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Increased non-fatal overdose risk associated with involuntary drug treatment in a longitudinal study with people who inject drugs

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Abstract

Aim—To assess the effect of involuntary drug treatment (IDT) on non-fatal overdose among people who inject drugs (PWID).

Design—Longitudinal study.

Setting—Tijuana, Mexico.

Participants—Baseline sample of 671 PWID included 258 (38.4%) women and 413 (61.6%) men.

Measurements—Primary independent variables were reported recent (i.e., past 6 months) non-fatal overdose event (dependent variable) and IDT. Substance use the day of the non-fatal overdose was also examined.

Findings—From 2011 to 2017, 213 participants (31.7%) reported a recent non-fatal overdose and 103 (15.4%) reported recent IDT. Heroin in combination with methamphetamine and tranquilizers were the drugs most reported at the day of the event. IDT significantly increased the odds of reporting a non-fatal overdose event (Adjusted Odds Ratio [AOR]: 1.76; 95% Confidence Interval [CI]: 1.04–2.96). Odds of overdose also independently increased for each additional injection per day (AOR: 1.05; 95% CI: 1.02–1.08), recent tranquilizer use (AOR: 1.92; 95% CI:

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1.41–2.61), and using hit doctors (AOR: 1.68; 95% CI: 1.29–2.18), and decreased with age (AOR: 0.97 per year, 95% CI: 0.95–0.99).

Conclusions—Recent involuntary drug treatment in Mexico is a risk factor for non-fatal drug overdose.

Keywords

people who inject drugs; non-fatal overdose; generalized estimating equation; involuntary treatment; cohort study; Tijuana

INTRODUCTION

Several countries have implemented some form of involuntary drug treatment (IDT), ranging from treatment administered within the civil commitment framework in the United States (1) to legally-mandated and enforced drug treatment such as forced labor camps in South-East Asia (2, 3). Although widely implemented, there is little evidence of the effectiveness of compulsory treatment in sustaining drug use remission (4). Globally, IDT has also been associated with high rates of relapse at the individual level and with forced labor and corporal punishment at the structural level, conflicting with fundamental human rights principles (5, 6).

Another potential detrimental effect of IDT is that it may increase the risk of overdose. Periods of involuntary drug abstinence (e.g., jail or prison (7)) among persons with opioid drug addiction have been associated with an increased risk for fatal opioid overdose (8). This may be related to a loss of tolerance and untreated addiction (8). Few studies have examined the relationship between drug treatment (voluntary and involuntary) and non-fatal overdose. There is inconclusive evidence for the association between overdose and drug treatment. For instance, with one-year of follow-up after treatment, an English sample of people who use drugs (PWUD; injecting and non-injecting) from the National Treatment Outcome Research Study, showed no association between rates of overdose with voluntary drug treatment (9). In San Francisco, Ochoa (10) found that last year overdose among PWID was associated with lifetime history of drug treatment. Also in San Francisco, Seal and colleagues (11) found that recent non-fatal overdose among PWID was associated with having been imprisoned but was not associated with drug treatment. A national cohort study in Italy among PWUD showed that retention in any drug treatment was protective against fatal overdose but also showed an excess mortality risk in the month following treatment (12). A study among PWID in Vancouver, Canada found that being denied drug treatment was significantly associated with recent non-fatal overdose (13).

To our knowledge, only one study has addressed the association between IDT outside of prison settings and overdose (14). This study was conducted among a Thai cohort of PWID and found no association between history of forced treatment and overdose (14). However, temporal understanding of the relationship between recent IDT and recent experiences of overdose among PWID is largely absent from the literature.

In Mexico, IDT may take the form of: (1) mandated treatment after a three-strike rule upon being presented to a judge for drug possession for personal consumption (15), (2) requests to a judge by a family member (16), and (3) requests made directly at a drug center by a family member (which is against the law but common) (17). There may be legal consequences (e.g., prison, fine, community service) only for those who, in addition to drug possession for personal consumption, have committed a crime. There are no exclusive centers for IDT; most of the voluntary and involuntary treatment is provided by abstinence-based residential centers run by small non-government agencies, often led by former drug users, their families, and/or religious groups. Informal treatment centers exist due to lack of infrastructure and human resources needed to meet the demand for treatment in the city (18). These centers operate outside of government oversight and are run with minimal or no cost to families (19, 20). In Mexico, overdose surveillance is dismally poor. In 2015 there were only 134 deaths nationwide that were registered as unintentional overdoses (21). To overcome the under-registration of fatal overdoses, we focus on non-fatal overdose events. Non-fatal overdose has been proved to be a predictor of overdose deaths (22, 23).

The specific aim of the present study is to assess the impact of IDT experiences on non-fatal overdose among PWID within a framework of a longitudinal study in Tijuana, Baja California, Mexico. Due to its nexus as a drug-trafficking point with the U.S., and subsequent drug availability, Tijuana is one of the cities with the highest prevalence of drug use; it is also located within Baja California, the state reporting the highest proportion of criminal justice mandated treatment nationwide (24). We hypothesized that PWID that have recently experienced IDT will be significantly more likely to also report recent non-fatal overdose events, compared to those with no IDT experience.

METHODS

Sample

PWID were recruited to the *El Cuete* IV cohort study in 2011 through targeted sampling, which consisted of street-based outreach in 10 neighborhoods across Tijuana. A full description of the cohort study is available elsewhere (25). Briefly, inclusion criteria comprised being 18 years of age or older, having injected drugs in the past month, speaking English or Spanish, currently living in Tijuana with no plans to move over the next 18 months, and not currently participating in an HIV intervention study. Participants completed interviewer-administered surveys at baseline and every six months (12 visits at the time of the analysis) and received $20 USD per visit. Recruitment and data collection activities took place from 2011 to 2017. Out of the 735 participants that completed baseline, for this analysis, we included participants with at least two visits (n=671; median=6.50; interquartile range [IQR]= 3.50–9.50; standard deviation [SD]= 3.45) within the observation period (Supplemental Table 1). The study protocol was approved by the Human Research Protections Program of the University of California, San Diego and by the Ethics Board at El Colegio de la Frontera Norte.

Measures

Data were collected by trained interviewers who administered surveys using computer-assisted participant interview (CAPI) technology. Survey items included sociodemographic characteristics, drug using behaviors and contextual factors surrounding drug use and treatment. Most of the interviews were conducted at the study site; when participants were not able to attend, they were interviewed at a place of their choice close to where they live. Interviews lasted approximately 45 minutes. The outcome variable was defined as having recently (i.e., 6-months) suffered a non-fatal overdose. We used the following question: "*In the last 6 months, how many times have you overdosed? This includes any situation where you passed out and couldn't wake up or your lips turned blue*". For the analysis, a binary dummy variable was created for reporting at least one non-fatal overdose. The primary independent variable was recent IDT, a variable we created for this analysis based on participants' reports of having been enrolled in rehabilitation center in the past 6 months ("*In the last 6 months, have you enrolled in a rehabilitation center? By rehabilitation center, I mean a place where you went and stayed overnight for help with your drug or alcohol problems*"), and to have been enrolled involuntarily at the rehabilitation center ("*The last time you enrolled in a drug rehab center over the last 6 months, did you go voluntarily to this most recent rehab center?*") or to have been forced by law enforcement officials ("*I was forced by law enforcement officials*" as answer to "*What are all the reasons that you decided to enroll in this most recent rehab center?*").

Sociodemographic variables included were: age, sex, housing status (i.e., living in a house or apartment owned by participants, their parents, friends, or partner vs. other), and marital status (i.e., married vs. other). Substance use-related variables included were: drug or drug combination most frequently injected (heroin, methamphetamine and heroin with methamphetamine), which are the main patterns of substance use among participants (26); recent heroin ("*In the last 6 months have you used heroin?*"), methamphetamine, cocaine, and tranquilizer use; hit doctor *("In the last 6 months, have you sought the help of a "hit doctor" to inject drugs?")* daily injection frequency, and type of drug most frequently injected. Daily frequency of injection was a variable created based on injection drug use questions on the following drugs: heroin, cocaine, heroin and cocaine, methamphetamine, methamphetamine and cocaine, methamphetamine and heroin, and methamphetamine and ketamine. For example, participants were asked "*During the last 6 months, have you injected heroin by itself?*" If the answer was positive, then they were asked "*During the last 6 months, how often have you injected heroin by itself?*" with the following possible answers: "*One per month or less*", *"2 or 3 days per month"*, *"once per week, 2 to 3 days per week"*, *"4 to 6 days per week"*, *"once per day"*, and *"more than one time per day every day*". If the answer was "*more than one time per day every day*" then the value of "*How many times a day do you inject heroin by itself?*" was used. Heroin was then coded as 0 for less than daily, and the number of times that participants reported injecting per day was entered. This was repeated for each of the drugs and drug combinations and summed.

Analyses

Descriptive summaries were performed for data on recent non-fatal overdose; chi-square tests were performed for categorical variables, and Wilcoxon tests for continuous variables

at baseline. Frequencies of type of substances the day of the non-fatal overdose event were also calculated. We also performed a sensitivity analysis to determine differences between participants with and without IDT at baseline (Supplemental Table 2).

Univariate and multivariable marginal models using generalized estimating equations (GEE) were also performed. This analytic technique models the outcome while taking into account the correlation between visits within subjects and provides an estimation of standard errors. The outcome variable was reporting a recent non-fatal overdose event and our primary independent variable was IDT. The marginal models were fitted specifying an exchangeable working correlation structure (27). First, univariate GEE analyses were generated to determine whether the main independent variable (i.e., recent IDT) and potential confounders (as listed above) were associated with recent non-fatal overdose. Second, based on the literature, the univariate and the sensitivity analysis, we entered variables into a multivariable logistic regression model in a manual forward stepwise fashion. Based on results from the variables that attained significance at $p<0.05$ in univariate GEE models, we manually entered each variable one at a time into the model, starting with the variable with the lowest p-value and ending with the variable that was least significant. The proportion of non-used observations was 9.58%. Therefore, we only included observations with valid information for all the variables used in the analysis. All analyses were performed in SAS 9.3 software (28).

RESULTS

The baseline sample of 671 PWID included 258 (38.4%) women and 413 (61.6%) men. The median age was 37 (Interquartile Range [IQR]:31–44) and the median number of injections per day was 4 (IQR: 3–6). There were 64 (9.5%) participants with at least one recent non-fatal overdose at baseline. The bivariate associations between recent overdose and sociodemographic characteristics are shown in Table 1. Those who reported a recent overdose were significantly younger than those with no recent overdose (median: 33.5 vs. 37; $p = <0.001$). There were no significant differences by sex, marital and housing status. Regarding drug-related variables, there were no significant differences in recent non-fatal overdose reporting by recent IDT, recently requiring help to inject from a hit doctor, and number of injections per day. Among those with recent tranquilizer and cocaine use there was a higher proportion of overdose than among those with no tranquilizer and cocaine use (14.6% vs. 8.4%; $p = 0.030$; 17.3% vs. 8.6%; $p = 0.009$ respectively). There were no significant differences in recent methamphetamine and heroin use.

From March 2011 to July 2017, a total of 213 (31.7%) participants experienced at least one overdose, of whom 95 (44.6%) suffered one event, 38 (17.8%) two events, 57 (26.8%) three to five events, 10 (4.7%) six events, and 13 (6.1%) seven to 17 events. The median number of overdoses among those who reported experiencing it at least once was 2 (IQR: 1–3). In addition, during the same period of observation, 103 participants (15.4%) reported recent IDT, of whom 80 (77.7%) were forced to enter once, 18 (17.5%) were forced twice, 4 (3.9%) were forced three times, and 1 (1.0%) was forced four times. All participants were taken to mutual aid/12-step programs and religious-based groups, none of them run by the government. The median number of recent experiences with IDT among those who

experienced it at least once was 1 (IQR: 1.0–1.0), and the median time spent at the drug center was 3 months (IQR: 1.61–5.00).

Table 2 shows substances used on the day of the non-fatal overdose event. Heroin was the most frequently injected drug either by itself (43.6%) or combined with other substances (46.9%). The most common combination was with methamphetamine and tranquilizers. Other drugs reported were alcohol, cocaine and few cases of crocodile/krokodil (i.e., mixture of several substances that is used as a cheap substitute for heroin), barbiturates, methadone, prescription opioids and PCP.

Table 3 shows the GEE univariate and multivariable analyses. Non-fatal overdose was significantly associated with younger age, having experienced IDT and greater daily injection frequency. Having been taken involuntarily to drug treatment increased the odds of non-fatal overdose (OR: 1.97; 95% CI: 1.15–3.36). The odds of non-fatal overdose also increased with recent cocaine (OR: 2.26; 95% CI: 1.54–3.31), methamphetamine (OR: 1.38; 95% CI: 1.02–1.87), tranquilizer use (OR: 2.11; 95% CI: 1.60–2.78), and getting help injecting from a hit doctor (OR: 1.82; 95% CI: 1.41–2.35). There was a decrease in the odds of non-fatal overdose for each additional year of age (OR: 0.96; 95% CI: 0.94– 0.98). For each additional injection per day the odds of non-fatal overdose were increased (95% CI: 1.04– 1.09). There were no significant associations between non-fatal overdose and sex and recent heroin and methamphetamine combo and heroin use. Controlling for time, age, daily injection frequency, and recent drug use there was a statistically significant association between IDT and overdose (Adjusted Odds Ratio [AOR]: 1.76; 95% CI: 1.04–2.96). Additionally, the odds of non-fatal overdose increased for every additional injection per day (AOR: 1.05; 95% CI: 1.02–1.08), tranquilizer use (AOR: 1.92; 95% CI: 1.41–2.61), and hit doctor (AOR: 1.68; 95% CI: 1.29–2.18); and that the decrease in the odds of non-fatal overdose for each additional year of age (AOR: 0.97 per year; 95% CI: 0.95– 0.99) were also maintained. Recent cocaine and methamphetamine use were no longer significant.

DISCUSSION

Study findings confirmed our hypothesis that PWID who have recently experienced IDT will be significantly more likely to also report recent non-fatal overdose events. Our study also highlights the common occurrence of non-fatal overdose among our sample of PWID in Tijuana. Over a period of six years, we found that almost one third suffered at least one non-fatal overdose, more than half of whom had more than one event. Additionally, more than one fifth experienced IDT.

Although we cannot conclusively determine a causal relationship between recent IDT and recent non-fatal overdose, qualitative analysis we conducted simultaneous to this paper (29) reveals that most of the PWID in our sample are not prepared to stop using drugs when they are taken involuntarily to drug treatment. This, in addition to the loss of tolerance related to abstinence periods, likely puts them at a higher risk of overdose. Furthermore, drug treatment centers in Mexico do not typically adhere to evidence-based modalities and are focused on abstinence-only models (30). In Tijuana, there are community organizations that sporadically distribute naloxone and train PWID to reverse overdoses. However, there is a

lack of public programs that include overdose prevention protocols among public hospitals and first responders. Moreover, drug treatment centers do not provide any type of discharge plans through which PWID could be referred to health or social services.

The proportion of non-fatal overdose in our sample is similar to what was found in a 7-year period among PWID in Vancouver (32.7%) (13). In contrast to that study, we found that more than half of the events occurred with a single drug, however, tranquilizer use was significantly associated with non-fatal overdose and was reported in 13% of the events. As previous research has shown (31–33), we also found that younger users were more likely to suffer a non-overdose compared to older population. We also found that PWID that inject more and those who asked a hit doctor for help injecting were more at risk of a non-fatal overdose. Higher frequency of injection may be related to the type of drug injected, since stimulants have a shorter half-life (34). However, stimulant use was not significant after adjusting for covariates. As such, frequency of injection may be related to drug dependence. Having to ask a hit doctor for help indicates less agency in the type and amount of drug injected and that PWID may no longer be able to inject by themselves because of a long drug injection trajectory (35). These findings suggest that overdose prevention efforts among this population should focus on young PWID that have recently experienced IDT and address frequent injecting and tranquilizer use as a risk factor.

The spiraling opioid overdose crisis in North America is fueling increased policy and programmatic emphasis on coercive treatment modalities (36). Although one study found that being denied access to drug treatment is significantly associated with an elevated risk of non-fatal overdose (13), our study extends this research by showing that experiencing IDT increases the odds of non-fatal overdose. Forced treatment is considered a type of low security imprisonment or deprivation of basic human rights (37). Accordingly, it is more adequate to compare our findings to those of imprisonment (13, 31). PWUD who are released from prison usually return to environments that trigger relapse to drug use and put them at risk of non-fatal and fatal overdose (7, 38–40).

The limited resources available for drug treatment need to be allocated to voluntary, evidence-based drug treatment. In Mexico, the median years of delayed treatment since the onset of a substance use disorder is of 10 years (41). That is, the general population would greatly benefit from the institutional strengthening and expansion of treatment services for those that are aware of their treatment need and willing to engage in treatment. Public and private efforts would be needed for a successful transition from involuntary to voluntary service provision in terms of changing treatment centers' protocols of admission, referrals and case management programs.

This study highlights several future research directions. First, future studies should analyze how IDT affects subsequent treatment seeking and whether in fact involuntary treatment is causally related to overdose risk. This may be addressed through mixed-methods research conducted specifically with people released from treatment centers. Second, we showed an association between IDT and non-fatal overdose, the next step is therefore to address fatal overdose after IDT. Indeed, there is sufficient evidence that non-fatal events are strong predictors of other non-fatal (42, 43) and fatal events, including fatal overdose (22, 23).

This study has several limitations. First, there is a possibility of residual confounding and a spurious association between the outcome and main independent variables. However, we controlled for the variables that, based on the sensitivity analysis, may be associated with IDT (i.e., age and substance use patterns) to limit it. Second, the definition provided to participants about overdose is more descriptive of opioid-related overdose and may have missed cases of stimulant-related overdose (26). Third, this analysis may have not taken full advantage of the longitudinal data by using lagged variables as predictors. Nevertheless, research suggests that substance use behavior and loss of tolerance that is most proximal to overdose is likely the most predictive (8, 12). Fourth, selection bias is possible due to attrition, but in the sensitivity analysis we did not find significant differences in the variables included in the analysis among those with more than one visit and those lost after baseline. Fifth, since we used self-reported measures, there may be recall bias. However, non-fatal overdoses and IDT are traumatic events that are unlikely forgotten. Finally, we grouped all the IDT experiences and it may be that differences exist depending on the nature of IDT (e.g., law enforcement, family or partner). However, people that are taken involuntarily to treatment by their relatives go to the same centers in which law enforcement officers involuntarily detain users (30). It is also possible that some PWID who reported having been in drug treatment voluntarily may have been coerced into agreeing to go into treatment, and therefore we would be underestimating the proportion of PWID forced into treatment.

Overall, IDT, as other type of forced abstinence, reduces drug tolerance putting PWID at risk of non-fatal overdose. Policy implications include government and treatment centers' respect for PWID and their right to choose the circumstances of treatment. Professionalization of treatment providers and oversight of addiction treatment agencies will reduce the potential consequences of being discharged into the same psychosocial context of previous drug use, and the need to include overdose prevention at drug treatment centers and upon release (38, 39, 44). This study highlights the life-threatening risks PWID experience in relation to IDT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline data on non-fatal overdose in the past 6-months among people who inject drugs. El Cuete IV. Tijuana, Mexico, 2011–2017 (n=671).

	No non-fatal overdose n= 607		Non-fatal overdose n= 64		p- value
	n/median	%/ IQR	n/median	%/ IQR	
Age median(IQR)	37	(31–44)	33.5	(27–40)	**<0.001**
Sex n(%)					
Women	226	(87.60)	32	(12.40)	0.05
Men	381	(92.25)	32	(7.75)	
Marital status n(%)					
Unmarried	330	(90.66)	34	(9.34)	0.850
Married	277	(90.23)	30	(9.77)	
Housing status n(%)					
Unstable	27	(81.82)	6	(18.18)	0.083
Stable	580	(90.91)	58	(9.09)	
Involuntary drug treatment n(%)					
No	597	(90.73)	61	(9.27)	0.066
Yes	9	(75.00)	3	(25.00)	
Hit doctor n(%) *					
No	264	(91.03)	26	(8.97)	0.281
Yes	121	(87.68)	17	(12.32)	
Drug most frequently injected n(%) *					
Heroin	382	(90.31)	41	(9.69)	0.664
Heroin and methamphetamine	198	(90.00)	22	(10.00)	
Methamphetamine	13	(100)	0	(0)	
Other	14	(93.33)	1	(6.67)	
Daily injection frequency median(IQR) *	4	(3–6)	5	(3–8)	0.339
Tranquilizer use n(%) *					
No	493	(91.64)	45	(8.36)	**0.030**
Yes	111	(85.38)	19	(14.62)	
Cocaine use n(%) *					

	No non-fatal overdose n= 607		Non-fatal overdose n= 64		p- value
	n/median	%/ IQR	n/median	%/ IQR	
No	275	(91.36)	26	(8.64)	**0.009**
Yes	105	(82.68)	22	(17.32)	
Methamphetamine use n(%)*					
No	121	(92.37)	10	(7.63)	0.348
Yes	325	(89.53)	38	(10.47)	
Heroin use n(%)*					
No	26	(81.25)	6	(18.75)	0.071
Yes	578	(90.88)	58	(9.12)	

Wilcoxon for continuous variables; Chi square for categorical variables. Change in sample size due to different number of observations.

*Past 6 months.

IQR= Interquartile range.

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Table 2

Substances used at the day of the non-fatal overdose events among people who inject drugs. El Cuete IV, Tijuana, Mexico, 2011–2017 (n=671).

Substances	N=326	%
One substance		
Heroin *	157	48.16
Methamphetamine	5	1.53
Crocodile	2	0.61
Alcohol	2	0.61
Two substances		
Heroin and methamphetamine *	88	26.99
Heroin and tranquilizers	20	6.13
Heroin and cocaine	9	2.76
Heroin and alcohol	6	1.84
Heroin and methadone	1	0.31
Methamphetamine and crocodile	1	0.31
Three or more substances		
Heroin, methamphetamine and tranquilizers **	16	4.91
Heroin, methamphetamine and alcohol	7	2.15
Heroin, methamphetamine, tranquilizers and alcohol	4	1.23
Heroin, methamphetamine and cocaine	3	0.92
Heroin, cocaine and barbiturates	1	0.31
Heroin, cocaine and tranquilizers	1	0.31
Heroin, cocaine and alcohol	1	0.31
Heroin, tranquilizers and methadone	1	0.31
Heroin, methamphetamine, prescription opioids and PCP	1	0.31

* One case with marijuana;

** Two cases with marijuana.

Crocodile or krokodil is a mixture of several substances that is used as a cheap substitute for heroin.

Table 3

Univariate and multivariable generalized estimating equation analyses for factors related to reporting non-fatal overdose in the past 6 months among people who inject drugs. El Cuete IV, Tijuana, Mexico, 2011–2017 (n=671).

	Univariate GEE				Multivariable GEE			
	OR	**95% CI**		**p-value**	**AOR**	**95% CI**		**p-value**
Age	0.96	0.94	0.98	**<0.0001**	0.97	0.95	0.99	**<0.001**
Women	1.15	0.86	1.55	0.353				
Involuntary drug treatment *	1.97	1.15	3.36	**0.013**	1.76	1.04	2.96	**0.034**
Hit doctor *	1.82	1.41	2.35	**<0.0001**	1.68	1.29	2.18	**<0.001**
Heroin use *	0.49	0.24	1.00	0.051				
Cocaine use *	2.26	1.54	3.31	**<0.001**	1.51	0.97	2.33	0.068
Methamphetamine use *	1.38	1.02	1.87	**0.035**	1.05	0.75	1.46	0.789
Heroin and methamphetamine combo use *	1.05	0.76	1.45	0.784				
Tranquilizer use *	2.11	1.60	2.78	**<0.0001**	1.92	1.41	2.61	**<0.0001**
Daily injection frequency *	1.06	1.04	1.09	**<0.0001**	1.05	1.02	1.08	**<0.001**

* Past 6 months.

GEE: Generalized Estimating Equation; OR: Odds Ratio; AOR: Adjusted Odds Ratio; CI: Confidence Interval. Significance at $p < 0.05$ bolded.