of the research supplement and pill counts. In addition, efforts were made to outreach those who were not compliant, and periodic checks were conducted in the Miami-Dade County Correctional system and the Vital Statistics Bureau to find those who did not show-up consecutively for their scheduled appointments. Our research participants also received a small incentive of about \$10 for attending the clinic monthly. These efforts resulted in substantially higher compliance with scheduled study visits by our participants. Although the current research is limited in that we were unable to directly measure adherence to ART treatment to make an effective comparison of adherence between our study pills and ART, the effect of the strategies implemented on compliance is clearly demonstrated.

Our current and past published (Jayaweera et al., 2004) findings corroborate the need to tailor ART programs using strategies such as active case management, incentives and Direct Observed Treatment to increase adherence to treatment and compliance with treatment visits. As has been found in the treatment of tuberculosis (Volmink et al., 2002), effective HIV-treatment in hard-to-reach populations, requires adaptation of DOT to the circumstances surrounding the patients by enriching the programs with active case management, modest incentives, and reminders, which allow for both the personal freedom of the patients, and the supervision by the medical staff needed to achieve treatment success.

The United States was one of the first countries to provide antiretroviral access for all HIV seropositive patients. To achieve control of the HIV epidemic in our country, it is paramount to assure that, beyond having access to treatment, effective and realistic interventions are also provided, in order to improve adherence to this costly and complex treatment regimen. The costs of providing

active case management and incentives to ensure compliance and adherence are minor compared to the costs of providing ART, especially when considering that a medication adherence of 95% or higher is required to attain viral suppression, and to avoid the development of resistant HIV strains, as well as to reduce HIV transmission (Barlett et al., 2005; Patterson et al., 2000; Haubrich et al., 1999; Montaner et al., 1998).

At a time when many developing countries are considering strategies for providing ART, our findings acquire new relevance, as they remind us that it is not enough to provide universal access to antiretroviral treatment, but that ART needs to be implemented in a manner that considers the social context (Lane et al., 2004; Berkman et al., 2000) and the distinctive circumstances and characteristics of the population served.

CONCLUSIONS

In patients who are at high risk for non-adherence, modified versions of the ART Direct Observed Therapy programs for viral control are needed to increase treatment success rates (Jayaweera et al., 2004). Our current research complements these findings, showing that, providing active case management and incentives, independently of DOT, greatly improves compliance with study visits among largely homeless, HIV+ drug users, possibly one of the most difficult to reach populations in the United States. Further studies are needed to investigate the synergistic effect of DOT programs for HIV+ patients (Jayaweera et al., 2004) combined with active case management strategies and incentives on adherence and compliance with antiretroviral treatment.

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