



Tobacco use and nicotine dependence among HIV-infected and uninfected injection drug users

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ABSTRACT

Introduction: Urban U.S. populations are burdened by intersecting epidemics of HIV infection, injection drug use, and cigarette smoking. Given the substantial morbidity attributable to tobacco in these populations, we characterized smoking behaviors, nicotine addiction, and tobacco exposure among HIV-infected and HIV-uninfected injection drug users (IDUs) in Baltimore, Maryland.

Methods: Smoking behaviors among participants in the ALIVE Study were assessed using interviewer-administered questionnaires. Smoking history and nicotine dependence (Fagerstrom Index scores) were compared by HIV and drug injecting status. Serum cotinine (a nicotine metabolite) was measured for a sample of participants by enzyme immunoassay.

Results: Among 1052 participants (29.7% HIV-infected, 39.8% active injectors), 85.2% were current smokers and 9.3% were former smokers. Smoking prevalence, age at smoking initiation, and cumulative tobacco exposure were similar by HIV status. Median Fagerstrom scores of 4 for HIV-infected and HIV-uninfected smokers indicated moderate nicotine dependence. Daily cigarette consumption was identical by HIV status (median 10 cigarettes), although HIV-infected participants were less likely to smoke 1+ pack daily compared to HIV-uninfected participants (18.0% vs. 26.9%, $p = 0.001$). Compared to former injectors, active injectors had higher smoking prevalence (90.5% vs. 81.7%, $p = 0.0001$), greater daily cigarette consumption (30.7% vs. 19.6% smoked 1+ pack daily, $p = 0.0001$), and slightly higher Fagerstrom scores (median 5 vs. 4). Cotinine levels paralleled self-reported cigarette consumption.

Discussion: Tobacco use is extremely common among inner-city IDUs. Smoking behavior and nicotine dependence did not materially differ by HIV status but were associated with active drug injection. Cessation efforts should target the dual dependence of cigarettes and drugs experienced among this population.

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1. Introduction

Human immunodeficiency virus (HIV) infection and injection drug use have long been recognized to coexist in contemporary urban populations. Tobacco use constitutes a third epidemic that may also impact urban populations with dramatic adverse health consequences. Cigarette smoking is common among HIV-infected individuals (prevalence estimates ranging from 35–70% compared to approximately 20% in the general U.S. population), (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005; CDC, 2007; Gritz, Vidrine, Lazev, Amick, & Arduino, 2004; Thompson, Nanni, & Levine, 1996) likely reflecting increased smoking in persons who engage in high-

risk sexual or drug use behaviors associated with HIV transmission. Given the success of highly active antiretroviral therapy (HAART) in prolonging survival among HIV-infected individuals, chronic smoking-related conditions such as lung cancer, chronic obstructive pulmonary disease (COPD), and cardiovascular disease account for a growing proportion of morbidity and mortality. (Braithwaite et al., 2005; d'Arminio Monforte et al., 2005; Lewden et al., 2005) An elevated risk of lung cancer, (Chaturvedi et al., 2007; Engels et al., 2006; Kirk et al., 2007) COPD, (Diaz, Clanton, & Pacht, 1992; Diaz et al., 2000; Sahebajami, 1992) and cardiovascular disease (Friis-Moller et al., 2003; Grunfeld et al., 2009; Lewden et al., 2005; Mary-Krause, Cotte, Simon, Partisani, & Costagliola, 2003; Saves et al., 2003) has been observed among HIV-infected individuals, and lung cancer is now the third most common malignancy in this population. (Chaturvedi et al., 2007; Kirk et al., 2007)

Injection drug users (IDUs) comprise one of the major HIV transmission groups. Independent of HIV infection, injection drug

Abbreviations: HIV, human immunodeficiency virus; AIDS, acquired immune deficiency syndrome; SHS, second hand smoke.

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use is associated with substantial morbidity and mortality, (McGinnis & Foege, 1999) although the burden of tobacco use and of smoking-related disease remains uncertain. Further, IDU's predisposition to addiction may confer an enhanced physiological dependence to nicotine. (Clemmey, Brooner, Chutuape, Kidorf, & Stitzer, 1997; Frosch, Shoptaw, Nahom, & Jarvik, 2000; Stark & Campbell, 1993) Although injection drug use represents a chronic, relapsing, medical condition, many IDUs are able to achieve injection cessation for prolonged periods. (Galai, Safaeian, Vlahov, Bolotin, & Celentano, 2003) The impact of injection cessation on the smoking behavior of former IDUs has not been fully explored.

Although the health consequences of HIV infection among IDUs have been well documented, the contribution of cigarette smoking to the disease process among this population is unclear. It remains unknown to what degree HIV status and injection drug use influence tobacco use. We, therefore, performed a cross-sectional study within a large inner-city cohort of IDUs in Baltimore, Maryland in which we collected detailed smoking histories to examine the prevalence of cigarette smoking. We determined whether smoking behavior and the level of nicotine dependence differed between HIV-infected and HIV-uninfected participants, and between active and former injectors. To further quantify tobacco exposure, we also measured serum levels of cotinine (a metabolite of nicotine) in a sample of participants.

2. Methods

2.1. Study participants and exposure assessment

The AIDS Linked to the Intra-Venous Experience (ALIVE) Study is a long-standing cohort study that has recruited and followed IDUs in Baltimore, Maryland since 1988. (Anthony et al., 1991) Eligibility criteria at enrollment include age of at least 18 years, ability to provide informed consent, and history of injection drug use. Cohort participants are seen at biannual visits, when data are obtained on recent drug use including intensity and route of use, medical illnesses, and HIV treatment. Blood samples are routinely collected for repository storage.

Participants in this study were evaluated at routinely scheduled follow-up visits from January 2007 to September 2008. In total, 1052 ALIVE participants underwent a structured interview regarding smoking history, exposure to second-hand smoke (SHS), symptoms of lung disease, and personal and family history of respiratory conditions. Additional questions on use of smoked illicit drugs were included. All participants provided written informed consent, and the study protocol was approved by institutional review boards of Johns Hopkins School of Public Health and the National Cancer Institute.

We defined active injection drug use as any reported drug injection within the last six months. Never smokers were individuals who had smoked fewer than 100 cigarettes over their lifetime. Former smokers were individuals who had smoked at least 100 lifetime cigarettes but none within the previous 30 days. Current smokers had both smoked 100 or more lifetime cigarettes and smoked at least once in the last 30 days. Individuals who lived with anyone who regularly smoked cigarettes in their home were considered exposed to SHS in the home. Individuals who regularly spent time when not at home where people smoked cigarettes were defined as exposed to SHS outside the home. To measure nicotine dependence, we used the Fagerstrom Index, (Fagerstrom & Schneider, 1989) which includes questions regarding time to first cigarette use after waking, difficulty refraining from smoking in prohibited areas, the cigarette one would most hate to give up, number of cigarettes smoked per day during the last week, smoking frequency during the beginning of the day, and smoking while sick.

Cotinine levels were measured in serum specimens collected on the same day as the interview. Because cotinine levels vary by race (Caraballo et al., 1998) and the majority of ALIVE participants are African American and male, only African American men were included in this sample. From those with available samples, 270 participants

were randomly selected for cotinine measurement based on current smoking patterns and HIV status. Current smoking categories included nonsmokers, light/moderate smokers (less than 1 pack [20 cigarettes] per day), and heavy smokers (1 pack [20 cigarettes] per day or greater). Among HIV-infected participants, sampling was further based on the degree of immune suppression (stratified as CD4 count 0–299 vs. 300+ cells/mm³). We randomly selected up to 50 participants in each stratum, if available. Cotinine was measured using an enzyme immunoassay (OraSure Technologies, Bethlehem, PA), which is calibrated across a range from 2 to 50 ng/ml. Because we tested serum samples diluted 1:20, the assay provided results corresponding to serum levels up to 1000 ng/ml. Cotinine levels measured using this assay are highly correlated with levels measured by gas chromatography. (Boffetta et al., 2006)

2.2. Statistical analysis

We compared demographic characteristics, smoking history, and measures of nicotine dependence in HIV-infected and HIV-uninfected participants using the chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. A total Fagerstrom score was calculated for each current smoker by assigning points to possible answers of each question of the Fagerstrom Index. (Fagerstrom & Schneider, 1989) Individuals with total scores of 7–10 points were considered to have high nicotine dependence, those with 4–6 points medium nicotine dependence, and those with 0–3 points low nicotine dependence. (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) Similar methods were employed for analyses comparing active to former injection drug users. Cotinine levels in HIV-infected and HIV-uninfected individuals as well as in active and former IDUs were compared within smoking strata (nonsmokers, light/moderate smokers, heavy smokers) using the Wilcoxon rank sum test. We also performed multivariate linear regression to determine whether HIV status or active injection drug use was independently associated with differing cotinine levels.

3. Results

3.1. Demographic characteristics

Demographic characteristics of the 1052 participants, stratified by HIV status (29.7% HIV-infected) are described in Table 1. The median age was 49 years among both HIV-infected and HIV-uninfected individuals, although HIV-infected participants were underrepresented at the extremes of the age distribution (less than 30 or greater than 60 years old). Compared with HIV-uninfected participants, HIV-infected individuals were more likely to be female and black, although only race differed significantly. Income levels did not vary by HIV status; however, there was limited variability in formal income reported, with 94.5% of HIV-infected and 91.5% of HIV-uninfected participants reporting less than \$10,000 annually.

As shown in Table 1, 419 participants (39.8%) reported actively injecting drugs in the prior 6 months. Compared to HIV-uninfected participants, HIV-infected individuals were less likely to be currently injecting drugs, and among those currently injecting, HIV-infected individuals were less likely to be injecting daily or more. HIV-infected participants were also less likely to be currently injecting heroin alone compared to HIV-uninfected participants. The age at initiation of injection drug use was significantly younger for HIV-infected individuals compared to HIV-uninfected individuals (median 20 vs. 21 years, $p = 0.026$).

3.2. Smoking behavior and nicotine dependence by HIV status

Overall, 85.2% of participants were current smokers and 9.3% were former smokers (94.5% were ever smokers), and no difference in

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