SHORT-TERM DECLINES IN CD4 LEVELS ASSOCIATED WITH COCAINE USE IN HIV-1 SEROPOSITIVE, MINORITY INJECTING DRUG USERS

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This study evaluates the association of cocaine use with short-term change in CD4 counts among human immunodeficiency virus type 1 (HIV-1) seropositive, minority injecting drug users prior to the introduction of zidovudine (AZT). Ninety-eight HIV-1 seropositive subjects were recruited from six inner-city, methadone maintenance clinics. A baseline assessment included a short questionnaire regarding drug behavior and quantitation of CD4 cell counts. These measures were repeated on all subjects 3 to 4 months later. Thirty-eight subjects reported using cocaine between baseline and 4-month follow-up evaluations. Males and African Americans were more likely to be cocaine users ($P<.01$). Cocaine users were more likely to engage in heroin and needle use ($P<.001$). Cocaine users experienced a significant decline in CD4 cells compared with nonusers ($P=.013$); no marked difference in CD4 decline was noted between heroin users and nonusers ($P=.19$). Multivariate analysis showed that a decline in CD4 counts was 2.82 times more likely to occur in cocaine users than in cocaine nonusers (90% two-sided confidence interval of 1.08, 7.37). These findings support the hypothesis of a possible link between cocaine use and short-term CD4 decline in HIV-1 seropositive injecting drug users. (*J Natl Med Assoc.* 1993;85:293-296.)

Key words • cocaine • human immunodeficiency virus (HIV) • intravenous drug users • CD4 counts

Infection with human immunodeficiency virus type 1 (HIV-1) represents an important cause of morbidity and mortality among injecting drug users. As we enter the second decade of the acquired immunodeficiency syndrome (AIDS) pandemic, intravenous drug users represent an important reason for the changing epidemiology of AIDS,[1] especially among Hispanic and African Americans.[2] As of July 1991, there were more than 40 000 cases of AIDS among female and heterosexual male intravenous drug users. Hispanic and African Americans comprise about 80% of AIDS cases in this exposure group.[3]

The study of the impact of intravenous drugs on the epidemiology of AIDS also has revitalized scientific curiosity about the relationship between psychoactive drug use and the immune system. These agents may make the host more susceptible to infection and accelerate clinical progression following HIV-1 infection. Certainly, the disinhibiting effects of many psychoactive substances may result in the conduct of high-risk behaviors that can lead to the acquisition of HIV-1 infection. In addition, the use of mood-altering substances with high drug injection frequency may alter

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TABLE 1. STUDY POPULATION AND LABORATORY CHARACTERISTICS BY COCAINE USE

	Total (n=98)	Cocaine Use: Yes (%) (n=38)	Cocaine Use: No (%) (n=60)	Two-Sided *P* Value
Age				
20 to 39 years	71	23 (60)	48 (80)	.06
40 to 55 years	27	15 (40)	12 (20)	
Sex				
Male	71	33 (87)	38 (63)	<.01
Female	27	5 (13)	22 (37)	
Race*				
Black	48	24 (65)	24 (40)	<.01
Other	50	14 (35)	36 (60)	
Income†				
≤$10 000	86	33 (89)	53 (88)	.92
>$10 000	11	4 (11)	7 (12)	
Education				
<12 years	56	21 (57)	33 (55)	.94
≥12 years	42	16 (43)	27 (45)	
Needle use				
Yes	45	33 (87)	12 (20)	<.001
No	53	5 (13)	48 (80)	
Heroin use				
Yes	29	24 (63)	5 (8)	<.001
No	69	14 (37)	55 (92)	
CD4 cells at baseline mean (standard error)		517 (56.5)	483 (41.3)	.93

*Other is predominantly Hispanic.
†Missing information on one person.

the distribution of the immune system cell types.[4,5]

This article reports the findings of a longitudinal study evaluating the relationship between short-term declines in CD4 cell counts and continued cocaine use in HIV-1 seropositive injecting drug users. The population selected and short length of follow-up were a consequence of our desire to focus on the natural history of CD4 changes in injecting drug users prior to the introduction of zidovudine (AZT), which often increases CD4 counts and thus would complicate the interpretation of any data relating to CD4 changes due to psychoactive drug use.

MATERIALS AND METHODS

Study Sample

Between January 1989 and June 1990, 98 consecutive HIV-1 seropositive subjects who consented to study inclusion and remained in the study for one follow-up interview were recruited from six methadone maintenance clinics located in the Brooklyn and Manhattan boroughs of New York City. These 98 subjects represent the total study population prior to the introduction of zidovudine (AZT) into the clinic who also had at least one follow-up visit at 4 months. This design feature allowed us to focus on the short-term effects of cocaine use in possibly altering CD4 cell counts and to eliminate the confounding effects of AZT. Subjects were required to meet the following criteria:

- 18 years of age or older,
- history of injecting drug use,
- HIV seropositivity,
- heterosexual orientation, and
- willingness to sign an informed consent.

The study sample was two thirds male, predominantly African American and Latino (94 of 98), and had a mean age of 37 years. The sample reflected the clinic population from which it was drawn. Several mechanisms were used to recruit study subjects, including referral from medical staff, recruitment by research assistants, and self-approach because of publicity.

Laboratory Studies

Laboratory testing for CD4 cells was done at a central location using standard methods (Smith Kline Bio-Science Laboratories, Syosset, New York).

Data Collection

A trained research assistant administered a structured questionnaire to study participants at the beginning of the study. The questionnaire included sociodemographic characteristics, HIV symptoms, drug use, and sexual behavior. Blood was collected to test for CD4 cells. All subjects were paid $15 for their time. A follow-up interview was conducted between 3 and 4 months after the baseline interview. The follow-up interview included a short questionnaire and blood testing to quantitate the number of CD4 cells. Subjects were defined to be cocaine users if they reported cocaine use between baseline (first) and follow-up (second) interviews. Similar definitions were applied to classification of patients as needle users or heroin users. Thus, if a subject reported previous cocaine use at baseline but no cocaine use since baseline when questioned at the follow-up, that subject was classified as a cocaine nonuser. Any subjects who reported cocaine use at follow-up were classified as a cocaine user.

Statistical Methods

Statistical analyses were performed using SAS.[6] For continuous-valued data, the nonparametric Kruskal-Wallis one-way analysis of variance test was used for between-group comparisons. The chi-square test was used for between-group comparisons involving categorical data. The logistic regression model was used to examine the interrelationship among several factors simultaneously. This model was used for the analysis of binary outcome data (increase versus decline in CD4 levels from baseline). All P values are of the two-sided type.

RESULTS

The demographic characteristics of the study participants with respect to cocaine use are presented in Table 1. Thirty-eight of 98 (39%) subjects reported using cocaine within the 3- to 4-month period between baseline and follow-up interviews. Mean age at baseline was 37 years (SD = 6.75). Participants under 40 years old tended to be less likely to be cocaine users ($P = .06$). Males and African Americans were more likely to be cocaine users than others ($P < .01$). Cocaine use was not associated with income and years of education ($P = .92$ and $P = .94$, respectively). There was no difference between cocaine users and nonusers with respect to the mean number of CD4 cells at baseline ($P = .93$). Among cocaine users, 58% had CD4 cell counts less than 500 while the same was true for 62% of nonusers ($P = .71$).

Participants who used cocaine also were more likely to engage in heroin and needle use during that time ($P < .001$). Among the 38 cocaine users, 33 (87%) engaged in needle use and 24 (63%) used heroin. Forty-eight (80%) of 60 cocaine nonusers did not engage in needle use, and 55 (92%) of 60 cocaine nonusers were not involved in heroin use.

Changes in CD4 cell counts between baseline and follow-up interviews for the cocaine nonusers and cocaine users were compared. There was a trend for cocaine nonusers to have a smaller decline from baseline (mean = −6 per cubic millimeter) than cocaine users (mean = −59 per cubic millimeter) ($P = .13$). There was no difference in CD4 change from baseline between heroin users and nonusers ($P = .73$).

There was substantial inter-subject variability in the change from baseline, which would tend to diminish the statistical significance of any difference between the cocaine users and nonusers. Thus, while the effect size in CD4 change from baseline was marked between cocaine users and noncocaine users (mean difference between groups: −53 per cubic millimeter), the large variability diminished the statistical significance associated with this between-group difference. These data were, therefore, reanalyzed by creating a coarser classification of change. In Table 2, the participants were categorized into one of two groups (a gain or loss in CD4 cells from baseline). Table 2 shows that while 54% of cocaine nonusers experienced an increase in CD4 count, only 36% of users experienced an increase. Overall, there was a significant difference between cocaine users and nonusers ($P = .013$). Table 2 also shows that there is no marked association between heroin use and change in CD4 cell counts.

TABLE 2. EFFECT OF DRUG USE ON CHANGE IN CD4 COUNT BETWEEN BASELINE AND 4 MONTHS

	Change in CD4 Count	
Drug Use	**Gain (%)**	**Decline (%)**
Cocaine		
Yes	13 (34)	25 (66)
No	32 (54)	28 (46)
Heroin		
Yes	12 (41)	17 (59)
No	33 (48)	36 (52)

To examine further the interrelationship of several factors simultaneously in terms of changes in CD4 level, a logistic regression analysis was performed. The logistic model assumes a binary outcome (ie, an increase or decrease in CD4 levels from baseline). For this regression analysis, the following set of independent variables were considered: cocaine use, heroin use, needle use, gender, age, and race. Both step-up and step-down regression approaches revealed that the only variable markedly related to an increase or decrease in CD4 level was cocaine use ($P = .094$). All other variables were nonsignificant at the $P > .20$ level. With this model, we found use of cocaine was associated with a decrease in CD4 cells between the baseline and follow-up interviews (odds ratio = 2.82, 90% two-sided confidence interval = 1.08, 7.37).

DISCUSSION

Our findings support the hypothesis of a link between cocaine use and short-term CD4 decline. Among users, the average decline was 59 mg/mm. In nonusers, the average decline was 6 mg/mm^3. While not striking clinically, one must note that this change occurred over a short 4-month period. If AZT had not been introduced into our clinic population so soon after the study

commenced, much more dramatic effects may have emerged with a prolonged period of follow-up. Moreover, our finding is relevant to the large number of injecting drug users not receiving AZT in any scheduled manner.

Cocaine users had an almost threefold increase of risk for short-term CD4 decline; this risk was largely independent of needle or heroin use. In addition, because we used self-reported use of cocaine, it is possible that misclassification with respect to cocaine use may have diluted the true association between cocaine use and CD4 decline from baseline. The assumption is that if a subject did not use cocaine, he or she would be unlikely to have reported use of cocaine. On the other hand, if a subject used cocaine, there is the possibility of not reporting its use. This would lead to selectively misclassifying cocaine users as nonusers and would dilute the true association.

Prior to the epidemic of AIDS, other investigators[7,8] had described substance-induced immunodeficiency among injecting drug users. Des Jarlais and colleagues[4] reported a correlation between drug injection frequency and CD4 cell decline in a cohort of injecting drug users. They found no association between decline of CD4 cells and noninjected cocaine use.[4] Flegg et al[5] also reported CD4 cell decline associated with continued drug injection. Kaslow et al[9] and other investigators[10-12] did not find any effect of psychoactive drug use on HIV-1 disease development or CD4 cell decline.

In our study population, the most common route of cocaine and heroin administration was by drug injection, which often leads to needle sharing. Not only does this activity increase the risk of multiple exposures to HIV, it also may be the source of the viral transmission to other HIV-seronegative persons. Furthermore, continued drug use may lead to participation in risky sexual behavior. Thus, our findings suggest that HIV-1 seropositive persons should be counseled against drug use.

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