Intentional cannabis use to reduce crack cocaine use in a Canadian setting: A longitudinal analysis

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ABSTRACT

Background: No effective pharmacotherapies exist for the treatment of crack cocaine use disorders. Emerging data suggests that cannabinoids may play a role in reducing cocaine-related craving symptoms. This study investigated the intentional use of cannabis to reduce crack use among people who use illicit drugs (PWUD).

Methods: Data were drawn from three prospective cohorts of PWUD in Vancouver, Canada. Using data from participants reporting intentional cannabis use to control crack use, we used generalized linear mixed-effects modeling to estimate the independent effect of three pre-defined intentional cannabis use periods (i.e., before, during and after first reported intentional use to reduce crack use) on frequency of crack use.

Results: Between 2012 and 2015, 122 participants reported using cannabis to reduce crack use, contributing a total of 620 observations. In adjusted analyses, compared to before periods, after periods were associated with reduced frequency of crack use (Adjusted Odds Ratio [AOR] = 1.89, 95% Confidence Interval [CI]: 1.02–3.45), but not the intentional use periods (AOR = 0.85, 95% CI: 0.51–1.41). Frequency of cannabis use in after periods was higher than in before periods (AOR = 4.72, 95% CI: 2.47–8.99), and showed a tendency to lower frequency than in intentional cannabis use periods (AOR = 0.56, 95% CI: 0.32–1.01).

Conclusions: A period of intentional cannabis use to reduce crack use was associated with decreased frequency of crack use in subsequent periods among PWUD. Further clinical research to assess the potential of cannabinoids for the treatment of crack use disorders is warranted.

1. Introduction

According to recent estimates, there are between 14 and 21 million current users of cocaine worldwide, of whom approximately seven million have a cocaine use disorder (Degenhardt et al., 2014; United Nations Office on Drugs and Crime, 2014). A substantial proportion of cocaine use is thought to occur in the form of crack cocaine, particularly among marginalized populations in urban settings in North and South America (Fischer, Cruz, Bastos, & Tyndall, 2013). Crack cocaine use, in turn, is associated with a number of health-, social-, and legal-related harms (DeBeck, Kerr, et al., 2009; DeBeck, Small, et al., 2009; Degenhardt et al., 2011; Fischer, Blanken, et al., 2015; Fischer & Coghlan, 2007; Fischer, Powis, Firestone Cruz, Rudzinski, & Rehm, 2008; Fischer et al., 2013; Shannon et al., 2008). Unfortunately, despite the substantial public health and social challenges posed by crack use, no effective pharmacotherapy exists for the treatment of crack cocaine use disorders, and the long-term effectiveness of available psychosocial interventions is limited (Fischer, Blanken, et al., 2015). Therefore, there is a critical need for continuous research on innovative therapeutic approaches for crack use disorders.

A growing body of evidence has described the key role of the human endocannabinoid system (ECBS) in the neurobiological adaptations and behavioral processes underlying substance use disorders (Prud'homme, Cata, & Jutras-Aswad, 2015). While data from small observational studies and animal models suggest that some cannabinoids may be effective in reducing craving — one of the major predictors of crack cocaine use (Paliwal, Hyman, & Sinha, 2008) — more robust data is currently lacking (Dreher, 2002; Fischer, Kuganesan, et al., 2015). Thus, the objective of this study was to investigate the potential impact

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of the intentional use of cannabis to reduce crack use on the subsequent crack use frequency in a community-recruited sample of people who use illicit drugs (PWUD) in Vancouver, Canada.

2. Materials and methods

2.1. Study design, procedures and population

Data for this study were drawn from three open and ongoing prospective cohorts of PWUD with harmonized procedures for recruitment, follow-up and data collection, in Vancouver, Canada. These include the Vancouver Injection Drug Users Study (VIDUS); the AIDS Care Cohort to Evaluate exposure to Survival Services (ACCESS); and the At-Risk Youth Study (ARYS). VIDUS began recruitment in 1996, and ARYS and ACCESS in 2005. Individuals are recruited through snowball sampling and extensive street outreach in the city's Downtown Eastside and Downtown South neighborhoods, both urban areas with high levels of illicit drug use, homelessness and marginalization. Where possible, all information gathering procedures are conducted in the same way regardless of a participant's cohort membership to allow for analysis of merged data of studies focusing on outcomes and behaviors that cut across cohorts, as is the case of the present analysis. In brief, to be eligible, individuals need to reside within the greater Vancouver region and have used illicit drugs (other than cannabis) in the previous month. In addition, each cohort has specific inclusion criteria. VIDUS consists of HIV-negative adults (≥ 18 years) who injected drugs in the month prior to enrolment, ACCESS of HIV-positive adults, and ARYS of street-involved youth (14–26 years old.) Recruitment and study procedures for the three studies have been described in detail previously (Strathdee et al., 1998; Wood, Stoltz, Montaner, & Kerr, 2006; Wood et al., 2008).

After providing written informed consent, at baseline and semi-annually thereafter, participants completed an interviewer-administered questionnaire, provided blood for HIV/HCV serological testing, and were examined by a study nurse who provides basic medical care and referrals to additional health services where appropriate. The questionnaire elicited data on socio-demographic characteristics, drug use patterns, health care access and utilization, including HIV and addiction care, as well as other relevant exposures. Participants received a $30 honorarium at each study visit. The VIDUS, ACCESS and ARYS studies have received ethical approval by the University of British Columbia/Providence Health Care Research Ethics Board.

For the present study, data from the three cohorts were combined to achieve sufficient power to examine the potential impact of intentional cannabis use on frequency of crack use. The analytic sample was restricted to participants who reported intentional use of cannabis to reduce their use of crack at least once during the study period. Specifically, individuals were included if they answered yes to the question "In the last 6 months, did you substitute one drug for another in order to control or slow down your use", and indicated that they were using cannabis to reduce their use of crack. As this question was added to the questionnaires in June 2012, we considered all observations collected between this date and May 2015. Of note, measurements of crack cocaine use were longitudinal and fully distinct and independent from measurements of cannabis use, and the "substitution" question was systematically asked after these assessments.

2.2. Measures

The primary outcome of interest was the self-reported frequency of crack use in the six-month period prior to each study interview. At each semi-annual follow-up interview, participants were asked to estimate their crack use since the last visit, using six predefined frequency categories: (1) $\geq$ daily, (2) 2–3 times a week, (3) about once a week, (4) 1–3 times a month, (5) less than once a month, and (6) no use. We defined a reduction in use as a change from one frequency category to any other lower frequency category.

The primary explanatory variable was the cannabis use period. Three periods were defined: (1) before, observations before the first report of intentional cannabis use to reduce crack use, (2) during, interview-periods where the participant reported using cannabis to control the use of crack, and (3) after, observations after the first report of intentional cannabis use where no intentional use was reported.

We also considered a set of socio-demographic variables that were hypothesized to potentially confound the relationship between intentional cannabis use and crack use. Time-fixed variables of interest at baseline included: gender (male versus non-male); ancestry (Caucasian versus non-Caucasian); highest educational attainment (high school or postsecondary education vs. less than high school completion). Time-varying variables (updated at each semi-annual follow-up) included age (per year older), place of residency (Downtown Eastside, one of the largest open drug scenes in North America, versus other neighborhoods), and seeking treatment for crack cocaine.

2.3. Statistical analyses

As a first step, we compared characteristics of participants stratified by daily crack cocaine use in the last 6 months prior to their first interview in the study period (e.g., June 2012). We used the Pearson's chi-squared (or Fisher's exact test in the presence of small cell counts) for categorical variables, and the Wilcoxon rank sum test for continuous variables. Next, we examined the frequency of crack and cannabis use in each of the three cannabis use periods. Then, we estimated the bivariable relationship between the primary explanatory variable (i.e., cannabis use period, using the before period as the reference category) and each secondary covariate on frequency of crack use. We used generalized linear mixed-effects models (GLMM), treating the frequency of crack use as an ordinal outcome, and incorporating random intercepts to account for repeated measurements from the same participants over time. The proportional odds assumption was checked using the score test. This approach (i.e., ordinal outcome, random intercept) also allows for an estimation of the odds of changes in the frequency of crack cocaine use, regardless of the frequency each participant started with. As we modeled lower frequency of crack use, Odds Ratio (OR) > 1 means decreased frequency of use compared to the "before" period, while OR < 1 means increased frequency of use. To assess the independent effect of the cannabis use period on reduced crack cocaine use, we then fit a fixed multivariable model with the main explanatory variable and all secondary covariates that were associated with the outcome in bivariable analysis at a p-value < 0.10. In addition, we forced into the multivariable model a variable representing calendar year of the interview to control for the cohort effect, and a variable representing cohort designation to control for possible heterogeneity of effect across cohorts.

Finally, to explore changes in cannabis use coinciding with the three cannabis use periods, we built an analogous 6-level cannabis use frequency variable and followed a similar approach as described above. The only difference is that for cannabis use, we modeled higher frequency of use instead of reduced frequency (i.e., OR > 1 = higher frequency of cannabis use, and OR < 1 = lower frequency). All statistical analyses were performed using the SAS software version 9.4 (SAS, Cary, NC), and two-sided p-values < 0.05 were considered statistically significant.

3. Results

Between June 2012 and May 2015, 837 VIDUS, 670 ACCESS, and 493 ARYS participants completed at least one follow-up interview. Of these, 122 participants (49 VIDUS, 51 ACCESS, and 22 ARYS participants) reported intentional use of cannabis to reduce crack use at least once and were thus included in the present analysis, contributing to a total of 620 observations. The median duration of follow-up per participant during the study period was 29.1 (Inter-Quartile Range [IQR]: 24.0–30.1) months, resulting in a total of 268.1 person-years of