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Injection Methamphetamine Use is Associated with an Increased Risk of Attempted Suicide: A Prospective Cohort Study

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Abstract

Background—Methamphetamine (MA) use is a growing public health concern in many settings around the world. While some physical and mental health effects associated with injection MA use have been well described, little is known about the relationship between injecting MA and suicidal behavior. We sought to determine whether MA injection was associated with an increased risk of attempting suicide among a prospective cohort of injection drug users (IDUs) in Vancouver, Canada.

Methods—Between 2001 and 2008, eligible participants enrolled in the Vancouver Injection Drug Users Study (VIDUS) completed semi-annual questionnaires that elicited information regarding sociodemographics, drug use patterns, and mental health problems including suicidal behavior. We used Cox proportional hazards models with time-dependent covariates to determine whether self-reported MA injection was an independent predictor of attempting suicide at subsequent time points.

Results—Of 1873 eligible participants, 149 (8.0%) reported a suicide attempt, resulting in an incidence density of 2.51 per 100 person-years. Participants who attempted suicide were more likely to be younger (median: 35 vs. 40, $p<0.01$), female (48.3% vs. 35.1%, $p<0.01$), and of Aboriginal ancestry (43.6% vs. 31.3%, $p<0.01$). In a Cox proportional hazards model, MA injection was associated with an 80% increase in the risk of attempting suicide (adjusted hazard ratio = 1.80, 95%CI: 1.08 – 2.99, $p=0.02$).

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Conclusions—These findings suggest that IDUs who inject MA should be monitored for suicidal behavior. Improved integration of mental health and suicide prevention interventions within harm reduction and drug treatment programs may be fruitful.

Keywords

methamphetamine; suicide; injection; drug use; Canada; epidemiology

1. INTRODUCTION

Over the past decade, the availability and use of methamphetamines (MA) has become a significant public health concern in many regions, with parts of North America, Eastern Europe, and Southeast Asia experiencing the greatest increases (Global SMART Programme, 2010; Gonzales et al., 2010; McKetin et al., 2008a). In fact, the global annual prevalence of MA use and other amphetamine-type substances (0.3% – 1.2% of the population aged 15 to 64) now exceeds that of opiates and cocaine combined (United Nations Office on Drugs and Crime, 2010). Although the majority of people who use MA do so through non-injection routes of consumption, parenteral use is increasingly common and of particular public health concern (Maxwell and Rutkowski, 2008). Previous studies have demonstrated that persons who inject MA are: more severely dependent than non-injectors (McKetin et al., 2008b), at an increased risk of non-fatal overdose (Fairbairn et al., 2008), more likely to engage in HIV risk behavior (Braine et al., 2005; Fairbairn et al., 2007; Hayashi et al., 2010; Lorvick et al., 2006), and more likely to experience social stigma (Semple et al., 2004).

Persons who inject MA are also more likely to have co-occurring psychiatric disorders compared to non-injection MA users (Hall et al., 1996; Zweben et al., 2004). Consistent with this observation, preliminary evidence from treatment samples indicates that MA injectors are more likely to attempt suicide than persons who snort or smoke the drug (Glasner-Edwards et al., 2008; Zweben et al., 2004). However, it is not clear if injecting MA augments what is already a greatly elevated risk of suicidal behavior among IDUs, compared to non-IDUs, in general (Havens et al., 2004).

Determining which subpopulations of IDUs are most likely to attempt suicide has important policy and programmatic implications, and may serve to inform suicide prevention efforts and mental health service delivery. However, we know of no longitudinal studies that have considered whether IDUs who use MA are more likely to attempt suicide than IDUs who do not use MA. The purpose of this study was thus to answer this question using data derived from a longstanding community-recruited prospective cohort of IDUs in Vancouver, Canada.

2. METHODS

2.1 Study Design

Data for this analysis were derived from an ongoing open prospective cohort known as the Vancouver Injection Drug Users Study (VIDUS). The study began enrolment in May 1996 and recruits individuals through word of mouth, street outreach, and referrals. Sampling and follow-up methodologies have been described in detail previously (Strathdee et al., 1997; Tyndall et al., 2003). Participants are eligible if they satisfy the following: are at least 14 years of age; reside in the Greater Vancouver region; injected drugs during the past six months; and provide informed consent. At baseline and at each six-month visit thereafter, participants complete an interviewer-administered questionnaire that elicits information pertaining to sociodemographic characteristics, drug use, treatment utilization, and HIV risk

behaviors. Nurses also assess participants for various health conditions (including suicidal behavior), and obtain blood specimens for HIV and hepatitis C serology. Participants receive $20 CAD for each visit. The study has been approved by the University of British Columbia/Providence Health Care Research Ethics Board.

2.2 Participants and Measures

Questions assessing lifetime and recent suicidal behavior were first added to the study instrument in May 2001; therefore, all participants who completed at least one interview after this date were eligible for inclusion. The study period was defined as the seven-year interval ending in May 2008.

The primary outcome for this analysis was time to first report of suicidal behavior, defined as a positive response to the question, “In the past 6 months, have you attempted suicide?” The primary exposure of interest was self-reported MA injection at least once in the past six months (yes vs. no). In a sub-analysis, we also considered MA injection as a categorical variable with the following levels: no MA injection, infrequent (i.e., <daily) MA injection, and frequent (i.e., ! daily) MA injection. We assessed as potential confounders measured variables that have been identified as risk factors for suicidal behavior in IDUs (Darke and Kaye, 2004; Havens et al., 2006; Havens et al., 2004). These included the following sociodemographics: age (per year older), years injecting (per year), sex (female vs. male), relationship status (married/common law/regular partner vs. single/dating), sexual orientation (lesbian, gay, bisexual, transgendered [LGBT] vs. heterosexual) and belonging to a minority group. We dichotomized participants as being Aboriginal (self-identified Aboriginal, First Nations, Inuit, or Métis ancestry) versus other due to increased rates of suicide in Aboriginal communities observed previously (Malchy et al., 1997). Other potential confounders examined included: homelessness, incarceration, current enrolment in a methadone maintenance program, experiencing physical violence, sex trade work, and any use of non-injection crack, injectable heroin, injectable cocaine, and non-injection methamphetamine (all yes vs. no). Non-injection heroin use and frequent (! daily) non-injection MA use are rarely reported by VIDUS participants and thus were not included as potential predictors of suicidal behavior. Unless otherwise indicated, all variables refer to behaviors occurring in the six-month period preceding the date of the interview.

2.3 Statistical analyses

As a first step, we compared the sociodemographic characteristics of those who reported attempting suicide over the study period versus those who did not using the Pearson chi-square test for categorical variables and the Wilcoxon test for continuous variables. We then used survival analysis to determine the association between MA injection and time to first suicide attempt among cohort participants. Since the study instrument assessed past six-month suicidal behavior, the exact date of first suicide attempt was estimated as occurring three months prior to the date of the interview. All participants who reported a suicide attempt were right-censored as of this date. Persons who never reported a suicide attempt were right-censored as of their last study visit. We used the person-time method to calculate the incidence of suicidal behavior over the study period.

In order to account for potential confounders and repeated measures over time, Cox proportional hazards models with time-dependent covariates were used to calculate the unadjusted and adjusted hazard ratios for each variable. To avoid associations attributable to reverse causation, the covariate values obtained at the follow-up prior to that in which a suicide attempt was recorded were used to predict the likelihood of this outcome. All covariates significant at an *a priori* cut-off of $p < 0.05$ were included in a final multivariate model. In order to determine whether polydrug use (i.e., injecting MA plus at least one other

drug concurrently during the past six months) further increased the risk of attempted suicide, interaction effects were assessed *post hoc*, and if significant, added to the final model. The variable corresponding to years injecting was excluded as it was found to be collinear with age. The proportional hazard assumption was assessed by examining time-by-covariate interactions (Hess, 1994). All statistical analyses were conducted using SAS 9.1.3, and all *p*-values are two-sided.

3. RESULTS

Over the study period, 1873 eligible participants contributed 5948 years of follow-up. The median age of the sample was 31 (interquartile range [IQR]: 32 – 46), 677 (36.2%) were female, and 601 (32.1%) were of Aboriginal ancestry. In total, 149 (8.0%) persons reported a suicide attempt, resulting in an incidence density of 2.51 per 100 person-years (95%CI: 2.13 – 2.93 per 100 person-years). Participants who attempted suicide were younger, reported fewer years injecting, and were more likely to be female and Aboriginal (Table 1). We did not observe differential loss to follow-up among study participants: the group who failed to return after their first visit did not differ with respect to age ($p = 0.67$), sex ($p = 0.67$), or ancestry ($p = 0.97$).

Factors associated with time to first suicide attempt are shown in Table 2. In a multivariate model, MA injection remained a strong predictor of attempting suicide (adjusted hazard ratio [AHR] = 1.80, 95%CI: 1.08 – 2.99, $p = 0.02$). Tests of time-by-covariate interactions demonstrated that the proportional hazards assumption was met. Each of three interaction effects (i.e., injecting MA plus injecting cocaine, injecting heroin, or crack) was non-significant, indicating that polydrug use neither increased nor decreased the risk of attempted suicide in this sample.

As a final step, we examined whether a dose-response relationship was observed between frequency of MA injection and increased likelihood of suicidal behavior. Considering MA injection as a categorical variable provided evidence that such a relationship exists. Compared to periods of no MA injection, infrequent MA injection was a predictor of attempting suicide (HR = 2.12, 95%CI: 1.23 – 3.66, $p = 0.01$), while frequent MA injection was associated with the greatest risk of attempting suicide (HR = 2.68, 95%CI: 1.08 – 6.60, $p = 0.03$).

4. DISCUSSION

In this seven-year study, we found that IDUs who injected methamphetamine had an 80% greater risk of attempting suicide than those who did not, even after taking into account a wide range of potential confounders. Sub-analyses indicated a dose-response relationship between frequency of injecting MA and suicidal behavior.

Our results support earlier cross-sectional analyses of persons participating in an MA outpatient treatment intervention demonstrating that, at program entry, IDUs reported more lifetime suicide attempts than non-IDUs (Glasner-Edwards et al., 2008; Zweben et al., 2004). Although an elevated prevalence of attempted suicide has been observed previously among populations of non-injection MA users in the US (Kalechstein et al., 2000) and Taiwan (Yen and Shieh, 2005), our results suggest that persons who inject MA should be considered at a very high risk of suicide among populations of MA users and the broader global IDU community. Further, this study both builds on previous findings and overcomes many of the limitations of cross-sectional designs by following individuals prospectively and using survival analysis to ensure that the exposure of interest preceded the reports of suicide attempt.

Although the etiologic pathway between injecting MA and suicidal behavior requires further investigation, it is likely that a combination of neurobiological, social, and structural mechanisms account for this association. For example, chronic MA users experience reduced dopamine neurotransmission (Volkow et al., 2001; Wang et al., 2004), which itself may play a role in inducing anhedonia, depression and suicidal behavior (Roy et al., 1992). However, given that these studies focus on non-injection MA users, it is not clear if similar neurobiologic mechanisms may explain the differential attempted suicide rates observed between MA using IDUs and non-MA using IDUs in this study. Compared to other IDU, it is possible that MA users have more isolated social networks and thus poorer social support systems (Shaw et al., 2008). MA injectors may also face unique barriers to accessing IDU-focused health and social services (Marshall et al., 2011). For example, addiction treatment programs and supportive housing services that cater to opioid injectors may be unable to accommodate the specific health needs of IDUs who use MA or are experiencing MA-induced withdrawal symptoms (Degenhardt et al., 2010). Future studies that combine neurobiologic analyses with social epidemiologic approaches may provide greater insight into these potential mechanisms.

This study has several limitations that should be noted. First, although a variety of techniques are undertaken to ensure that the sample is representative, caution is recommended when generalizing these findings to other settings. A second limitation is that both the exposure and outcome of interest are self-reported. Given that suicide is a highly stigmatized behavior, it is likely that the observed incidence of attempted suicide is an underestimate. Third, although previous studies have shown that suicidal ideation is elevated among MA-using women (Kalechstein et al., 2000), we were unable to conduct gender-stratified analyses due to the relatively small number of events and females in our sample. Fourth, we were unable to control for several previously identified risk factors for suicide among MA users. For example, although history of prior suicidal behavior, comorbid mental health conditions including depressive disorder, and history of abuse are important predictors of suicide attempts (Dube et al., 2001; Forman et al., 2004; Henriksson et al., 1993), this information was either not collected or not available for the entire study period. It is therefore possible that residual confounding may explain some of the observed association between MA injection and suicidal behavior, and thus our results should be interpreted with caution.

This study has a number of implications for clinic- and community-based services for IDUs. The high rate of attempted suicide observed in this and in other studies suggests that suicide prevention efforts should be an integral part of substance abuse treatment programs (Glasner-Edwards et al., 2008; Lloyd et al., 2007). Further, out-of-treatment IDUs who inject MA, particularly frequently, would likely benefit from improved suicide risk assessment and other mental health support services within health care and community-based settings. Although the incorporation of harm reduction principles within community-based mental health programs is a relatively new phenomenon (Mancini and Linhorst, 2010), improved integration between harm reduction interventions and mental health programs including suicide prevention efforts for this population may be fruitful.

In summary, these results demonstrate an increased risk of attempted suicide among IDUs who use methamphetamine. While the precise mechanisms underlying the association between MA injection and suicidal behavior remain to be elucidated, this study provides preliminary evidence that persons who inject methamphetamine should be a major focus of future suicide prevention efforts.

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Table 1

Sociodemographic characteristics of injection drug users (IDU) who did and who did not attempt suicide, 2001–2008 (*N* = 1873).

Characteristic	Attempted Suicide N (%) *N* = 149[¶]	Did Not Attempt Suicide N (%) *N* = 1724[¶]	*P*-value
Age[†] (median, IQR)	35 (29 – 43)	40 (33 – 46)	<0.01
Years injecting[‡] (median, IQR)	17 (14 – 21)	19 (16 – 26)	<0.01
Sex (*n*, %)			
Female	72 (48.3)	605 (35.1)	<0.01
Male	77 (51.7)	1119 (64.9)	
Ethnicity (*n*, %)			
Caucasian	73 (49.0)	1042 (60.8)	0.01
Aboriginal[*]	65 (43.6)	536 (31.3)	
Asian	7 (4.7)	59 (3.4)	
Other	4 (2.7)	78 (4.5)	
Sexual Orientation (*n*, %)			
LGBT[a]	19 (16.1)	139 (10.4)	0.06
Heterosexual	99 (83.9)	1199 (89.6)	

Note:

[†] age at first interview during follow-up;

[‡] number of years injecting at first study visit;

[*] Aboriginal includes self-identified First Nation, Inuit, or Métis ancestry; a LGBT = lesbian, gay, bisexual, or transgendered/transsexual;

[¶] note: columns do not add to 100% due to missing or unavailable data.

Table 2

Cox proportional hazards model of time to first suicide attempt among a cohort of injection drug users in Vancouver, 2001–2008 (*n* = 1873).

Characteristic	Unadjusted HR* (95% CI)	*P* – value	Adjusted HR* (95% CI)	*P* – value
Age (per year older)	0.96 (0.95 – 0.98)	<0.01	0.98 (0.96 – 1.00)	0.05
Sex (female vs. male)	1.59 (1.15 – 2.19)	0.01	1.32 (0.91 – 1.92)	0.15
Ethnicity (Aboriginal ancestry vs. other)	1.59 (1.15 – 2.19)	0.01	1.36 (0.93 – 1.97)	0.11
Sexual Orientation (LGBT[a] vs. heterosexual)	1.55 (0.95 – 2.54)	0.08		
Relationships Status (married vs. single/dating)	1.14 (0.76 – 1.69)	0.53		
Homeless† (yes vs. no)	1.74 (1.17 – 2.59)	0.01	1.22 (0.79 – 1.87)	0.37
Non-injection Crack Use† (yes vs. no)	1.61 (1.09 – 2.38)	0.02	1.28 (0.79 – 1.87)	0.21
Injection Heroin Use† (yes vs. no)	1.47 (1.01 – 2.16)	0.04	1.16 (0.78 – 1.71)	0.46
Injection Cocaine Use† (yes vs. no)	1.54 (1.07 – 2.23)	0.02	1.29 (0.87 – 1.92)	0.21
Injection Methamphetamine Use† (yes vs. no)	2.15 (1.32 – 3.49)	<0.01	1.80 (1.08 – 2.99)	0.02
Non-injection Methamphetamine Use† (yes vs. no)	1.48 (0.69 – 3.17)	0.32		
Incarceration† (yes vs. no)	1.13 (0.71 – 1.78)	0.61		
Methadone Maintenance Therapy‡ (yes vs. no)	0.81 (0.56 – 1.17)	0.26		
Experience Physical Violence† (yes vs. no)	1.54 (1.04 – 2.28)	0.03	1.38 (0.92 – 2.06)	0.12
Sex Trade Work† (yes vs. no)	1.46 (0.94 – 2.26)	0.09		

Note:

*HR = Hazard Ratio; a LGBT = lesbian, gay, bisexual, transgender/transsexual;

†refers to activities in the past 6 months;

‡refers to current experiences.