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Risk factors associated with benzodiazepine use among people who inject drugs in an urban Canadian setting

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HIGHLIGHTS

- We asked persons who inject drugs about illicit benzodiazepine use.
- Almost 40% of our sample reported illicit benzodiazepine use over the study period.
- Benzodiazepines use was associated with addiction severity and health/social risks.
- Treatment of benzodiazepine misuse and safer prescribing are important priorities.

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ABSTRACT

Background: Though known to have abuse potential, benzodiazepine medications remain widely prescribed. Furthermore, issues related to benzodiazepine use by people who inject drugs (PWID) remain to be fully characterized. We therefore sought to examine the prevalence of and risk factors associated with benzodiazepine use in a street-involved urban population.
Methods: Between May 1996 and November 2013, data were derived from two open prospective cohort studies in Vancouver, Canada, restricted to PWID. Multivariable logistic regression with generalized estimating equations (GEE) was used to determine factors independently associated with benzodiazepine use.
Results: Over the study period, 2806 individuals were recruited, including 949 (34%) women. Of these, 1080 (38.5%) participants reported benzodiazepine use at least once during the study period. In the multivariable analysis, Caucasian ethnicity, ≥ daily heroin injection, ≥ daily cocaine injection, non-fatal overdose, incarceration, syringe sharing, and unsafe sex were all independently associated with benzodiazepine use. Conversely, older age, homelessness, and ≥ daily crack smoking were negatively associated with benzodiazepine use.
Conclusions: Use of benzodiazepines was common in this urban setting and was associated with several markers of addiction severity and significant health and social vulnerabilities including syringe sharing and unsafe sex. These findings underscore the need to promote treatment for benzodiazepine use, safer benzodiazepine prescribing, including greater recognition of the limited indications for evidence-based use of this medication class.

1. Introduction

The diversion and illicit misuse of physician-prescribed medicines constitutes a significant and growing health problem (Paulozzi, 2012). Indeed, the U.S. Centers for Disease Control and Prevention (CDC) estimates that hospital emergency room visits for misused opioid and benzodiazepine (BZD) prescriptions increased by 111% and 89%, respectively, between 2004 and 2008 (Centers for Disease, C. and Prevention, 2010).

The misuse and abuse of BZD medication has been previously documented to be widespread, particularly among people who use drugs recreationally (Jones, Mogali, & Comer, 2012). Non-medical prescription of BZDs in a Baltimore cohort of PWID was reported to be 12% (Khosla, Juon, Kirk, Astemborski, & Mehta, 2011), while lifetime illicit and prescription tranquilizer misuse was 11% in people who had ever injected drugs in two large US centers (Lankenau et al., 2012). Moreover, risks associated with the combination of opioids and BZDs were recently raised as a public health concern by the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA) (Substance Abuse and Mental Health Services Administration, 2014). Co-administration of methadone or buprenorphine with BZDs by patients receiving opioid replacement therapy has also been shown to be

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associated with marked increases in death by overdose (Reynaud, Petit, Potard, & Courty, 1998; Ernst et al., 2002). Additional data from SAMHSA demonstrate that treatment admissions for co-abuse of BZDs and narcotic pain relievers have risen by over 500% between 2000 and 2010 (The TEDS Report, 2012).

While several studies investigating the abuse of BZDs by recreational drug users and patients receiving opioid replacement therapy were conducted in the 1980's and 1990's, data regarding BZD use (whether prescription or non-prescription) among PWID is lacking, and risk factors associated with BZD use among street-involved populations has not yet been fully described (Jones et al., 2012). We therefore undertook the present study to examine the prevalence and factors associated with BZD use among PWID in a major Canadian city, looking at a number of markers reflective of drug use severity and social vulnerability.

2. Material and methods

2.1. Study sample

Data from two open prospective cohorts of persons who use drugs in Vancouver, Canada, were used for this study: the Vancouver Injection Drug Users Study (VIDUS), and the AIDS Care Cohort to Evaluate access to Survival Services (ACCESS). With the exception of recruitment related to HIV status, recruitment and follow-up procedures for VIDUS and ACCESS are identical, allowing for combined analysis. The ACCESS cohort includes HIV-positive individuals who have used illicit drugs other than cannabis in the previous month, whereas HIV-negative individuals who report having injected drugs in the month prior to enrollment are followed in VIDUS. The present study was restricted to individuals from the VIDUS and ACCESS cohorts with a history of drug injecting and who were recruited between May 1996 and November 2013. The VIDUS and ACCESS sampling and recruitment procedures have been described previously (Strathdee et al., 1998; Tyndall et al., 2003). Briefly, enrollment in the cohorts is through self-referral, word of mouth, and street outreach; participants must be 18 years of age or older and reside in the greater Vancouver region. All participants provided written informed consent; a stipend ($20 CDN) was given at each study visit to compensate time and transportation. VIDUS and ACCESS have received ethics approval from the University of British Columbia/Providence Healthcare Research Ethics Board.

2.2. Measures

Participants completed an interviewer-administered questionnaire at baseline and at six-month intervals that elicited data concerning demographic characteristics, injection and non-injection drug use patterns, and various risk behaviors. In addition, HIV and hepatitis C virus (HCV) antibody testing was performed at baseline and at each follow-up visit for individuals with negative test results to date. Interviews were conducted in private and included comprehensive pre- and post-test counseling by trained nurses.

The primary outcome of interest was self-reported BZD use in the previous six months (yes vs. no). The following demographic characteristics, drug use patterns, social and structural-level risk factors were considered to be potentially associated with the outcome: age (per year older), gender (female vs. male), ethnicity (Caucasian vs. non-Caucasian), homelessness (yes vs. no), ≥ daily heroin injection (yes vs. no), ≥ daily crack smoking (yes vs. no), ≥ daily cocaine injection (yes vs. no), overdose (yes vs. no), sex work (yes vs. no), incarceration (yes vs. no), syringe sharing (yes vs. no), unprotected vaginal and anal sex (yes vs. no). Except for gender and ethnicity, all variables were treated as time-updated and referred to behaviors and activities in the six months predating the interview.

2.3. Statistical analysis

We first summarized the baseline characteristics of participants, stratified by baseline BZD use in the past six months. Comparisons were made by using Pearson's Chi-square test (or Fisher's exact test) for categorical variables and the Wilcoxon rank-sum test for continuous variables.

Next, variables potentially associated with active BZD use during follow-up were evaluated using generalized estimating equations (GEE) with a logit-link function and exchangeable working correlation structure, since serial measures for cohort participants were available. This approach serves to examine behaviors and characteristics that correlated with BZD use at each follow-up period throughout the study. First, using GEE, we examined the bivariable associations between each explanatory variable and BZD use. Next, we fitted a multivariable model, considering all variables with $p < 0.10$ in bivariable GEE analyses as the full model. A backward model selection procedure was used to construct the final model, as indicated by the lowest quasi-likelihood under the independence model criterion (QIC) value (Cui, 2007). All statistical analyses were performed using the SAS software version 9.3 (SAS, Cary, NC, USA). All p-values are two-sided.

3. Results

Between May 1996 and November 2013, 2806 persons who inject drugs (PWID) met criteria for inclusion in the present study from the VIDUS (n = 2020) and ACCESS cohorts (n = 786). Over time, the median number of study visits per participant was 9 (interquartile range [IQR]: 4–15). These participants generated 31,961 observations for this analysis. There were 1080 (38%) participants who reported BZD use at least once during the study period.

The median age of the cohort at baseline was 37 years (IQR: 29–44), 1713 (61%) of respondents were Caucasian, and 949 (34%) were female. Table 1 shows the sample characteristics stratified by BZD use in the previous six months at baseline. As shown, at baseline, those reporting BZD use were younger, more likely to be female, HIV positive, and homeless. Additionally they injected heroin or cocaine at least daily, smoked crack as least daily, had experienced a non-fatal overdose and reported incarceration, syringe sharing, sex work, and unprotected sex in the preceding six months (all $p < 0.05$).

The results of the bivariable and multivariable GEE analyses of factors associated with BZD use are shown in Table 2.

In the multivariable GEE analysis, Caucasian ethnicity, ≥ daily heroin injection, ≥ daily cocaine injection, non-fatal overdose, sex work, incarceration, syringe sharing, and unprotected sex remained independently and positively associated with BZD use. Conversely, age, HIV status, homelessness, and ≥ daily crack smoking were negatively associated with BZD use.

A separate analysis stratified by HIV status was also performed. When analyses were restricted to HIV positive participants, Caucasian ethnicity, ≥ daily heroin injection, ≥ daily cocaine injection, non-fatal overdose, sex work, incarceration, syringe sharing, and unprotected sex were positively associated with BZD, use whereas age, homelessness, and ≥ daily crack smoking were negatively associated. When analyses were restricted to HIV negative participants, the results were common, although sex work was no longer associated with BZD use.

4. Discussion

The present study demonstrated that approximately 40% of our sample of PWID in Vancouver, Canada, reported BZD use throughout the study period. In addition, the present study found that BZD use was associated with several markers of addiction severity and significant health and social vulnerabilities, including syringe sharing and unsafe sex.