**ABSTRACT**

The use of alcohol or illicit drugs is common among adolescents and adults in the United States, especially among those with HIV infection. The use of opioids, cocaine, marijuana, and other illicit drugs has been associated with several adverse health outcomes among patients with HIV infection, including lower utilization of antiretroviral therapy, higher rates of opportunistic infections, poor treatment adherence, and high-risk sexual behaviors. Alcohol use is often overlooked in clinical practice, but also increases the risk of treatment failure and high-risk behaviors. In patients with HIV infection and substance use problems, interventions that reduce substance use have been shown to improve treatment adherence and survival. All patients with HIV infection should be regularly screened for substance use problems. Individuals with substance use problems who do not have evidence of dependence may be successfully managed using a brief patient-centered intervention. The focus for these patients is generally on reducing substance use rather than complete abstinence. Individuals with evidence of dependence may require referral to a specialist. Opioid substitution with methadone or buprenorphine may help to improve treatment adherence and viral suppression for patients who misuse opioids. Mental health disorders are also common among those with HIV and substance use problems, and the combination of substance use and mental health problems presents a significant challenge in HIV care. These patients are less likely to enter care, to remain adherent, and to attain complete viral suppression. Minority patients are generally less likely to receive mental healthcare, and may be at especially high risk of complications due to substance use problems and mental illness. Effective communication among an interdisciplinary treatment team is essential to improve long-term treatment outcomes for these challenging patients.


**PROCEEDINGS**

**ASSESSING SUBSTANCE USE AMONG PATIENTS LIVING WITH HIV/AIDS: THE ROLE OF HARM REDUCTION AND TREATMENT**

Geetanjali Chander, MD, MPH

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Substance use is common in the United States, and often complicates the management of HIV infection. For the US population as a whole, the nationwide National Survey on Drug Use and Health found that approximately 20% of the population aged 12 or older reported the use of 1 or more illicit drugs during the previous month, including marijuana (15.2%), prescription medications (6.2%), cocaine (1.9%), hallucinogens (1.1%), inhalants (0.6%), or heroin (0.2%). When substance use was examined by race/ethnicity, the rate of self-reported illicit drug use during the previous month was highest for individuals who described themselves as being of 2 or more races (14.7%), followed by blacks (10.1%), American Indians and Alaskan Natives (9.5%), non-Hispanic whites (8.2%), Native Hawaiians and Pacific Islanders (7.3%), Hispanics (6.2%), and Asians (3.6%; Figure 1). Current alcohol use was reported by 51.6% of those surveyed, with 23.3% reporting binge drinking...
at least once in the 30 days before the survey, and 6.9% reporting heavy drinking. The prevalence of substance use is even greater among individuals with HIV or AIDS. Nationwide surveys have reported illicit drug use by approximately 40% of those with HIV infection, and hazardous alcohol use during the previous month by 8% to 11%. In addition, tobacco use is reported by approximately 50% to 75% of those with HIV infection, which is approximately 3 times the rate among the noninfected population.

Many studies have documented that substance use problems significantly increase the risk of adverse health outcomes in patients with HIV infection. The use of heroin or prescription opioids has been linked to lower rates of highly active antiretroviral therapy (HAART) utilization, treatment adherence, and viral suppression, and to higher rates of opportunistic infections, disease progression, and HIV-related mortality. Persistent cocaine use has been associated with increased AIDS-related mortality and accelerated disease progression, and binge cocaine use increases the risk of high-risk sexual behaviors. Marijuana use is very common among HIV-infected individuals, and has been associated with decreased medication adherence. Hazardous alcohol use, although often not detected in HIV clinical settings, may significantly influence clinical outcomes for patients with HIV infection. Hazardous alcohol use has been defined by the National Institute of Alcohol Abuse and Alcoholism (NIAAA) as more than 7 drinks per week or more than 3 drinks per occasion in women; and more than 14 drinks per week, or more than 4 drinks per occasion in men. Individuals with HIV who have hazardous alcohol use patterns are significantly less likely to use HAART or to attain complete viral suppression when HAART has been prescribed. In addition, alcohol use has been associated with decreased odds of medication adherence. In a recent meta-analysis, the odds ratio for medication adherence was 0.47 (95% confidence interval [CI] = 0.41–0.55) for those with high-risk alcohol use compared with moderate drinkers or nondrinkers. Alcohol use also has been associated with high-risk sexual behaviors. In another recent meta-analysis, the odds ratio for unprotected intercourse was 1.69 (95% CI = 1.45–1.97) for problem drinkers, and 1.98 (95% CI = 1.63–2.39) for those who consume alcohol in sexual contexts. Another recent study performed in urban sexually transmitted disease clinics found that binge drinking was associated with a very high risk of unprotected anal intercourse among women. Thus, although alcohol is often overlooked in the context of HIV prevention and treatment, patterns of unhealthy alcohol use substantially alter the risk of HIV infection and the success of treatment.

Although substance use is a clear risk factor for worse clinical outcomes in patients with HIV infection, substance abuse treatment has been shown to improve clinical outcomes. A longitudinal study of drug and alcohol use among individuals with HIV infection found that switching from active substance use to nonuse was followed by a significant improvement in HAART adherence and HIV viral suppression. In a study of 659 patients who were using HAART, patients with a history of substance use problems who were currently in treatment were as adherent to HAART as individuals who had no history of substance use. In a recent longitudinal study from Vancouver, Canada, survival rates for intravenous drug users were the same as for nonusers after adjusting for differences in medication adherence.
HARM REDUCTION STRATEGIES

Interventions to reduce harm associated with substance use in HIV-infected patients include identification of substance abuse, treatment of the substance abuse disorder, treatment of HIV infection, identification and treatment of co-occurring mental health disorders, and steps to improve retention in treatment.

All patients with HIV infection should be screened for possible substance misuse. Patients with negative screen results should be rescreened annually at a minimum; substance misuse should be queried at each visit among those with a positive screen. The NIAAA recommends a 1-question screen for alcohol misuse: “How often, in the last year, have you had 4 or more drinks (women) or 5 or more drinks (men)?” A report of more than 1 episode should be followed with questions about the frequency and quantity of use. The Alcohol Use Disorders Identification Test is an interviewing tool to assess more detailed patterns of unhealthy alcohol consumption, including frequency, quantity, and consequence of use. This instrument is available online at http://whqlibdoc.who.int/hq/2001/who-msd-msb_01.6a.pdf. A similar screening question can be used for illicit drug use: “How many times in the last year have you used an illegal drug or used a prescription drug for nonmedical reasons?” Patients reporting more than 1 use should be questioned in more detail about the specific patterns of drug use.

In developing a management strategy, it is essential to distinguish substance use from substance dependence, which is defined by the presence of 3 or more of the following:

- Tolerance, (a) A need for markedly increased amounts of the substance to achieve intoxication or the desired effect or (b) Markedly diminished effect with continued use of the same amount of the substance.
- Withdrawal, as manifested by (a) The characteristic withdrawal syndrome for the substance or (b) The same (or closely related) substance is taken to relieve or avoid withdrawal symptoms.
- The substance is often taken in larger amounts or over a longer period than intended.
- There is a persistent desire or unsuccessful efforts to cut down or control substance use.
- A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
- Important social, occupational, or recreational activities are given up or reduced because of substance use.
- The substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance (eg, current cocaine use despite recognition of cocaine-induced depression or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

A brief intervention by the primary care physician may be effective for patients with a positive screening result but who do not meet criteria for alcohol or drug dependence. Patients with signs of alcohol or drug dependence should be referred for specialist treatment. The goal of the brief intervention is not necessarily abstinence, but the reduction of substance use to safer levels. The brief intervention uses a patient-centered approach and emphasizes the “4 A’s”:

- Ask about substance use
- Assess for alcohol use disorders
- Advise and assist in cutting down or abstinence, with goal setting and further treatment when necessary. A brief, directive interaction is developed based on the assessment of substance use and related problems, and patient readiness to change. Personalized feedback and goal-setting is based on individual patient circumstances (eg, elevated liver function tests, depressive symptoms, or increasing conflicts with others).
- Arrange follow-up to monitor progress and continue support

As with alcohol, harm reduction in patients who use illicit drugs should not focus exclusively on abstinence, but also includes needle exchanges; safe disposal of needles; emphasizing the importance of not sharing needles, syringes, or cookers; and cleaning needles with bleach if no clean needles are available. Pharmacologic treatment is often an important component of harm reduction. In opioid substitution therapy, patients receive a long-acting opioid agonist in place of heroin or other nonprescription narcotics to
block the sensation of euphoria associated with short-acting opioid drugs. The goals of opioid substitution are to reduce or eliminate opioid use, prevent future harms associated with continuing use, improve the quality of life and well-being of the opioid-dependent patient, reduction or cessation of injecting and associated risk of bloodborne virus transmission, and to reduce the risk of overdose.23,24

Options for opioid substitution therapy include methadone and buprenorphine. Methadone is an opioid receptor agonist that is used to prevent symptoms of withdrawal and reduce craving for opioids. In opioid-dependent patients with HIV infection, methadone has been shown to improve HAART use, treatment adherence, and viral suppression (Figure 2).25,26 In the United States, methadone administration is restricted to highly regulated treatment settings. In addition, methadone is associated with potentially significant interactions with HAART medications. For example, efavirenz may reduce methadone levels by as much as 50%, which may precipitate withdrawal in some patients. Buprenorphine is a µ-opioid receptor partial agonist that may be prescribed in office-based settings, and is therefore more easily integrated into addiction treatment in HIV primary care settings. Although buprenorphine is metabolized by CYP3A4, there is little or no significant clinical interaction between buprenorphine and HAART medications. Buprenorphine is often combined with naloxone, which is inactive when the drug is taken sublingually but precipitates withdrawal symptoms if injected.27 A recent randomized clinical trial compared buprenorphine integrated into an HIV clinic with referral to an opioid treatment program in 93 patients with HIV infection.28 Patients in the office-based buprenorphine group were more likely to participate in opioid agonist therapy, less likely to have urine drug screen results that were positive for cocaine or opioids (Figure 3), and also exhibited greater engagement in primary care compared to those referred to an off-site treatment program. There was no difference in use of antiretroviral therapy between the 2 groups.

Harm reduction approaches also are available for other drugs of abuse. For cocaine abuse, counseling has been the mainstay of therapy. Some studies have demonstrated reduced cocaine use with disulfiram or with the use of behavior modification approaches.29 For cigarette smoking, nicotine replacement therapy, pharmacotherapy (eg, with bupropion), or supportive therapy all have been used with success to help patients stop smoking.29

Regardless of the specific approach, drug treatment programs are important for patients with HIV infection and substance use problems to remain engaged in care. In a recent study of women with HIV, improved treatment adherence was noted with a variety of specific substance abuse approaches, including Alcoholics Anonymous, Narcotics Anonymous, and inpatient treatment programs.30

IDENTIFICATION AND TREATMENT OF CO-OCCURRING MENTAL HEALTH DISORDERS

Mental health disorders are common among individuals living with HIV infection. A positive screen for depression was reported for 36% of patients with HIV in one study,31 and a second study found that the likelihood of a diagnosis of depression was approximately doubled among those with HIV compared with the general population.32 Patients with HIV exhibit high rates of anxiety disorders, including generalized anxiety disorder (16% of patients), panic attacks (10%), and posttraumatic stress disorder (PTSD; 16%–54%).31,33 Schizophrenia or other severe mental illnesses have been associated with high rates of HIV

Figure 2. Initiation of HAART in Patients Using MMT

Mental health disorders significantly diminish patient quality of life, and they also complicate HIV treatment. For example, depression has been associated with delays in initiating HAART, decreased treatment adherence, HAART interruption, virologic failure, and increased risk of death. Greater psychological trauma and PTSD have been associated with several adverse health outcomes among those with HIV infection, including AIDS-defining illnesses or death, substance use, high-risk behaviors (eg, intercourse with multiple partners or inconsistent condom use), and decreased medication adherence.

Several studies have demonstrated lower rates of mental health service use by minority patients with HIV infection, including psychotropic medications and psychiatric treatment. These observations are especially important because when patients with psychiatric disorders are effectively engaged in care, they may actually have better outcomes than other patients. For example, in a study from The John Hopkins University HIV clinic, patients with psychiatric disorders were 37% more likely to receive HAART, and 40% more likely to survive, than patients without psychiatric disorders. Screening for and treatment of mental health disorders is therefore an integral part of HIV treatment.

Mental health and substance use disorders often occur together. It has been estimated that approximately 50% of individuals with a lifetime history of drug use disorders also are affected by at least 1 mental disorder. Conversely, nearly 25% of individuals with major depressive disorder also meet diagnostic criteria for a substance abuse disorder. In a study of a nationally representative sample of individuals with HIV infection in the United States, 13% had psychiatric symptoms in combination with heavy drinking, drug dependence, or both. Psychiatric disorders and drug or alcohol dependence may interact with one another to further complicate treatment. In a study of 5119 patients in care for HIV infection, a concurrent mental health disorder and illicit drug use was associated with lower use of HAART, and more than a doubling in the likelihood of using inpatient services. In a second study of more than 10,000 patients with HIV infection, concurrent illicit drug use and a mental health disorder was associated with lower odds of

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**Figure 3. Probability of Positive Results for Opioid and Cocaine Use in Clinic-Based Buprenorphine Program vs Referral to Traditional Opioid Treatment Program**

Observed estimates are shown for clinic-based buprenorphine-naloxone (BUP; circles) and referred treatment (triangles); vertical lines represent 95% confidence intervals. Mixed-effects model-based estimates for positive urine drug test results are shown for clinic-based BUP (squares) and referred treatment (diamonds); shading represents 95% confidence bands. The average model-based estimates for opioid-positive results and cocaine-positive results were significantly lower for clinic-based BUP than for referred treatment ($P = 0.015$ and 0.012, respectively). Reprinted with permission from Lucas et al. Ann Intern Med 2010;152:704-711.
attaining complete HIV viral suppression compared to patients with either illicit drug use or mental health disorders alone, or with neither condition.31

Treatment approaches for these patients with triple diagnoses of HIV, substance use, and mental health disorders must overcome the substantial barriers to care that patients face in trying to navigate a variety of different healthcare settings and services. The integrated care approach is one method that has been developed to help patients to overcome these barriers by combining HIV primary care, mental health treatment, and substance abuse services into a single coordinated treatment program that simultaneously addresses the clinical complexities associated with multiple needs and conditions. This approach also might include ancillary services such as housing assistance, case management, transportation, or child care. Effective communication among a multidisciplinary treatment team is also essential to the successful implementation of this approach, with shared decision-making among several collaborating clinicians.

CONCLUSIONS

Substance misuse and mental health disorders are common among persons with HIV and AIDS, and are associated with worse HIV treatment outcomes. Screening for substance use, patient-centered interventions for those without evidence of dependence, and referral to specialist care when needed should be integral to HIV therapy. In patients who misuse opioids, opioid substitution therapy has been shown to improve HIV outcomes. Concurrent mental health and substance use disorders may be associated with even worse treatment outcomes than either alone. Combining substance abuse treatment, psychiatric treatment, and HIV care may help to improve outcomes for HIV infection.

REFERENCES


