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Pain and Risk Behaviors Among HIV-Infected Persons in St. Petersburg, Russia

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Abstract

We analyzed baseline data from an observational cohort of HIV-infected ART-naïve patients in St. Petersburg, Russia to explore whether pain was associated with HIV risk behaviors. The primary outcomes were (1) unprotected vaginal or anal sex in the past 90 days and (2) sharing of needles or equipment in the past month. Secondary outcomes included: use of alcohol prior to sex, current injection drug use, number of unprotected sex and sharing episodes, and days injected in the past month. The main independent variable was any past week pain. Multivariable regression models were fit for outcomes. After adjustment, the association with unprotected sex was of borderline significance (AOR = 2.06; 95 % CI 0.98–4.36, $p = 0.058$); there was no significant association

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Conflict of interest: The authors declare that they have no conflicts of interest.

Compliance with Ethical Standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

between any past week pain and sharing of needles/equipment (AOR = 1.52; 95 % CI 0.65–3.59, $p = 0.33$). Participants with pain had higher odds of reporting alcohol use prior to sex (AOR = 2.42; 95 % CI 1.10–5.28, $p = 0.03$).

Keywords

Pain; HIV; Risk behaviors

Introduction

Pain is common among persons living with human immunodeficiency virus (HIV) [1–13]. Pain remains a major clinical problem even in the era of highly active anti-retroviral therapy [14], and research has shown that over time painful symptoms increase even after initiation of anti-retroviral therapy (ART) [15]. There is a close relationship between pain and substance use. Pain is strongly associated with substance use in studies of both HIV-infected [16–18] and uninfected populations [19]. Substance use may be a maladaptive coping response to pain [20, 21] and thus pain can serve as a trigger for relapse [22, 23]. And yet substance use may also play a role in the generation or persistence of pain either indirectly through association with painful co-morbidities (trauma, neuropathy, etc.) or more directly such as through opioid-related hyperalgesia.

In many parts of the world, including Eastern Europe, HIV epidemics are driven by injection drug use. As such, relationships between pain and substance use have major implications for HIV transmission. In a previous study of HIV-infected persons in St. Petersburg we demonstrated that individuals with pain were more likely to report current use of illicit drugs, with the association being strongest for heroin use [24], and similar results have since been reported among HIV-infected injection drug users in the U.S. [25]. In a subsequent study, we demonstrated associations between pain and heavy drinking in the same cohort [26]. Alcohol and drugs can lower inhibitions that may lead to both high risk sex and drug risk behaviors. As such, HIV-infected persons with pain might be more likely to engage in high-risk behaviors due to increased use of these substances. Furthermore, engaging in sex or drug use could potentially cause transient euphoria or distraction from pain [27], and as such persons with pain might pursue these activities with less regard for risk. Among persons with chronic pain, the term “chemical coping” has been coined to describe maladaptive drug seeking behaviors that are response to pain [28]. We are unaware of prior studies that have examined associations between pain and sex and drug risk behaviors among persons with HIV. Given the high prevalence of pain among persons with HIV, it is important to understand how pain might impact risk for HIV transmission through its effects on using alcohol and other drugs.

In a sample of HIV-infected persons not on ART in St. Petersburg, Russia, we examined whether any self-reported pain or pain that interfered with daily living was associated with HIV sex and drug risk behaviors.

Methods

Study Design and Participants

We performed a secondary analysis of baseline data from the Russia ARCH cohort, an observational prospective cohort study conducted to assess the longitudinal association between alcohol consumption and biomarkers of microbial translocation and inflammation/ altered coagulation. Russia ARCH is part of the Uganda, Russia, Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS (URBAN ARCH) Consortium. A total of 351 participants were recruited between November 2012 and June 2015 from clinical HIV and addiction care sites, non-clinical sites, and via snowball recruitment in St. Petersburg, Russia. Eligibility criteria included the following: 18–70 years old; documented HIV-infection; documented ART-naïve status; the ability to provide contact information for two contacts to assist with follow-up; stable address within St. Petersburg or districts within 100 km of St. Petersburg; possession of a home or mobile phone. Participants were excluded if they were not fluent in Russian or had a cognitive impairment resulting in inability to provide informed consent. After eligibility was verified and informed consent obtained, participants provided a blood sample and were administered an interview assessment. Institutional Review Boards of Boston University Medical Campus and First St. Petersburg Pavlov State Medical University approved this study.

Data Collection

Participants were assessed at baseline, 12- and 24-months post enrollment; this study used data from the baseline visit only. The baseline assessment included: demographics [29]; Russian Brief Pain Inventory [30]; Sex Behaviors [31]; Sexual Partners; The Center for Epidemiologic Studies Depression Scale (CES-D) [32, 33]; 30 Day Timeline Follow Back [34]; Drug Use (modified Risk Behavior Survey) [35, 36]; and VR-12 Health Survey [37]. All assessments were conducted by trained research assessors and administered in Russian. Particularly sensitive sections of the assessment (including Sex Behaviors; Sexual Partners; HIV Risk Categories; and Depressive Symptoms) were self-administered by the participant.

Measures

Outcome Measures—The two primary outcomes of interest were: (1) any unprotected sex episode (vaginal or anal) within the past 90 days and (2) any sharing of needles/syringes or injecting equipment (cookers, cotton, or rinse water) in the past 30 days. Secondary outcomes were: any drinking alcohol prior to or during sex within the past 90 days, any injection drug use in the past 30 days, number of days injected in the past 30 days, number of episodes sharing needles/equipment in the past 30 days and number of episodes of unprotected sex in the past 90 days.

Main Independent Variable—The main independent variable of interest was self-report of any pain that occurred in the past week. This was based on the initial question in the Brief Pain Inventory (“Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain in the last 7 days?”). Secondary analyses were conducted examining the independent variable—pain that interfered with daily living in the past month. This was

based on a question from the VR-12, which asks, “During the past month, how much did pain interfere with your normal work, including housework?”. The range of possible responses were “not at all/a little bit/moderately/quite a bit/extremely”, and responses were dichotomized at the threshold above “not at all”.

Covariates—Covariates included in the adjusted models as potential confounders were the following: age, sex, education (less than or greater than 9th grade), married or living with a partner, heavy drinking, cannabis use, depression and opioid use. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) and a threshold of 16 was used to define moderate to severe symptoms of depression. Use of alcohol and illicit drugs (cannabis and opioids) in the past 30 days was assessed using the modified Risk Behavior Survey. Definitions of heavy drinking were based on NIAAA guidelines (i.e., drinking greater than 14 standard drinks per week/greater than 4 drinks in a day for men; greater than 7 drinks in the past week/greater than 3 drinks in a day for women) [38].

Statistical Analysis

Descriptive statistics were used to characterize study participants overall and by pain status at baseline, and χ^2 and Student's *t* tests were used to assess differences between groups. Multiple logistic regression models were used to evaluate the association between reporting any pain in the past week/any pain interference in the past month and each dichotomous HIV sex and drug risk behavior at baseline. Odds ratios (OR) and 95 % confidence intervals are reported from the logistic regression models. Count outcomes were analyzed using negative binomial regression models to account for overdispersion in the data. Incidence rate ratios and 95 % confidence intervals are reported from the negative binomial models. Prior to regression modeling, Spearman correlation coefficients were calculated for independent variables and covariates, and no pair of variables had a correlation >0.40. We fit preliminary unadjusted models for each outcome. The main analyses were adjusted for age, marital status, gender, education, heavy drinking, cannabis use, and depression. Models of sex outcomes were additionally adjusted for opioid use. Two-tailed tests and a significance level of 0.05 were used for all hypothesis testing. Post hoc exploratory analyses assessed gender interaction; they were not significant at alpha of 0.10 and are not reported here.

Results

At baseline, participants (*n* = 351) had a mean age of 33.7 (SD $\pm$ 5.6) years, 29.3 % were female, 78.9 % had a >9th grade education and 43.3 % were married/living with a partner (Table 1). A minority of participants reported any pain in the past week (44/351; 12.5 %), and of those, 30 % reported that their current pain had been present for at least 3 months. One-quarter (91/351; 25.9 %) of the sample reported pain that had interfered with daily living in the past month. At baseline the frequency of self-reported sex risk behaviors among this HIV-infected cohort was relatively high: 167/351 (47.6 %) reported an unprotected sex episode in the past 90 days and 194/351 (55.3 %) reported an episode of drinking alcohol prior to sex. Sharing of needles or syringes in the past 30 days was reported among 52/351 (14.8 %), and 130/351 (37.0 %) reported injecting drugs within the past 30 days. Past 30 day

heavy drinking was reported by 250/351 (71.2 %), opioids by 121/351 (34.5 %) and cannabis by 50/351 (14.2 %).

Tables 1 and 2 describe the overall differences at baseline between participants with and without pain in the past week and with and without past month pain that interfered with daily living, respectively. There were no significant differences between age, sex, education and marital status among participants who did and did not have past week pain, or past month pain interference. Participants who reported having pain in the past week appeared more likely to have used opioids (47.7 vs. 32.6 %, $p = 0.05$) and cannabis (27.3 vs. 12.4 %, $p < 0.01$) in the past month. Participants with past month pain that interfered with daily living also appeared more likely to report past month use of cannabis (22.0 vs. 11.5 %, $p = 0.01$), however, they were less likely to report past month heavy alcohol use (54.9 vs. 76.9 %, $p < 0.01$). Depressive symptoms were significantly more common among participants with any past week pain and any past month pain interference. At baseline, participants with pain in the past week reported more HIV risk behaviors compared to those who did not report pain: any unprotected sex (65.9 vs. 46.3 %, $p = 0.02$), alcohol prior to having sex (72.7 vs. 53.1 %, $p = 0.01$), sharing of needles or syringes (27.3 vs. 13.0 %, $p = 0.01$) and injected drugs in the past month (54.5 vs. 34.5 %, $p = 0.01$) (Table 1). Participants with past month pain that interfered with daily living were more likely to report sharing needles or equipment in the past month compared to those without pain interference (24.2 vs. 11.5 %, $p < 0.01$), but there were no significant differences in other HIV risk behaviors (unprotected sex, drinking prior to sex and injection drug use) (Table 2).

In the unadjusted logistic regression models shown in Table 3, past week pain was associated with a greater than 2-fold higher odds of unprotected sex and sharing needles/equipment (primary outcomes). After adjustment for age, sex, education, marital status, depressive symptoms, heavy alcohol, cannabis, and opioid use, the association with unprotected sex was attenuated and of marginal significance (AOR = 2.06; 95 % CI 0.98–4.36, $p = 0.058$); there was no significant association between any past week pain and sharing of needles/equipment (AOR = 1.52; 95 % CI 0.65–3.59, $p = 0.33$). Among other secondary dichotomous outcomes, the association between any pain and reporting alcohol use prior to or during sex remained significant after adjustment (AOR = 2.42; 95 % CI 1.10–5.28, $p = 0.03$) (Table 3). Results from the negative binomial models examining associations between pain and count outcomes (days injected in the past 30 days, episodes sharing needles/equipment in the past 30 days and episodes of unprotected sex in the past 90 days) are presented in Table 4. Having pain that interfered with daily living was significantly associated with more episodes of sharing needles or equipment in the adjusted analysis (AIRR = 4.40; 95 % CI 1.18–16.42, $p = 0.02$); no other associations were statistically significant.

Discussion

In this study of HIV-infected adults not on ART, we observed that after adjustment for other factors, past week pain was not significantly associated with sharing needles/equipment. There was a clinically notable association between pain and unprotected sex although the result did not quite meet statistical significance ($p = 0.058$). Participants with past week pain

had a higher odds of reporting alcohol use prior to or during sex. In addition, it appeared that pain which interfered with daily living in the past month is associated with more episodes of sharing needles and syringes. These results point to a possible relationship between pain and risk behaviors that lead to HIV transmission.

We are unaware of any prior studies that have examined associations between pain and HIV risk behaviors. Given that pain is common, it is important to understand how pain impacts risk behaviors among persons with HIV. In a prior study of symptoms among HIV-infected persons in the UK, it was observed that psychological, but not physical symptoms, were associated with increased risk of unprotected sex [39]. Previously, we demonstrated that individuals with pain were more likely to use illicit drugs (particularly heroin) and alcohol over time [24, 26]. This study adds to the current literature linking pain to substance use, demonstrating that pain is associated with use of alcohol prior to or during sex.

Alcohol use prior to or during sex increases the likelihood of high risk sexual behaviors and thus may facilitate HIV transmission [40]. As such, unaddressed pain may be a factor contributing to HIV transmission. Alcohol has analgesic effects, elevating pain tolerance in healthy volunteers [41]. Given that opioids are infrequently prescribed in Russia, it is plausible that HIV-infected person might “self-medicate” their pain with alcohol, including in the settings of sexual encounters. Surveys of adults without HIV in the United States have reported use of alcohol to self-medicate pain [20, 42] and a Russian study of premature deaths related to alcohol noted that alcohol was used for pain and other ailments [43]. It is of note that the particular population examined was not receiving ART. Given that HIV prevention has expanded to include both behavioral and biomedical combined approaches (e.g., ART suppression of HIV viral load), that the presence of pain could be yet another reason to expedite the delivery of ART, from an HIV prevention perspective.

This study had limitations. The study was not designed to answer the specific research hypotheses explored here and we were likely underpowered to detect differences. The proportion of participants who reported pain was relatively low (12.5 % with current pain, 3.7 % with chronic pain; 25.9 % with any past month pain interference), which likely reflects the characteristics of the sample being relatively young and ART-naïve. Given that our study is the first to report associations between pain and HIV risk behaviors, our results should be viewed as exploratory and hypothesis-generating, and the results should be confirmed in other samples. Further research examining the relationship between types of pain and HIV risk behaviors is warranted, as it was not feasible to undertake in this study, given the small numbers of participants reporting pain, particularly chronic pain. The time frame for assessing risk behaviors (90 days for sex risk, 30 days for drug risk), was not the same as that assessed for our primary independent variable (any pain in the past 7 days). However, it is interesting to note that the secondary independent variable (pain that interfered with daily living in the past 30 days) which had a more similar timeframe had fewer associations with risk behaviors. The study questionnaire did not specifically ask participants whether they used alcohol (or other drugs) to self-treat their pain, or expectancies for pain relief with use of alcohol. Therefore, we cannot be certain that participants were self-medicating as it is also plausible that unhealthy drinking, including

drinking prior to and during sex, could lead to pain as alcohol withdrawal is associated with increased sensitivity to pain (hyperalgesia) in animal and human studies [44, 45].

In summary, in this study of pain and HIV-risk behaviors among HIV-infected Russian adults in St. Petersburg we found that after adjustment for potential confounders there was a marginal significant association between any past week pain and unprotected sex, but no significant association with sharing needles/equipment. Among our secondary outcomes, any pain in the past week was independently associated with a higher odds of reporting using alcohol prior to having sex, and past month pain interference was associated with increased episodes of sharing needles and injecting equipment within the same time frame. Providers who care for HIV-infected persons should be attentive to relationships between pain, substance use and HIV risk behaviors. Although pain may not be independently associated with all HIV-risk behaviors, given the many unadjusted associations we observed, it may be a useful marker for HIV-infected individuals at increased risk of transmitting HIV.

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Table 1
Demographics and HIV risk behaviors by any pain in the past 7 days (Brief Pain Inventory)

	Overall (n = 351)	No pain past 7 days (n = 307)	Pain past 7 days (n = 44)	Test statistic	p value
Age (mean ± SD)	33.7 (5.6)	33.8 (5.7)	33.0 (4.6)	t = 0.83	0.41
Female	103 (29.3 %)	85 (27.7 %)	18 (40.9 %)	$\chi^2 = 3.24$	0.07
> 9th grade education	277 (78.9 %)	246 (80.1 %)	31 (70.5 %)	$\chi^2 = 2.17$	0.14
Married or living with a partner	152 (43.3 %)	132 (43.0 %)	20 (45.5 %)	$\chi^2 = 0.09$	0.76
Past month opioid use	121 (34.5 %)	100 (32.6 %)	21 (47.7 %)	$\chi^2 = 3.91$	0.05
Past month heavy drinking	250 (71.2 %)	222 (72.3 %)	28 (63.6 %)	$\chi^2 = 1.41$	0.23
Past month cannabis use	50 (14.2 %)	38 (12.4 %)	12 (27.3 %)	$\chi^2 = 6.99$	0.01
Depressive symptoms	161 (46.1 %)	134 (43.9 %)	27 (61.4 %)	$\chi^2 = 4.70$	0.03
Any sharing needles/equipment (30 days)	52 (14.8 %)	40 (13.0 %)	12 (27.3 %)	$\chi^2 = 6.19$	0.01
Any unprotected sex (90 days)	167 (48.8 %)	138 (46.3 %)	29 (65.9 %)	$\chi^2 = 5.89$	0.02
Any recent IDU (30 days)	130 (37.0 %)	106 (34.5 %)	24 (54.5 %)	$\chi^2 = 6.61$	0.01
Any alcohol prior to sex (90 days)	194 (55.6 %)	162 (53.1 %)	32 (72.7 %)	$\chi^2 = 5.99$	0.01
Number of unprotected sex episodes (90 days) (mean ± SD)	13.4 (30.0)	12.8 (29.4)	17.7 (33.9)	t = -1.02	0.31
Days injected in past month (mean ± SD)	4.2 (8.1)	3.9 (7.8)	6.7 (9.5)	t = -2.21	0.03
Number of episodes sharing needles/equipment in past month (mean ± SD)	2.2 (11.3)	2.0 (11.5)	3.4 (10.2)	t = -0.76	0.45

Table 2

Demographics and HIV risk behaviors by pain interference in the past month

	Overall (n = 351)	No pain interference (n = 260)	Pain interference (n = 91)	Test statistic	p-value
Age (mean ± SD)	33.7 (5.6)	33.6 (5.6)	33.9 (5.4)	t = -0.47	0.64
Female	103 (29.3 %)	74 (28.5 %)	29 (31.9 %)	$\chi^2 = 0.38$	0.54
> 9th grade education	277 (78.9 %)	211 (81.2 %)	66 (72.5 %)	$\chi^2 = 3.01$	0.08
Married or living with a partner	152 (43.3 %)	115 (44.2 %)	37 (40.7 %)	$\chi^2 = 0.35$	0.55
Past month opioid use	121 (34.5 %)	83 (31.9 %)	38 (41.8 %)	$\chi^2 = 2.89$	0.09
Past month heavy drinking	250 (71.2 %)	200 (76.9 %)	50 (54.9 %)	$\chi^2 = 15.89$	<0.001
Past month cannabis use	50 (14.2 %)	30 (11.5 %)	20 (22.0 %)	$\chi^2 = 6.01$	0.01
Depressive symptoms	161 (46.1 %)	102 (39.5 %)	59 (64.8 %)	$\chi^2 = 17.33$	<0.001
Any sharing needles/equipment (30 days)	52 (14.8 %)	30 (11.5 %)	22 (24.2 %)	$\chi^2 = 8.53$	<0.01
Any unprotected sex (90 days)	167 (48.8 %)	118 (46.6 %)	49 (55.1 %)	$\chi^2 = 1.87$	0.17
Any recent IDU (30 days)	130 (37.0 %)	89 (34.2 %)	41 (45.1 %)	$\chi^2 = 3.39$	0.07
Any alcohol prior to sex (90 days)	194 (55.6 %)	143 (55.4 %)	51 (56.0 %)	$\chi^2 = 0.01$	0.92
Number of unprotected sex episodes (90 Days) (mean ± SD)	13.4 (30.0)	12.8 (30.2)	15.1 (29.7)	t = -0.63	0.53
Days injected in past month (mean ± SD)	4.2 (8.1)	4.0 (8.0)	4.9 (8.2)	t = -0.99	0.32
Number of episodes sharing needles/equipment in past month (mean ± SD)	2.2 (11.3)	1.2 (5.4)	5.0 (20.2)	t = -2.77	0.01

Table 3
Unadjusted and adjusted* associations between pain and HIV risk behaviors (logistic regression models)

	Any pain (past 7 days)				Pain interference (past month)			
	OR (95 % CI)	p-value	AOR (95 % CI)	p-value	OR (95 % CI)	p-value	AOR (95 % CI)	p-value
Any unprotected sex (90 days)	2.24 (1.15, 4.35)	0.02	2.06 (0.98–4.36)	0.058	1.40 (0.86–2.28)	0.17	1.51 (0.85–2.78)	0.16
Any sharing needles/equipment (30 days)	2.50 (1.19, 5.26)	0.02	1.52 (0.65, 3.59)	0.33	2.44 (1.33, 4.51)	0.004	1.64 (0.81, 3.35)	0.17
Any alcohol prior to sex (90 days)	2.35 (1.17, 4.74)	0.02	2.42 (1.10, 5.28)	0.03	1.03 (0.63, 1.66)	0.92	1.19 (0.67, 2.09)	0.55
Any recent IDU (30 days)	2.28 (1.20, 4.31)	0.01	1.81 (0.90, 3.65)	0.10	1.58 (0.97, 2.56)	0.07	1.33 (0.76, 2.32)	0.32

* Adjusted for age, sex, education, married/partnered status, heavy drinking, cannabis use, depression, and opioids (sex outcomes only)

Unadjusted and adjusted* associations between pain and HIV risk behaviors (negative binomial models)

Table 4

	Any pain (past 7 days)				Pain interference (past month)			
	IRR** (95 % CI)	p-value	AIRR [†] (95 % CI)	p-value	IRR** (95 % CI)	p-value	AIRR [†] (95 % CI)	p-value
Days injected (30 days)	1.74 (0.74, 4.11)	0.21	1.46 (0.62, 3.44)	0.38	1.25 (0.65, 2.39)	0.51	0.90 (0.45, 1.81)	0.78
Episodes of unprotected sex (90 days)	1.39 (0.62, 3.10)	0.42	1.55 (0.68, 3.49)	0.28	1.18 (0.64, 2.18)	0.59	1.32 (0.68, 2.57)	0.41
Episodes of sharing needles/equipment (30 days)	1.70 (0.35, 8.21)	0.51	1.10 (0.20, 6.20)	0.91	4.22 (1.34, 13.23)	0.01	4.40 (1.18, 16.42)	0.02

* Adjusted for age, sex, education, married/partnered status, heavy drinking, cannabis use, depression, and opioids (sex outcomes only)

** Incidence rate ratio

[†] Adjusted incidence rate ratio