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Risk factors for recent non-fatal overdose among HIV-infected Russians who inject drugs

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Abstract

Overdoses and HIV infection are common among Russians who inject drugs, yet risk factors have not been studied. We analyzed baseline data of 294 participants with 30 day injection drug use from an HIV secondary prevention trial for persons reporting “heavy” alcohol use (NIAAA risky drinking definition) and risky sex in the past 6 months. The outcome was any self-reported overdose in the previous 3 months. We examined demographic, HIV-related, criminal justice, mental health, substance use and injection risk factors. Participants’ characteristics included median age 29 years, 117/294 (40%) female, and median CD4 cell count 345/ μ l. Over three quarters 223/294 (76%) reported a history of overdose; 47/294 (16%) reported overdose in the past 3 months. Past month injection frequency (AOR 4.77, 95%CI: 1.63-14.0 highest vs. lowest quartile; AOR 3.58, 95%CI: 1.20-10.69 second highest vs. lowest quartile) and anti-retroviral therapy at time of interview (AOR 3.96 95%CI: 1.33-11.83) were associated with 3-month

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overdose. Nonfatal overdose among HIV-infected Russians who inject drugs is common. Risk factors include injection frequency and anti-retroviral therapy, which warrant further study. Overdose prevention efforts are needed among HIV-infected Russians who inject drugs.

Keywords

Overdose; Russia; injection drug use; anti-retroviral therapy; HIV

Introduction

Among people who inject drugs (PWID), overdose is almost twice as common in people with HIV-infection compared to those without (Green, McGowan, Yokell, Pouget, & Rich, 2012). In Russia overdose is a major cause of premature and preventable death, and overdose death rates exceed death rates from HIV (Coffin, 2008; Grau et al., 2009). Up to 1.3 million Russians are infected with HIV and injection drug use (IDU) is the primary cause of HIV transmission (Coffin, 2008; Grau et al., 2009; Rhodes, Sarang, Bobrik, Bobkov, & Platt, 2004; UNAIDS, 2011; World Health Organization, 2005). It is common in Russia for treatment providers to withhold anti-retroviral therapy (ART) from actively using PWIDs (Rhodes & Sarang, 2012; Wolfe, Carrieri, & Shepard, 2010) and to require periods of abstinence before offering ART (Simona, 2010; Wolfe, 2007).

Established overdose risk factors include previous overdose (Coffin et al., 2007; Powis et al., 1999), polydrug use (Coffin et al., 2007; Green et al., 2009; Milloy et al., 2010; Powis et al., 1999), greater injection frequency, longer duration of drug use (Yin et al., 2007), abstinence due to arrest (Seal et al., 2001), incarceration (Milloy et al., 2010; Ochoa et al., 2005), detoxification or treatment (Milloy et al., 2010; Seal et al., 2001) and female gender (Powis et al., 1999). Factors associated with overdose have not been investigated in HIV-infected Russian PWID. The HERMITAGE (HIV Evolution in Russia - Mitigating Infection Transmission and Alcoholism in a Growing Epidemic) study, which included subjects at HIV and addiction treatment sites as well as needle exchange, provided an opportunity to identify risk factors associated with recent non-fatal overdose among a high risk HIV-infected population.

Methods

Design and population

We conducted a cross-sectional analysis of data collected from 294 PWID of 700 total subjects at the baseline assessment in the HERMITAGE Study, which has been described previously (Pace et al., 2012). Eligibility criteria included: 18 years of age or older; HIV infected; anal or vaginal sex without a condom in the past 6 months; and past 6 months heavy alcohol use, defined as >14 drinks/week or >4 drinks/occasion for men, and >7/ week or >3/occasion, for women (National Institute on Alcohol Abuse and Alcoholism, 2007). Researchers screened 921 people and excluded 221; 31 eligible declined and one was too ill. Of the 189 remaining who were not eligible, 110 did not meet alcohol criteria and 134 did not meet sex risk criteria. Other reasons for ineligibility were an inability to provide contact

information (n=30); legal issues (n=17); ongoing efforts to conceive (n=4); or HIV infection status unconfirmed (n=2). Institutional Review Boards of Boston University Medical Campus and Pavlov State Medical University approved this study.

Measures

The dependent variable was any overdose in the last 3 months, defined as “Any overdose you may have had including accidental and deliberate (on purpose) overdoses on illegal drugs, over the counter medications, prescription medications, or alcohol.”

Potential risk factors examined included demographic, HIV-related, mental health and substance use characteristics. Demographics included age (categorized into tertiles), gender, marital status and employment. HIV-related factors included years since HIV diagnosis, treatment with ART at the time of the interview and CD4 cell count. Mental health factors included depressive symptoms by the Beck Depression Index (BDI) II (categorized as none, mild, moderate, or severe) and any lifetime suicidal thoughts or attempts (Beck et al., 1996). Using timeline follow-back, 30 day alcohol consumption was measured (Sobell & Sobell, 1992) and categorized as 30 day heavy alcohol use. Alcohol dependence over the last 12 months was evaluated using the Composite International Diagnostic Interview Short-Form (CIDI-SF) (Kessler, Andrews, Mroczek, Ustun, & Wittchen, 1998). Drug use was categorized as heroin use only, heroin and other drug use, and non-heroin drug use only over the last year according to the CIDI-SF. For modeling, we dichotomized the variable as “drug use other than heroin” (yes vs. no). Measures of periods of abstinence included drug or alcohol treatment in the past year and previous incarceration ever. Injection risk factors were all reported for the previous 30 days and included daily injection frequency (categorized into quartiles), any distributive sharing, any receptive sharing, and any other substance use before injecting. Sex trade involvement was defined as any exchange of drugs or money for sex in the previous 3 months.

Analysis

To identify potential risk factors for recent overdose, a series of logistic regression models were fit using an iterative model building approach. We first conducted unadjusted logistic regression models for each independent variable. Factors with a p-value <0.15, were then included together in a single multivariable model. Age and gender were forced into the models as important potential confounders. Factors in the multivariable model with a p-value greater than 0.15 were removed one at a time. Finally, factors not selected based on the unadjusted analyses were included one at a time in the current multivariable model to assess their importance in adjusted analyses. To minimize collinearity, we assessed the correlation between all pairs of independent variables and verified that no pair of variables included in the same regression model was highly correlated (i.e., $r > 0.40$). Analyses were performed using SAS software (version 9.1; SAS Institute, Cary, NC).

Results

Among 294 Russian HIV-infected PWID, previous incarceration (49% (144/294)), past year drug or alcohol treatment (60% (176/294)), depressive symptoms (78% (229/294)) with at

least mild symptoms), distributive and receptive needle and syringe sharing were common at 39% (115/294) and 47% (138/294), respectively.

ART was reported by 7% (21/294). Anti-retrovirals were reported in the following frequencies: lamivudine 21/21, zidovudine 15/21, efavirenz 12/21, stavudine 7/21, lopinavir/ritonavir 3/21, and 1/21 for nevirapine, atazanavir, didanosine, abacavir and ritonavir.

Sixteen percent (47/294) reported a recent overdose (past 3 months) and 76% (223/294) reported a lifetime non-fatal overdose. Subjects with recent overdose were more likely to be on ART (15% vs. 6%) and had greater median injection frequency (60 vs. 40 injections in the last 30 days).

Variables significantly associated with recent overdose in the final multivariable model were frequency of injections in the past month (AOR 4.77, 95% CI: 1.63-14.0 highest vs. lowest quartile; AOR 3.58, 95% CI: 1.20-10.7 second highest vs. lowest quartile) and current treatment with ART (AOR 3.96 95% CI: 1.33-11.83).

Discussion

Non-fatal overdose was a common experience among this Russian sample of HIV-infected PWID with over three quarters reporting a lifetime non-fatal overdose and 16% reporting one in the last 3 months. Those who injected more frequently were more likely to have an overdose. Although few were taking ART (7%); these subjects had almost 4 times the odds of having an overdose in adjusted analysis, an unexpected finding.

The association between ART and increased odds of non-fatal overdose may be due to periods of abstinence required by treatment providers to qualify for ART in Russia (Simona, 2010; Wolfe, 2007). Abstinence in a population of PWIDs that later relapses would increase the risk of overdose. Alternatively, ART may potentiate the overdose risk of drugs of abuse, like heroin, by altering hepatic metabolism or via direct interactions. ART may be a marker of pulmonary or hepatic illness which could increase susceptibility to overdose. We did not find a clear association with odds of overdose and CD4 cell count. Regardless of the mechanism of the ART-overdose association, these findings are notable given that scaling up ART is a key strategy to lengthening and improving the lives of PWID with HIV and reducing HIV transmission in Russia. Over 50% of the sample in this study had CD4 cell counts under 350, yet only 7% were receiving ART. Given the reality of the scale up of ART in Russia, the relationship between ART and overdose risk among PWIDs warrants further study.

Study strengths included thorough measures of substance use and examination of a population at high risk for overdose, not previously studied. Outcomes were limited to non-fatal overdose, a reasonable proxy for fatal overdose. We restricted our analyses to HERMITAGE subjects who reported injection drug use because overdoses reported among subjects who did not report injection were substantially less common (4% vs. 16% in PWID). Although we report on ART status at the time of the study interview, participants were not necessarily on ART at the time of the overdose. Among injection drug users in Russia, heroin is the primary drug of choice and thus most likely one of, if not the, major

contributors in most overdoses (Coffin, 2008). Study limitations included an overdose definition that was not substance-specific and did not distinguish intentional from unintentional; CD4 cell counts were available on only 57% (169/294) of subjects.

This study demonstrates that nonfatal overdose is common among HIV-infected PWID in Russia. Risk factors identified were injection frequency and current ART. Qualitative and longitudinal studies investigating both the structural and individual relationships between ART access, drugs of abuse, overdose, and health status are needed to fully understand the mechanisms of overdose among HIV-infected PWID.

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Table 1
 Characteristics of Russians with HIV infection, injection drug use and heavy drinking by 3-month overdose status and by anti-retroviral treatment (ART) status

N (%) ^a	Total N=294	3-month OD N=47	No 3-month OD N=247	On ART N=21	Off ART N=273
Age in years, median (IQR)	29 (27-33)	29 (27-33)	29 (27-33)	31 (27-33)	29 (27-33)
Tertile 1: 18-27	98 (33%)	17 (36%)	81 (33%)	8 (38%)	90 (33%)
Tertile 2: 28-31	93 (32%)	12 (26%)	81 (33%)	4 (19%)	89 (33%)
Tertile 3: 32-57	103 (35%)	18 (38%)	85 (34%)	9 (43%)	94 (34%)
Female	117 (40%)	21 (45%)	96 (39%)	8 (38%)	109 (40%)
Married or living with partner	81 (28%)	11 (23%)	70 (28%)	11 (52%)*	70 (26%)*
Unemployed	88 (30%)	12 (26%)	76 (31%)	4 (19%)	84 (31%)
Previous incarceration	144 (49%)	27 (57%)	117 (47%)	11 (52%)	133 (49%)
Past year drug or alcohol treatment	176 (60%)	30 (64%)	146 (60%)	9 (45%)	167 (61.4%)
ART at time of interview	21 (7%)	7 (15%)*	14 (6%)*	21 (100%)*	273 (0%)*
CD4 cell count,** median (IQR)	345 (186-550)	358 (243-533)	328 (180-580)	327 (180-520)	351 (186-580)
<200	45/169 (27%)	5/30 (17%)	40/139 (29%)	4/15 (27%)	41/154 (27%)
200-349	41/169 (24%)	9/30 (30%)	32/139 (23%)	5/15 (33%)	36/154 (23%)
350-499	30/169 (18%)	7/30 (23%)	23/139 (17%)	2/15 (13%)	28/154 (18%)
500 or greater	53/169 (31%)	9/30 (30%)	44/139 (32%)	4/15 (27%)	49/154 (32%)
Years since HIV diagnosis, median (IQR)	4.0 (1.3-7.8)	5.1 (1.2-7.8)	3.9 (1.4-7.9)	7.6 (6.8-8.1)*	3.7 (1.1-7.6)*
Lifetime suicide attempt or thoughts	172 (59%)	30 (64%)	142 (58%)	13 (62%)	159 (58%)
Beck Depression Index II, median (IQR)	20 (14-28)	22 (13-31)	20 (14-28)	20 (15-26)	20 (14-28)
No depression	65 (22%)	12 (25%)	53 (22%)	4 (19%)	61 (22%)
Mild depression	74 (25%)	8 (17%)	66 (27%)	6 (29%)	68 (25%)
Moderate depression	88 (30%)	14 (30%)	74 (30%)	8 (38%)	80 (29%)
Severe depression	67 (23%)	13 (28%)	54 (22%)	3 (14%)	64 (23%)
Risky drinking, 30 days	257 (87%)	45 (96%)	212 (86%)	18 (86%)	239 (88%)
Alcohol dependent, 12 months	183 (62%)	32 (68%)	151 (61%)	13 (62%)	170 (62%)
Heroin use, 12 months					
Heroin use only	38 (13%)	2 (4%)	36 (15%)	1 (5%)	37 (13%)
Heroin and other drug use	248 (84%)	44 (94%)	204 (83%)	17 (81%)	231 (85%)

N (%) ^a	Total N=294	3-month OD N=47	No 3-month OD N=247	On ART N=21	Off ART N=273
Non-heroin drug use only	8 (3%)	1 (2%)	7 (3%)	3 (14%)	5 (2%)
Sex trade involvement, 3 months	64 (22%)	14 (30%)	50 (20%)	2 (10%)	62 (23%)
Injection frequency, 30days, median (IQR)	50 (10-81)	60 (30-93) [*]	40 (10-70) [*]	5 (2-60) [*]	50 (13-81) [*]
Quartile 1: 1-10	76 (26%)	6 (13%)	70 (28%)	11 (52%)	65 (24%)
Quartile 2: 12-48	70 (24%)	9 (19%)	61 (25%)	3 (14%)	67 (25%)
Quartile 3: 50-81	75 (25%)	15 (32%)	60 (24%)	2 (10%)	73 (27%)
Quartile 4: 85-200	73 (25%)	17 (36%)	56 (23%)	5 (24%)	68 (25%)
Distributive sharing, 30 days	115 (39%)	17 (36%)	98 (40%)	6 (29%)	109 (40%)
Receptive sharing, 30 days	138 (47%)	26 (55%)	112 (46%)	9 (43%)	129 (48%)
Other substance use before injecting, 30 days ^{**}	213/285 (75%)	39/46 (85%)	174/239 (73%)	13/18 (72%)	200/267 (75%)
Lifetime overdose	223 (76%)	47 (100%) [*]	176 (71%) [*]	19 (91%)	204 (75%)

ART – Anti-retroviral treatment

IQR – Interquartile range

* p<0.05

** N=169 for CD4 cell count and N=285 for other substance use before injecting, all other denominators indicated by column headings

^a Except where medians and IQRs are given, as noted

Table 2

Logistic regression models for recent non-fatal overdose among Russians with HIV infection, injection drug use and 6-month heavy drinking

	Unadjusted Odds Ratio	95% CI	Adjusted [†] Odds Ratio	95% CI
Age in years (tertiles)				
18-27	1.0		1.0	
28-31	0.71	0.32-1.57	0.95	0.40-2.23
32-57	1.01	0.49-2.09	1.09	0.50-2.39
Male vs. Female	0.79	0.42-1.48	0.77	0.39-1.52
Married or living with partner	0.77	0.37-1.60		
Employed	1.30	0.64-2.63		
Previous incarceration	1.50	0.80-2.82		
Drug or Alcohol treatment, past year	1.20	0.63-2.29		
ART at time of interview	2.91	1.11-7.66	3.96	1.33-11.83
CD4 cell count *				
<200	1.0			
200-349	2.25	0.69-7.38		
350-499	2.43	0.69-8.56		
500 or greater	1.64	0.51-5.29		
Years since HIV diagnosis, per year	1.01	0.92-1.11		
Lifetime suicide attempt or thoughts	1.30	0.68-2.49		
Beck Depression Index II				
No depression	1.0			
Mild depression	0.54	0.20-1.41		
Moderate depression	0.84	0.36-1.95		
Severe depression	1.06	0.44-2.54		
Heavy alcohol use, 30 days	3.71	0.86-16.0	3.80	0.84-17.1
Alcohol dependent, 12 months	1.36	0.70-2.64		
<u>Drug use other than heroin</u> , 12 months	3.84	0.89-16.5	4.32	0.96-19.4
Sex trade involvement, 3 months	1.67	0.83-3.36		
Injection frequency, 30 days (quartiles)				
1-10	1.0		1.0	
12-48	1.72	0.58-5.11	2.15	0.68-6.85
50-81	2.92	1.07-7.99	3.58	1.20-10.7
85-200	3.54	1.31-9.58	4.77	1.63-14.0
Distributive sharing, 30 days	0.86	0.45-1.64		
Receptive sharing, 30 days	1.47	0.78-2.75		
Other <u>substance</u> use before injecting, 30 days *	2.08	0.89-4.69		

[†]The final multivariable model included age, gender, current ART use, heavy drinking, heroin use, and injection frequency

* N=169 for CD4 cell count and N=285 for other substance use before injecting. N=294 for all other variables.