Cannabis use correlates of syringe sharing among injection drug users

Didier Jutras-Aswad[1,2], Geng Zang[1], Julie Bruneau[1,3]

1. CRCHUM, Centre Hospitalier de l'Université de Montréal, Québec, Canada
2. Department of Psychiatry, Université de Montréal, Québec, Canada
3. Department of Family Medicine, Université de Montréal, Québec, Canada

Address for all three authors:

CRCHUM, Centre Hospitalier de l'Université de Montréal

264 René-Lévesque est

Montreal, QC

CANADA H2X 1P1

Corresponding author:

Julie Bruneau

CRCHUM, Centre Hospitalier de l'Université de Montréal

264 René-Lévesque est, room 313

Montreal, QC

CANADA H2X 1P1

TR: 514-890-8000 #35882

FAX : 514-412-7280

julie.bruneau@umontreal.ca

Abstract

This study examines whether the relation between acute cannabis use and syringe sharing during single injection days is similar among regular and non-regular users, participating in a cohort study of injection drug users in Montréal, Canada. 236 (36.6%) subjects were classified as regular cannabis users (RCUs), 227 (35.2%) as non-regular cannabis users (NRCUs) and 181 (28.1%) were abstinent. Cannabis use during a single injection day was associated with a fivefold increased risk of sharing (OR 4.92; 1.83-13.22) in NRCUs compared to RCUs. Our results indicate that cannabis use history should be considered when evaluating its potential effect on risk-taking behaviors.

Keywords: cannabis, injection drug users, syringe sharing, HIV

Introduction

Injection drug users (IDUs) are vulnerable to numerous social and health problems, including HIV and viral hepatitis infections (1, 2). In both cases, viral transmission occurs mainly through sharing of contaminated syringes (3, 4). In spite of the availability of an extensive syringe exchange network, with access sites situated in the places where they are most needed (5), Montreal surveillance data have shown an increase in the incidence of HIV from 3.5 cases per 100 person-years between 1998 and 2002 to 4.9 cases per 100 person-years between 2003 and 2006 (6). These results indicate the need to continually fine-tune and update our understanding of correlates of syringe sharing to improve prevention and treatment strategies in IDUs (3).

Binge drug use (7), high injection frequency (8) and co-use of non-injecting drugs, such as alcohol and benzodiazepines (8-10), are all significantly correlated to syringe sharing. The relation between cannabis use and syringe sharing, on the other hand, has been the object of much less attention, although cannabis is one of the most commonly non-injecting drug used among IDUs, second only to alcohol (11). The few studies that examined the relation between cannabis use and syringe sharing showed inconsistent results. Studies conducted in opiate-dependent patients in treatment showed null to modest positive association between cannabis use and risky behaviors including syringe sharing (12-14). Conversely, a protective effect of cannabis use was found on HIV seroconversion among IDUs who were mostly out-of-treatment cocaine users, after adjustment for other individual covariates (15).

A recent study may provide insights into the difficulty encountered by the published studies in understanding the possible effect of cannabis on syringe sharing. Ramaekers et al. showed that cannabis use history strongly determines the behavioral response to a single dose of THC. An acute dose of THC 500 μg/kg induced a significant alteration of critical tracking, divided attention and motor impulse control in occasional cannabis users. In contrast, heavy users experienced a limited loss of motor impulse control, and these changes only occurred when they were exposed to high THC concentrations (16). These findings are consistent with other studies suggesting that regular cannabis users are tolerant to some of the acute effects of cannabis on cognition in laboratory setting (17-21), notably decision-making alteration

which disrupts the ability to balance the immediate consequences of choices with their future consequences (18, 22). Altogether, these studies provide valuable clues as to how the relation between cannabis use and risky behaviors such as syringe sharing could be examined.

Most of the published research on cannabis use and HIV risk (12-15) did not examine different patterns of cannabis use (e.g. regular *vs.* irregular use), which could partly explain the inconsistent results obtained thus far. In addition, most epidemiological studies have used aggregated measures of cannabis use over the course of the three or six months preceding the survey, not allowing for the study of the acute effect of cannabis on behaviors during a specific injection episode. Event-level methodology in IDU research is novel, and offers an interesting alternative for the investigation of correlates of risky behavior as they ensure that the risky behavior occurred at the time of a specific event (23). Event-level research involves questioning participants about the circumstances and behaviors related to a single "incident" or set of incidents that presented an opportunity for high-risk behavior, as opposed to asking about factors that might have occurred at multiple times over the months preceding a survey.

In this report, we examined the association between cannabis use patterns and syringe sharing among IDUs, using i) self-reported behavioral measures over 6-months, and ii) self-reported data on the type of drug used and syringe sharing taking place during single injection days (event-level journal). We hypothesize that the pattern of cannabis use, measured over 6 months, will not be associated with syringe sharing. Conversely, we postulate that cannabis use during an injection day will moderate the association between cannabis use patterns and sharing.

Methods

The study population was drawn from the St. Luc Cohort, an open cohort established in 1988 to study factors associated with HIV transmission among IDUs in Montreal, and which has already been described (24). Cohort eligibility criteria included being 18 years of age or older, having injected drugs within the past six months, and providing informed consent as approved by the institutional review board of the Centre Hospitalier de l'Université de Montréal. Overall, 60% of cohort participants have

volunteered to participate in response to street-level recruitment and by word-of-mouth referral, while recruitment of the remaining subjects was done through addiction treatment agencies and other community programs. Interviewer-administered questionnaires elicited information on socio-demographic and health characteristics, drug use and injection behaviors in the past 6 months. At each visit, participants were also asked to fill a journal including information on drug use, injection and sharing behaviors during each of the 7 days preceding their last injection day. Venous blood samples were drawn and tested for HIV and HCV antibodies. Participants were asked to return for their HIV and HCV serostatus test results two weeks after their interview, at which time post-test counseling and referral for medical care were provided as needed. Participants were given a $15.00 CDN stipend at each interview as compensation for their time and to facilitate transportation to the study centre.

The present analysis was restricted to active IDUs, defined as participants who reported injecting drugs in the six months prior to their study visit, interviewed between November 2004 and December 2006. A total of 697 IDUs were eligible for this investigation. For each participant, data from a single visit was used for analysis. For participants who entered the cohort prior to the study visit, the first visit during the study period was considered for this investigation. We excluded 53 participants for whom information on key variables was missing. Excluded participants did not differ from those included except for the two following variables (all p value < 0.05): frequent alcohol use (59.1% vs. 40.1%), and IV heroin use (6.1% vs. 16.9%).

Patterns of cannabis use: Regular cannabis users (RCU) were defined as IDUs having reported cannabis use on average every second day, e.g. 90 days or more of cannabis use in the past six months. Non-regular cannabis users (NRCU) reported cannabis use between 1 and 89 days over the same period, and cannabis abstinent IDUs did not report cannabis use in the past six months. This categorization was used to differentiate users who had a continuous cannabis brain exposure from those who were exposed intermittently, and was selected in order to overcome concerns raised by the imprecise definition of "heavy cannabis use" used in other studies (25).

6-month analysis: The primary end-point for this analysis was "syringe sharing", defined as having injected with a syringe used by someone else at least once in the past six months. Similar outcomes were used in studies on cannabis use among IDUs (12, 15) and our measure of sharing was chosen to help comparisons with the existing literature. The main explanatory variable was cannabis use patterns, RCU and NRCU compared to cannabis abstinent IDUs. Other potential explanatory variables included injection duration (time elapsed between the first and the last reported injection), and frequent alcohol or drug use (at least 45 days of each substance's use in the past six months). Consistent with previous studies, unstable housing arrangement was defined as living on the street, in shelters, or in apartment-hotels rented on a monthly basis, where rapid turnover prevails compared to a more typical rental accommodation leased on a yearly basis in Montreal (5), and binge drug use was assessed by asking the following question: "In the past six months, did you go on runs/binges where you injected drugs more than usual?" (26). Participants were asked whether they had needed help injecting themselves in the past 6 months. Age, gender and HCV/HIV status were also examined and are self-explanatory.

Event-level journal: The data were collected over seven consecutive days in the journal; only days where at least one injection was reported were used for analysis. The relation between pattern of cannabis use and any syringe sharing during an injection day was examined, stratified by the use of cannabis (yes/no) on each given day. Only days during which the participant reported having injected were included. Covariates of interest included other drug used (cocaine, heroin, alcohol, crack, tranquillizers), each treated dichotomously, and the number of injections reported during each injection day, along with age, gender, and housing status.

Statistical analyses: Chi-square and F-test analysis were conducted to examine socio-demographic characteristics, drug use and injection behaviors in the past 6 months according to pattern of cannabis use. Logistic regression was conducted to calculate the crude and adjusted odds ratio (OR) and corresponding 95% confidence intervals (95%CI) of the association between syringe sharing, 6-months cannabis use patterns and potential risk factors. Variables that had a p-value of less than 0.25 in univariate analysis were considered in a multivariate analysis in addition to age and gender, expected to be important based on

substantive knowledge, after assessment of collinearity. Binge drug use was almost exclusively reported by cocaine users (81/96), therefore only the former was kept in the analyses.

Since analyses of the relation between cannabis use patterns and syringe sharing in the journal included up to seven measures for each subject, we used generalized estimating equations (GEE) with logit link for the analysis of correlated data to determine which factors were independently associated with syringe sharing (27, 28). We examined associations between syringe sharing, cannabis use patterns and covariates of interest using univariate and multivariate logistic GEE analyses. Analyses were computed using SPSS 16.0 and SAS 9.1 programs.

Results

Six hundred forty-four IDUs were included in this investigation. Participants were predominantly male, Caucasian (n=541, 84.0% and n=573, 89.0% respectively) and almost half (n=297, 46.1%) lived in unstable conditions. They have been injecting for 14.46 (SD 9.38) years on average. Nearly one third of IDUs (n=202, 31.4%) reported having shared a syringe at least once in the previous six months. 74.2% (n=478) were HCV positive and 13.2% (n=85) were HIV positive. The numbers of participants in each of the three sub-groups were as follows: 236 (36.6%) RCUs, 227 (35.2%) NRCUs and 181 (28.1%) abstinents. Sub-groups were also similar for most socio-demographic and drug use characteristics. RCUs were slightly younger than NRCUs and cocaine abstinent IDUs (36.3 +/- 9.0 *vs.* 39.0 +/- 9.6 years and 40.2+/-10.2, respectively; $p<0.001$) and more likely to be male (89.0 *vs.* 81.1% and 81.2%; $p<0.05$). Cannabis abstinent IDUs were less likely than RCUs and NRCUs to live in unstable housing conditions (37.0% *vs.* 48.7% and 50.7%; $p<0.05$). The only drug use characteristic differing between sub-groups was frequent alcohol use (32.6%, 46.6% and 39.2% for cocaine abstinent IDUs, RCUs and NRCUs, respectively; $p<0.05$).

Table 1 shows the logistic regression model of the association between syringe sharing and explanatory variables measured at 6-months intervals. The association between sharing and cannabis use

patterns was not significant. In the multivariate analysis, syringe sharing was positively associated with unstable housing, frequent IV heroin and alcohol use, need help to inject and binge drug use.

Overall, the 644 participants contributed to a total of 4,494 days in the event-level journal analysis, of which 1880 injection days were reported. Syringe sharing happened on 124 of those days. As shown in Table 2, there was no significant difference between the sub-groups regarding syringe sharing on injection days. Predictably, RCUs were more likely to use cannabis, compared to NRCUs (82.1% vs. 17.5%, $p<0.0001$). Sub-groups were similar in terms of other drug used and injection practices.

Figure 1 shows the proportion of IDUs reporting syringe sharing during an injection day in each sub-group, accounting for cannabis use on that same day. On days where subjects did not use cannabis, all three groups showed similar syringe sharing frequency. On days where they used cannabis, this frequency raised from 7.6% to 14.6% in NRCUs, while it decreased in RCUs, from 8.3% to 3.1%.

Table 3 shows univariate and multivariate adjusted GEE analysis of the association between syringe sharing and cannabis use patterns in reported days of the journal, stratified by cannabis use on any given day. Compared to RCUs, NRCUs were more likely to have shared a syringe on days where they used cannabis (OR 4.92; 95% CI 1.83-13.22), this difference not being observed on days without cannabis use, even after adjustment for other covariates.

Discussion

The possibility that cannabis use has an influence on risky behaviors among IDUs remains poorly documented although this substance's use is widespread in this population. As expected, we did not find a significant relation between cannabis use and syringe sharing, using the aggregated 6-month cannabis use pattern and syringe sharing measures. Other factors previously reported in the literature on sharing such as to need help to inject (8), binge drug use (7) and unstable housing (29) were independently associated with syringe sharing. Yet, compared to regular cannabis users, the risk of sharing was five times higher among non regular cannabis users if using cannabis on a given injection day, this relation not being observed

within non-cannabis days.

Experienced users appear to be tolerant to some of the cognitive and behavioral effects of cannabis in laboratory settings (16-21). Ramaekers et al. proposed that this habituation phenomenon of THC-induced alteration of neurocognitive performance could have an impact on traffic injuries and death, stating that cannabis use history modulates the acute effect of THC on performance and thus may explain current controversies in studies showing contradictory results as to whether THC increases crash risk or not (16). The present study could be another illustration of how such controlled-setting neuropsychological findings can translate into subjects' behaviors in a naturalistic setting. Indeed, acute alteration of neurocognitive performance by THC could mediate the relation between cannabis use and syringe sharing during injection episodes in our study sample, which appears to be more deleterious in irregular users. A differential effect of THC on cognition according to pattern of use could explain the difference that we found between NRCUs and RCUs, the latter being more tolerant to these effects. Unfortunately, the absence of molecular or other neurobiological markers in our study prevented us from characterizing the potential mechanisms, which are numerous. CB1 is the main receptor associated with cannabinoid effects on central nervous system and its activation, such as the supra-physiological stimulation induced by THC, modulates several neurotransmission systems in mesocorticolimbic structures and pathways critical to decision-making cognition (30-33). Interestingly, the CB1 receptors down-regulation induced by a prolonged exposure to cannabis (34) appears to be in line with our findings.

Although the aforementioned "tolerance" hypothesis is appealing, other differences, aside from cannabis use pattern, could contribute to explain our findings. The use of heroin, for example, could mediate the association between pattern of cannabis use patterns and syringe sharing. On one hand, irregular cannabis use is positively related to the severity of addiction among opiate dependent subjects (35, 36), while frequent use of heroin is associated with syringe sharing (8). NRCUs could be more likely to engage in risky behaviors like syringe sharing because of a higher risk of using other drugs, notably heroin, compared to RCUs. On the other hand, RCUs may be somewhat protected in regard to syringe sharing by using cannabis to control problematic heroin use (36). In our study however, the increased odds

of syringe sharing among NRCUs when compared to RCUs remains significant after controlling for other drug use including heroin and cocaine in the multivariate analysis. We also found no significant association between syringe sharing and cannabis use patterns on "non-cannabis" days, suggesting that the RCUs and NRCUs showed a similar general pattern of behaviors, except when they use cannabis during an injection episode. Moreover, the positive relation between cannabis use patterns and syringe sharing on injection days was significant even after controlling for the frequency of injection, a proxy of binge use, one of the factors most strongly associated with syringe sharing in the 6-month analysis and in existing literature (7). Such confounder is thus less likely to entirely mediate the relation between cannabis use and syringe sharing in our cohort, further supporting the potential relevance of alternative mechanisms such as the modulation of neurocognitive performance by THC.

This study has several limitations that need to be mentioned. Self-report of drug use and behaviors may be suspected of causing an information bias, but it has been showed to be a reliable source of information in drug users (37) and allowed us to obtain day-to-day measures of cannabis use in the journal. Relatively little information was available to describe the injection episode. The study's design did not allow for the determination of cannabis use chronology during injection episodes or the amount, potency and composition of cannabis that was used. Also, a relatively small number (124) of syringe sharing episode were reported in the journal. It prevented us from conducting a more complete set of analysis, which would have notably allowed examining more broadly the relation between acute cannabis use and syringe sharing for each subgroup based on cannabis use patterns, controlling for adequate covariates.

Altogether, our findings suggest a differential effect of cannabis on syringe sharing between IDU who are regular vs. non regular chronic cannabis users. These results indicate that inexperienced users could be more affected by acute cannabis effects than regular users, who are reported as being more tolerant to cannabis-related performance-impairing effects. Although much remains to be learned on the effect of cannabis among IDUs, our data add to the existing literature to begin establishing a foundation on which a prevention platform can be built in guiding drug users about the potential impact of cannabis use

on risky behaviors. Understanding the mechanisms underlying why some IDUs are more affected by the deleterious effects of cannabis than others could lead to a better understanding of this substance's impact in these vulnerable individuals, and maybe provide some clues on new treatment strategies. An integrative effort of behavioral and basic sciences appears as being the best approach to go further in that direction, using samples sufficiently large to take into account both acute cannabis effect and chronic pattern of use.

ACKNOWLEDGMENTS

We would like to acknowledge Élisabeth Deschênes, Travis Hottes, Martin Rioux, and the other staff at the St. Luc Cohort research site for sharing their wisdom and expertise during the data analysis and interpretation phases of this project. We extend a special thank you to the St. Luc Cohort participants, without whom this research would not be possible.

DECLARATION OF INTERESTS

All authors declare no competing interests, including no financial, personal or other relationships with people or organisations that could inappropriately influence, or be perceived to inappropriately influence, the work.

FUNDING

This study was supported by a project grant from the Canadian Institutes of Health Research, with additional support from the Réseau SIDA et Maladies Infectieuses du Fonds de la Recherche en Santé du Québec. D^{r} Bruneau holds a clinical research career award from the Fonds de la Recherche en Santé du Québec. D^{r} Jutras-Aswad holds a Research Fellowship award from the CRCHUM, Centre Hospitalier de l'Université de Montréal. Funding sources had no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

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Table 1: Crude and Adjusted Odd Ratios (OR) and 95% Confidence Intervals (CI) of the association between syringe sharing and selected risk factors, by logistic regression.

VARIABLE CATEGORIES (N)	% SYRINGE SHARING	CRUDE OR AND 95%CI	MULTIVARIATE MODEL ADJUSTED OR AND 95%CI
Cannabis use patterns	29.3	1	1
Cannabis abstinent users (181)	38.7	1.34 (0.9-2.0)	1.16 (0.7-1.8)
Non regular cannabis users* (227)	28.8	0.98 (0.6-1.5)	0.85 (0.5-1.4)
Regular cannabis users ** (236)			
Age (1 year increment)		0.98 (0.96-1.00)	0.99 (0.97-1.01)
Gender			
Male (541)	29.2	1	1
Female (103)	42.7	1.81 (1.2-2.8)	1.41 (0.9-2.3)
Unstable Housing			
No (347)	28.0	1	1
Yes (297)	35.4	1.41 (1.0-2.0)	1.58 (1.1-2.3)
IV heroin			
Infrequent (535)	28.4	1	1
Frequent *** (109)	45.9	2.14 (1.4-3.3)	1.75 (1.1-2.8)
Alcohol			
Infrequent (386)	27.2	1	1
Frequent *** (258)	37.6	1.61 (1.2-2.3)	1.72 (1.2-2.5)
Binge			
No (548)	27.7	1	1
Yes (96)	52.1	2.83 (1.8-4.4)	2.41 (1.5-3.9)

VARIABLE CATEGORIES (N)	% SYRINGE SHARING	CRUDE OR AND 95%CI	MULTIVARIATE MODEL ADJUSTED OR AND 95%CI
Need help to inject	26.3	1	1
No (506)	50.0	2.81 (1.9-4.1)	2.55 (1.7-3.8)
Yes (138)			

*: NRCUs = cannabis use between 1 and 89 days in the past six months

**: RCUs = cannabis use on average every second day, e.g. 90 days or more of cannabis use in the past six months.

***: frequent= 45 days or more of drug use in the past six months

Table 2: Type of drug used and injection practices reported during injection days by IDUs according to their pattern of cannabis use in the past six months

VARIABLES	REGULAR CANNABIS USERS Observations=674 N (%)	NON REGULAR CANNABIS USERS Observations=705 N (%)	CANNABIS ABSTINENT USERS Observations=501 N (%)	*P*-value*
Cannabis	553 (82.1)	123 (17.5)	-	<.0001
IV Cocaine	417 (61.9)	423 (60.0)	296 (59.1)	0.85
IV Heroin	185 (27.5)	212 (30.1)	177 (35.3)	0.42
Crack	77 (11.4)	92 (13.1)	44 (8.8)	0.43
Tranquilizers	76 (11.3)	123 (17.5)	75 (15.0)	0.14
Alcohol	224 (33.2)	202 (28.7)	118 (23.6)	0.65
Syringe sharing	27 (4.0)	62 (8.8)	35 (7.0)	0.20
Mean number of daily injections (mean and SD)	6.20 (7.40)	6.33 (6.87)	6.25 (5.97)	0.85

*: *P*-values for difference from F-test for continuous variables and Chi-square test for categorical variables.

Table 3: GEE logistic regression analysis of the association between syringe sharing and chronic cannabis use (NRCU vs. RCU) during an injection day, stratified by use of cannabis on that given day

VARIABLES	CRUDE OR (95%CI)	*P*-VALUE	ADJUSTED* OR (95% CI)	*P*-VALUE
Using cannabis during the day				
RCUs	1		1	
NRCUs	5.00 (1.88-13.36)	0.001	4.92 (1.83-13.22)	0.002
Not using cannabis during the day				
RCUs	1		1	
NRCUs	0.99 (0.25-4.00)	0.99	0.94 (0.20-4.40)	0.94
Abstinents	1.03 (0.26-4.16)	0.97	1.17 (0.25-5.53)	0.84

*: adjusted for age, sex, housing status, IV cocaine, IV heroin, crack, tranquilizers, alcohol use (use of each substance during the same day) and injection frequency

Figure 1: Frequency of syringe sharing according to cannabis use pattern, accounting for cannabis use during single days of injection.