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The Association between Cigarette Smoking, Virologic Suppression, and CD4+ Lymphocyte Count in HIV-Infected Russian Women

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Abstract

Cigarette smoking among people living with HIV/AIDS is associated with significant morbidity and mortality, but findings regarding the association between cigarette smoking and HIV viral load and CD4+ lymphocyte counts have been inconsistent. This study characterized the prevalence of cigarette smoking among HIV-infected Russian women and examined the association between smoking frequency and quantity and HIV viral load and CD4+ lymphocyte counts. HIV-infected Russian women (N=250; *M*age = 30.0) in St. Petersburg, Russia, completed an audio computer-assisted self-interview survey assessing cigarette use, antiretroviral medication adherence, and provided blood samples assayed for HIV viral load and CD4+ lymphocyte counts. The majority (60.4%) reported cigarette smoking in the past month; 49.0% of recent smokers were classified as moderate or heavy smokers, defined as smoking ≥10 cigarettes daily. Viral load status did not differ between infrequent smokers and regular smokers. However, moderate/heavy smokers (relative to light smokers) were more likely to have a detectable viral load (AOR = 2.3, 95% CI: 1.1, 5.1). There were no significant differences in CD4+ lymphocyte counts by smoking frequency or quantity of cigarettes smoked. Results highlight the need for additional research to examine the association between cigarette smoking and virologic suppression and markers of HIV disease

progression. Adverse health consequences of cigarette smoking coupled with a potential link between heavy smoking and poor virologic suppression highlight the need for assessment of cigarette use and provision of evidence-based smoking-cessation interventions within HIV medical care.

Keywords

Cigarette smoking; HIV-infected; antiretroviral medication adherence; virologic suppression

Introduction

Russia has the highest number of cigarette smokers per capita; 39.1% of adults are current smokers (Russian Federation, 2009; WHO, 2009). HIV prevalence is increasing with approximately 980,000 HIV-infected Russians and increasing incidence among Russian women (Burruano & Kruglov, 2009; Federal AIDS Center, 2014; UNAIDS, 2010). Smoking prevalence among HIV-infected Russians is unknown; however, among people living with HIV/AIDS (PLHIV) in the U.S., estimates suggest 40% – 70% smoke (Reynolds, 2009; Tesoriero, Gieryic, Carrascal, & Lavigne, 2010), a rate two to three times higher than the general population (Kalman, Morissette, & George, 2005).

Smoking among PLHIV is associated with significant morbidity and mortality (Crothers et al., 2005; Feldman et al., 2006; Gordin et al., 2008; Helleberg et al., 2013; Lifson et al., 2010; Pines, Koutsky, & Buskin, 2011; Rahmanian et al., 2011). This may be due, in part, to smoking's direct, negative biological effects on the efficacy of specific antiretroviral (ARV) medications (Feldman et al., 2009; Higgins et al., 2007; Miguez-Burbano et al., 2003). Smoking may increase PLHIV's susceptibility to opportunistic infections (e.g., pulmonary infections; Miguez-Burbano et al., 2003; Ompad et al., 2014). HIV-infected smokers may also be less adherent to their ARV medications, which may accelerate HIV disease progression (Shuter & Bernstein, 2008).

Findings regarding the association between smoking and HIV disease status markers and viral suppression have been mixed. Poorer immunologic and viral response to ARVs have been found in smokers, relative to non-smokers (DeFino, Clark, Mogyros, & Shuter, 2004; Feldman et al., 2006; Wojna et al., 2007). In a longitudinal examination of HIV-infected women, smokers had poorer viral responses, poorer immunologic response, and greater risk of virologic rebound (Feldman et al., 2006). However, other studies have not found an association between smoking and CD4+ lymphocyte counts (CD4) or viral load (VL; Akhtar-Khaleel et al., 2016; Kabali et al., 2011; Webb, Vanable, Carey, & Blair, 2007). Research is needed to examine the association between smoking and HIV disease markers. This study characterized smoking prevalence and examined the association between current smoking frequency and quantity and CD4 and VL among HIV-infected Russian women.

Methods

Participants

Participants were Russian HIV-infected women ($N = 250$) who had been diagnosed with HIV for a mean (SD) of 7.1 (4.1) years. Participants had a mean (SD) age of 30.0 (3.0) years; 44.0% were married, 61.2% were employed, and 32.0% were below the Russian poverty line.

Procedures

Participants were recruited during medical appointments at an HIV care center in Saint Petersburg, Russia. A staff member approached female patients, described the study, and assessed eligibility. Eligibility criteria included: (a) 18–35 years old; (b) report vaginal sex in the previous three months (for study aims examining sexual risk); (c) not pregnant; and (d) prescribed ARVs. Data collection consisted of a 45-minute computerized survey. Participants provided biological specimens to test for prevalent STIs, VL, CD4, and recent alcohol use. Written informed consent was obtained from participants. Institutional Review Boards of the participating institutions approved study procedures.

Measures

Demographics—Participants reported their age, marital status, current employment status, and average monthly income in rubles.

Cigarette use—Participants indicated whether they had ever smoked cigarettes in their lifetime (no/yes). Participants reporting a lifetime smoking history then reported the number of days they smoked in the past month. For participants indicating 1 day of past month smoking, a dichotomous variable was created to distinguish: (a) infrequent smokers (<20 days smoking; coded as 0) or regular smokers (≥20 days smoking; coded as 1). Participants indicated the average number of cigarettes per day (CPD) smoked. Consistent with prior research (Okuyemi et al., 2002, 2004; Webb et al., 2007), we created a dichotomous variable to distinguish light smokers (<10 CPD; coded as 0) and moderate/heavy smokers (≥10 CPD; coded as 1).

Length of time since HIV diagnosis—Participants self-reported number of years since HIV diagnosis.

ARV adherence—Participants reported their level of ARV adherence during the past month using a visual analog scale (percentage of medications taken from 0%–100%; Simoni et al., 2006).

Viral load (VL) and CD4+ lymphocyte count (CD4)—Participants provided a blood sample that was tested for VL (undetectable: <50 copies/mL, coded as 0; detectable: ≥50 copies/mL, coded as 1) and CD4.

Data Analytic Approach

Analyses were performed using IBM SPSS version 23.0 (IBM Corporation, 2015). Descriptive statistics were calculated to characterize study variables. Separate logistic regression analyses examined whether regular smoking or moderate/heavy smoking were associated with differences in VL status, adjusting for ARV adherence and number of years since HIV diagnosis. Separate linear regression analyses examined whether regular smoking or moderate/heavy smoking were associated with differences in CD4, adjusting for ARV adherence and number of years since HIV diagnosis.

Results

Most (94%; $n = 235$) indicated a lifetime smoking history. 60.4% ($n = 151$) reported 1 day of past month smoking. Among the effective sample size of recent smokers ($n = 151$), 77.5% ($n = 117$) were regular smokers, smoking on 20 days during the past month. 49.0% ($n = 74$) were moderate/heavy smokers, smoking 10 CPD. Participants self-reported high ARV adherence ($M = 91.4$, $SD = 18.4$, $Median = 100.0$, $Range: 0-100$). The majority (70.9%, $n = 107$) had an undetectable VL ($Range: 0$ copies/mL – 92,283.0 copies/mL; $M = 1507.8$, $SD = 8353.8$). The mean (SD) CD4 was 460.2 (230.5) and ranged from 53.0 to 1436.0.

Separate logistic regression analyses examined whether VL status differed by smoking frequency or quantity. VL status did not differ between infrequent and regular smokers (see Table 1a). Moderate/heavy smokers (relative to light smokers) were more likely to have a detectable VL (AOR = 2.3, 95% CI: 1.1, 5.1; see Table 1b). Separate linear regression analyses examined whether CD4 differed by smoking frequency or quantity. CD4 did not differ between infrequent smokers and regular smokers (see Table 2a) and light and moderate/heavy smokers (see Table 2b).

Discussion

Approximately 60% of Russian HIV-infected women reported recent cigarette use. Half were moderate/heavy smokers, smoking an average of 10 CPD. While there were no differences between infrequent and regular smokers on VL status, moderate/heavy smoking was associated with a greater likelihood of having a detectable VL. This finding may reflect the effect of smoking on metabolic enzyme activity that cause interactions with ARVs, which may reduce plasma concentrations of certain ARV classes (e.g., protease inhibitors; Higgins et al., 2007) and adversely affect virologic suppression. However, there were no differences on CD4 by smoking frequency or quantity.

Findings mirror inconsistencies regarding the association between smoking and virologic suppression and markers of HIV disease progression. Inconsistent findings may, in part, be accounted for by the use of different smoking measures. Smoking has been classified comparing smokers to non-smokers (DeFino et al., 2004; Shuter & Bernstein, 2008), while others have employed alternative measures (e.g., CPD, Akhtar-Khaleel et al., 2016; Kabali et al., 2011; Webb et al., 2007; nicotine dependence measures, Wojna et al., 2007). The majority had an undetectable VL and CD4 counts not indicative of advanced HIV disease progression and reported high levels of ARV adherence, consistent with virologic

suppression. The limited variability in VL and CD4 coupled with high self-reported ARV adherence may have limited our ability to detect differences by smoking status. It may also be important to consider additional factors that may mediate the associations between smoking, ARV adherence, and virologic suppression and the directionality of these associations. Factors including co-occurring substance use (King et al., 2012; Peretti-Watel, Spire, Lert, & Obadia, 2006), chronic pain (Ditre et al., 2011), or depression (King et al., 2012; Webb, Vanable, Carey, & Blair, 2009) and anxiety (Nguyen et al., 2016) symptoms may be important to consider in future research (Gonzalez, Barinas, & O'Cleirigh, 2011).

Strengths and Limitations

To our knowledge, this is the first study to examine the association between smoking and immunosuppression among HIV-infected Russian women. Strengths include the use of a validated adherence measure and collection of blood samples to measure VL and CD4. Limitations included enrolling a sample of HIV-infected women aged 18–35 years in HIV care in St. Petersburg, Russia who were currently prescribed ARVs with high levels of reported adherence; thus, findings may not generalize to other PLHIV. Our measure of cigarette use focused on self-reported past month usage, which limited our ability to examine whether smoking patterns over extended time periods were associated with differential immunosuppression levels. The operationalization of undetectable VL as 50 copies/mL is a conservative measure of immunosuppression and we did not have access to previous VL and CD4 data. A final potential weakness was the lack of assessment of other tobacco forms (e.g., e-cigarettes) and an objective measure for cigarette exposure (e.g., cotinine).

Conclusions

Findings highlight the elevated smoking prevalence among HIV-infected Russian women. Cigarette use poses a number of negative health consequences and may also be associated with adverse long-term health consequences for PLHIV. There is a clear need to integrate evidenced-based smoking-cessation interventions within ongoing HIV clinical care. Results highlight the need for additional research examining mechanisms that may underlie the association between smoking and immunosuppression and the directionality of these relations among PLHIV.

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Table 1

Multivariable logistic regression analyses modeling the effects of cigarette smoking frequency and quantity on detectable viral load (N = 151) *

Predictor	95% CI		p
	Odds ratio	Lower	Upper
<i>1a. Cigarette smoking frequency</i>			
Number of days smoking: Past month			
Infrequent: < 20 days	Reference ^a		
Regular: 20 days	1.6	.62	4.3 .32
Model $\chi^2 =$	18.7		<.001
<i>1b. Cigarette smoking quantity</i>			
Average number of cigarettes per day: Past month			
Light: < 10 cigarettes	Reference ^a		
Moderate/Heavy: 10 cigarettes	2.3	1.1	5.1 .03
Model $\chi^2 =$	22.3		<.001

Notes:

* : Analyses control for self-reported antiretroviral adherence and number of years since HIV diagnosis, which were included in the models as continuous measures.

CI: Confidence Interval;

^a : The reference group is the group against which the other category is compared.

Table 2

Multivariable linear regression analyses modeling the effects of cigarette smoking frequency and quantity on CD4+ cell count (cells/mL; N = 151)*

Predictor	Unstandardized <i>b</i>	SE	<i>t</i>	<i>p</i>
<i>2a. Cigarette smoking frequency</i>				
Number of days smoking: Past month				
Infrequent: < 20 days	Reference ^a			
Regular: 20 days	-25.5	44.9	-.57	.57
<i>2b. Cigarette smoking quantity</i>				
Average number of cigarettes per day: Past month				
Light: < 10 cigarettes	Reference ^a			
Moderate/Heavy: 10 Cigarettes	-58.3	37.1	-1.6	.12

Notes:

* : Analyses control for self-reported antiretroviral adherence and number of years since HIV diagnosis, which were included in the models as continuous measures.

SE: Standard Error;

^a: The reference group is the group against which the other category is compared.