The impact of illicit drug use and substance abuse treatment on adherence to HAART

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Abstract

High levels of adherence to highly active antiretroviral therapy (HAART) are essential for virologic suppression and longer survival in patients with HIV. We examined the effects of substance abuse treatment, current versus former substance use, and hazardous/binge drinking on adherence to HAART. During 2003, 659 HIV patients on HAART in primary care were interviewed. Adherence was defined as 95% adherence to all antiretroviral medications. Current substance users used illicit drugs and/or hazardous/binge drinking within the past six months, while former users had not used substances for at least six months. Logistic regression analyses of adherence to HAART included demographic, clinical and substance abuse variables. Sixty-seven percent of the sample reported 95% adherence or greater. However, current users (60%) were significantly less likely to be adherent than former (68%) or never users (77%). In multivariate analysis, former users in substance abuse treatment were as adherent to HAART as never users (Adjusted Odds Ratio (AOR) 0.82; *p*>0.5). In contrast, former users who had not received recent substance abuse treatment were significantly less adherent than never users (AOR=0.61; *p*=0.05). Current substance users were significantly less adherent than never users, regardless of substance abuse treatment (*p*<0.01). Substance abuse treatment interacts with current versus former drug use

status to affect adherence to HAART. Substance abuse treatment may improve HAART adherence for former substance users.

Introduction

High levels (>95%) of adherence to HAART are necessary to achieve virologic suppression and ultimately improve survival (Bangsberg et al., 2000; Gifford et al., 2000; Paterson et al., 2000; Pound-stone et al., 2001). Active substance use is associated with non-adherence (Arnsten et al., 2002; Tucker et al., 2003), which may lead to failure to achieve viral suppression (Ickovics et al., 2002; Lucas et al., 2001; Mannheimer et al., 2002; Palepu et al., 2003).

The effect of substance abuse treatment on adherence to HAART is not well understood (Moatti et al., 2000; Moreno et al., 2001; Palepu et al., 2004; Sambamoorthi et al., 2000; Warden & Hunter, 2005). We examined the association between adherence to HAART and participation in substance abuse treatment, controlling for time frame of substance use (current/former/never) and alcohol consumption.

Methods

Site selection

The HIV Research Network (HIVRN) is a consortium of 21 sites that provide primary and subspecialty care to HIV-infected adult and pediatric patients. To participate, sites had to have a minimum data set available, including the patient's age, sex, race, HIV transmission risk factor, CD4 level and use of antiretroviral medication. Data elements were abstracted from HIV-infected patients' medical records at each site and sent in electronic format to a data co-ordinating center after personal identifying information was removed. Methods for the collection of the HIVRN clinical dataset have been presented elsewhere (Gebo et al., 2005a; 2005b).

During 2003, 951 adult (18 years old) patients in primary care at 14 HIVRN sites participated in face-to-face interviews. The sites are located in the Eastern (6), Midwestern (3), Southern (2) and Western US (3). Seven of the sites have academic affiliations; seven are community-based. The median sample size per site was 59 patients (range: 38–172 patients).

Sampling and data collection

We drew random samples from de-identified patient lists in each of the 14 sites. Staff at each site determined the sampled patient's name and address and mailed an invitation to participate. Of 5363 letters of invitation sent, we successfully conducted interviews with 717 (13%) patients. In all but three sites, we supplemented mail recruitment by approaching patients as they waited for treatment; this yielded interviews with another 234 patients. The distributions of gender, race/ethnicity and HIV transmission in the interviewed sample were similar to the larger population of patients at these sites. Nevertheless, the sample may have differed in other characteristics from the population of patients in these sites.

Data collection methods have been described elsewhere (Josephs et al., in press). Participants were reimbursed $30 for the approximately one-hour interview.

Measures

All data are from the patient interview except HIV risk factor and CD4 count, which were obtained from the clinical database. Age, as of July 1, 2003, was calculated from self-reported month and year of birth and categorized as 18–34, 35–44 and 45 years or older. Racial/ethnic group was categorized as white, African-American, Hispanic and other (American Indian or Alaskan native, Asian or Pacific Islander). Respondents reported the number of years of education completed, employment status and insurance status at the time of the interview.

Based on HIV transmission risk factor, we classified patients as IDU or non-IDU. The IDU category included patients with other risk factors.

Self-reported CD4 nadir was categorized as less than or equal to 50 cells/mm^3, 51–200 cells/mm^3, 201–500 cells/mm^3 and greater than 500 cells/mm^3. AIDS diagnosis was defined as either CD4 nadir <200 or a self-reported AIDS-defining illness. Current CD4 count was the first recorded value in calendar year 2003.

Current illicit drug use was assessed by asking participants whether they had, in the past six months, used any drugs without a doctor's prescription, in larger amounts than prescribed or for longer than prescribed. Patients were specifically asked about use of sedatives, amphetamines, analgesics, marijuana, cocaine, inhalants, LSD and heroin. We categorized patients as current, former or never users of illicit drugs. Former substance use was defined as ever using illicit drugs with last use being more than six months prior to the interview.

Alcohol use was ascertained from questions asking: (1) how many days in the past four weeks the respondent drank alcohol, (2) how many drinks the respondent consumed on a typical day when drinking and (3) the number of days the respondent consumed more than five drinks (Galvan et al., 2002). Per national guidelines, the definition of hazardous drinking was greater than 14 drinks per week for men and greater than seven drinks per week for women; binge drinking was five or more drinks per occasion (National Institute of Alcohol Abuse and Alcoholism [NIAAA], 1995). Hazardous and binge drinkers were classified in one category; social drinking was any alcohol consumption not hazardous or binge drinking. Given high rates of potential non-adherence with hazardous/binge drinking (HBD), those reporting HBD within the last four weeks were classified with current illicit drug users.

A dichotomous variable for any substance abuse treatment in the last six months was defined as self-reported participation in any drug or alcohol treatment/counselling (including 12-step, methadone maintenance, outpatient or residential) and/or self-reported inpatient hospitalisation for treatment of a drug or alcohol problem.

HAART was defined as concomitant use of ≥ 3 antiretroviral drugs either from ≥ 2 classes (NRTIs, NNRTIs, PIs or a fusion inhibitor) or 3 NRTIs. We opted to be as inclusive as

possible in our definition of HAART; this definition is unlikely to exclude any preferred drug combinations.

For each prescribed antiretroviral we asked: 'How many doses of [drug name] did you miss altogether in the past two weeks?' (Chesney et al., 2000). Adherence was defined as taking greater than or equal to 95% of prescribed doses of all antiretroviral drugs in the HAART regimen (Paterson et al., 2000).

Analysis

Analyses were based on 659 respondents who reported using HAART. We performed χ^2 tests to examine bivariate associations between individual demographic and clinical variables and substance use. Logistic regression analyses of adherence to HAART included demographic, clinical and substance abuse variables. To examine the combined effect of substance abuse and receipt of treatment, we derived an interaction variable with the following categories: (1) never used substances; (2) current users who had not recently participated in substance abuse treatment; (3) former users who had not participated in substance abuse treatment; (4) current users who had participated in substance abuse treatment; and (5) former users who had participated in substance abuse treatment.

Analyses were conducted using STATA 9.2 (College Station, Texas, US). In all regressions adjustment was made for site of care to account for variations in practice patterns and demographic differences across sites.

Results

Table I describes characteristics of the 659 respondents on HAART. The median age was 44, with a range of 20 to 85 years (results not shown). The median current CD4 count was 373 cells/mm^3, with a range of 0 cells/mm^3 to 1720 cells/mm^3 (results not shown).

Forty-two percent were current substance users, 30% were former users and 28% had never used substances. Current substance users were more likely to be younger ($p<0.001$), male ($p<0.001$) and to have men who have sex with men (MSM) as their HIV risk factor ($p<0.001$) than former or never users. Nearly half of the sample had ever used cocaine (41%), 14–19% used other drug classes and 57% had ever used marijuana. Forty-two percent of the sample reported any alcohol use in the last four weeks: 31% social drinking and 11% HBD. Current users were significantly more likely to have used alcohol in the last four weeks (62% versus 25%; $p<0.001$) than former users.

Overall, 15% had been in any drug or alcohol treatment/counselling in the last six months. More former users reported participating in any drug or alcohol treatment in the past six months than current users (25% versus 15%, $p=0.005$) (Table I).

Sixty-seven percent of the sample reported 95% adherence or greater. However, current users (60%) were significantly less likely to be adherent than former (68%) or never users (77%) ($p=0.001$) (data not shown).

Table II shows bivariate associations of each independent variable with adherence. Significant bivariate predictors were included in a multivariate logistic regression. Table III shows significant predictors in the multivariate model. Current users who had not received substance abuse treatment in the last six months (adjusted odds ratio [AOR]=0.49; 95%CI: 0.31, 0.78), former users who had not received substance abuse treatment (AOR=0.61; 95%CI: 0.37, 1.00) and current users who had received substance abuse treatment (AOR=0.24; 95%CI: 0.11, 0.51) were all significantly less likely to be adherent than never users after adjusting for age, race and AIDS diagnosis. However, former users who had recently participated in substance abuse treatment were not statistically significantly different from never users (AOR=0.82; 95%CI: 0.39, 1.72). Black race (AOR=0.54; 95%CI: 0.33, 0.88), Hispanic ethnicity (AOR=0.51; 95%CI: 0.28, 0.94) and AIDS diagnosis (AOR=0.63; 95%CI: 0.43, 0.93) also remained significant in the multivariate model and were associated with lower odds of being adherent to HAART regimen.

Discussion

This study suggests that illicit drug use and substance abuse treatment may interact to affect adherence to HAART. Current substance users were significantly less adherent than never users, regardless of substance abuse treatment. Former illicit drug users' adherence to HAART after recently participating in substance abuse treatment was not significantly different from never users' adherence. In contrast, former users who had not received recent substance abuse treatment were significantly less adherent than never users. The results support the critical distinction between current users, who have not sufficiently stabilized to achieve adherence or other clinical gains resulting from treatment for substance abuse, and former users, who show clear improvements in these areas.

Substance abuse treatment appears to be most beneficial to HAART adherence when patients both achieve and maintain abstinence from illicit drugs for at least six months. However, a causal impact of treatment cannot be estimated from these observational data. It is possible that unmeasured variables, such as attitudes about health or life circumstances, affect both adherence and participation in substance abuse treatment.

Consistent with past work, alcohol use was also an important predictor of non-adherence (Cook et al., 2001; Galvan et al., 2002). Hazardous/binge drinking within the last four weeks was strongly associated with non-adherence in bivariate analysis of the whole sample and, among former illicit drug users, social drinking was significantly associated with non-adherence. These findings reiterate the importance of alcohol as a possible detriment to adherence. Providers should be aware of the potentially negative impact of alcohol on adherence and should assess alcohol use at each visit.

This study has several important limitations. First, the data are observational, therefore we cannot assess whether cessation of drug use or substance abuse treatment is responsible for improved adherence. However, the findings establish an association and warrant further investigation into a possible causal relationship between substance abuse treatment and better adherence. Although the response rate for the interview was low, this study has one of the largest and most recent samples used to assess adherence among HIV-infected patients

in the US. Also, the sample is not nationally representative and does not generalize to all HIV patients though the 14 sites encompass a broad geographic distribution. The data are based on patient self-report; however, other studies with more rigorous measures of substance abuse treatment utilization have shown similar findings on the effect on adherence (Turner et al., 2003). Finally, we were unable to assess known confounders such as depression and incarceration, which have been shown to be associated with non-adherence.

The results have several important implications for HIV care and substance abuse treatment. Any current substance use (illicit drugs and/or hazardous/binge drinking) is negatively associated with adherence and even social drinking strongly predicts non-adherence in former illicit drug users. Additionally, former illicit drug users who recently participated in substance abuse treatment were not statistically less adherent than never users. Substance abuse treatment may be an effective strategy for improving adherence and possibly clinical outcomes for adults with HIV. Further research is needed to evaluate the efficacy of substance abuse treatment as an adherence intervention.

Acknowledgments

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Table I

Overall demographics, clinical variables, illicit drug and alcohol use, and substance abuse treatment by drug use category.

| | Overall *n* = 659 | Substance use category | | | |
| | | Current *n* = 275 | Former *n* = 198 | Never *n* = 185 | *p*-value |
	n (%)	n (%)	n (%)	n (%)	
	n = 655	*n* = 274	*n* = 197	*n* = 184	<0.001
Age					
18–39	169 (26)	79 (29)	39 (20)	51 (28)	
40–49	313 (48)	144 (53)	101 (51)	68 (37)	
50	173 (26)	51 (19)	57 (29)	65 (35)	
	n = 659	*n* = 275	*n* = 198	*n* = 185	0.253
Race					
White	207 (31)	98 (36)	59 (30)	50 (27)	
Black	336 (51)	131 (48)	106 (54)	100 (54)	
Hispanic	92 (14)	33 (12)	28 (14)	31 (17)	
Other/missing	24 (4)	13 (5)	5 (3)	5 (3)	
					<0.001
Sex					
Female	198 (30)	50 (18)	76 (38)	72 (39)	
Male	461 (70)	225 (82)	122 (62)	113 (61)	
	n = 652	*n* = 274	*n* = 196	*n* = 182	0.526
Education					
<High school degree	156 (24)	59 (22)	48 (25)	49 (27)	
High school grad/ junior college	404 (62)	180 (66)	117 (60)	107 (59)	
College/post-college	92 (14)	35 (13)	31 (16)	26 (14)	
	n = 655	*n* = 274	*n* = 197	*n* = 184	
Employment					
Full time or part time job	165 (25)	70 (26)	53 (27)	42 (23)	0.647
	n = 652	*n* = 270	*n* = 198	*n* = 183	0.847
Insurance					
Private insurance	162 (25)	71 (26)	48 (24)	43 (24)	

	Overall $n = 659$	Current $n = 275$	Former $n = 198$	Never $n = 185$	p-value
	n (%)	**n (%)**	**n (%)**	**n (%)**	
Medicaid	236 (36)	96 (36)	76 (38)	63 (34)	
Medicare	62 (9)	23 (9)	20 (10)	19 (10)	
Medicaid & Medicare	134 (21)	60 (22)	37 (19)	37 (20)	
No insurance	58 (9)	20 (7)	17 (9)	21 (11)	<0.001
	$n = 659$	$n = 274$	$n = 198$	$n = 185$	
HIV Risk Factor-hierarchy					
IDU	94 (14)	36 (13)	46 (23)	12 (6)	
MSM	238 (36)	126 (46)	43 (22)	68 (37)	
MSM/IDU	16 (2)	7 (3)	7 (4)	2 (1)	
HET	203 (31)	61 (22)	66 (33)	76 (41)	
HET/IDU	44 (7)	20 (7)	17 (9)	7 (4)	
Other/unknown/missing	64 (10)	24 (9)	19 (9)	20 (11)	
AIDS diagnosis	449 (68)	203 (74)	131 (66)	114 (61)	0.018
	$n = 628$	$n = 262$	$n = 188$	$n = 177$	0.365
CD4 nadir (cells/mm^3)					
50	194 (31)	90 (34)	57 (30)	46 (26)	
51–200	218 (35)	92 (35)	66 (35)	60 (34)	
201–500	167 (27)	60 (23)	49 (26)	58 (33)	
>500	49 (8)	20 (8)	16 (9)	13 (7)	
	$n = 659$	$n = 275$	$n = 198$	$n = 185$	0.660
CD4 count in 2003 (cells/mm^3)					
50	30 (5)	16 (6)	9 (5)	5 (3)	
51–200	81 (12)	39 (14)	19 (10)	23 (12)	
201–500	221 (34)	92 (33)	69 (35)	60 (32)	
>500	159 (24)	60 (22)	49 (25)	50 (27)	
Unknown/missing	168 (25)	68 (25)	52 (26)	47 (25)	
Illicit drug use *					
Amphetamines	116 (18)	68 (25)	48 (24)	N/A	0.904
Analgesics	103 (16)	68 (25)	35 (18)	N/A	0.067

Table header: Substance use category

| | Substance use category | | | | |
	Overall $n = 659$	Current $n = 275$	Former $n = 198$	Never $n = 185$	p-value
	n (%)	n (%)	n (%)	n (%)	
Cocaine	269 (41)	143 (52)	126 (64)	N/A	0.012
Hallucinogens	113 (17)	66 (24)	47 (24)	N/A	0.947
Heroin	122 (19)	57 (21)	65 (33)	N/A	0.003
Inhalants	93 (14)	58 (21)	35 (18)	N/A	0.357
Marijuana	377 (57)	223 (81)	154 (78)	N/A	0.377
Sedatives	117 (18)	72 (26)	45 (23)	N/A	0.390
	$n = 657$	$n = 274$	$n = 197$		<0.001**
Alcohol use					
No drinking	379 (58)	104 (38)	147 (75)	N/A	
Social drinking	206 (31)	98 (36)	50 (25)	N/A	
Hazardous/binge drinking (HBD)	72 (11)	72 (26)	N/A	N/A	
	$n = 659$	$n = 275$	$n = 198$		
Substance abuse treatment					
Any drug or alcohol treatment	97 (15)	40 (15)	49 (25)	N/A	0.005
Type of substance abuse treatment					
12-step	69 (10)	27 (10)	35 (18)	N/A	0.012
Non-12-step	31 (5)	16 (6)	14 (7)	N/A	0.581
Methadone maintenance	15 (2)	8 (3)	7 (4)	N/A	0.701
Outpatient	16 (2)	10 (4)	7 (4)	N/A	0.701
Residential	6 (1)	5 (2)	1 (1)	N/A	N/A***

*
Lifetime use of a particular illicit drug. In the 'Overall' and 'Current' columns indicates current or former use; in the 'Former' column, indicates former use only by definition of a former substance user.

**
Chi-square excludes HBD.

***
Chi-square test not performed due to small sample size.

Table II

Bivariate odds ratios for factors associated with adherence in overall sample on HAART ($n = 659$).[†‡§]

	Overall sample	
	OR	95%CI
Age	$n = 655$	
18–39	1.0	Ref
40–49	1.00	0.67–1.51
50	1.11	0.70–1.78
Race	$n = 659$	
White	1.0	Ref
Black	0.60	0.38–0.96
Hispanic	0.59	0.32–1.06
Other/missing	0.86	0.33–2.23
Sex		
Females	1.0	Ref
Males	0.98	0.67–1.42
Education		
<high school degree	1.0	Ref
High school grad/ junior college	0.81	0.53–1.22
College/ post-college	1.07	0.58–1.97
Unknown/missing	0.89	0.16–4.96
HIV risk factor: IDU vs non-IDU	0.76	0.51–1.12
AIDS diagnosis	0.65	0.44–0.94
CD4 nadir (cells/mm^3)		
50	1.0	Ref
51–200	1.22	0.80–1.84
201–500	1.53	0.96–2.43
>500	1.22	0.62–2.41
Unknown/missing	1.80	0.74–4.35
CD4 count in 2003 (cells/mm^3)		
50	1.0	Ref
51–200	1.39	0.58–3.32
201–500	1.63	0.73–3.62
>500	3.46	1.49–8.04
Unknown/missing	1.70	0.71–4.11
Substance use	$n = 658$	
Never	1.0	Ref
Former	0.66	0.41–1.05
Current	0.44	0.29–0.68
Alcohol use		
No drinking	1.0	Ref
Social drinking	0.74	0.50–1.08

	Overall sample	
	OR	**95%CI**
Hazardous/binge drinking (HBD)	0.45	0.26–0.76
SA tx* Substance use		
Never user	1.0	Ref
(−) SA tx in current users	0.50	0.32–0.78
(−) SA tx in former user	0.62	0.38–1.02
(+) SA tx in current users	0.23	0.11–0.48
(+) SA tx in former users	0.82	0.40–1.71

[†] Adjusted for site.

[‡] Employment status and insurance were not significantly associated with adherence in bivariate analysis.

[§] OR = 1 indicates no difference in adherence between categories; OR < 1 = poorer adherence; OR > 1 = better adherence.

Table III

Multivariate model for effects of substance abuse treatment on adherence to HAART in overall sample on HAART (n=659).[**][††]

	Overall sample	
	OR	95%CI
Age	n = 655	
18–39	1.0	Ref
40–49	1.01	0.66–1.54
50	0.98	0.60–1.60
Race		
White	1.0	Ref
Black	0.54	0.33–0.88
Hispanic	0.51	0.28–0.94
Other/missing	0.86	0.32–2.30
AIDS diagnosis	0.63	0.43–0.94
Substance abuse treatment (SA tx)		
Never user	1.0	Ref
(−) SA tx in current users	0.49	0.31–0.78
(−) SA tx in former user	0.61	0.37–1.00
(+) SA tx in current users	0.24	0.11–0.51
(+) SA tx in former users	0.82	0.39–1.72

[**] Adjusted for site.

[††] OR = 1 means no difference in adherence between categories; OR < 1 means poorer adherence; OR > 1 means better adherence.