The Relationship Between Depressive Symptoms and Nonfatal Overdose Among a Sample of Drug Users in Baltimore, Maryland

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ABSTRACT   *Nonfatal drug overdoses are common among heroin users. While several factors that increase risk of overdose have been identified, there is little research on the role of mental health status. The purpose of this study was to examine the association between depressive symptoms and history of overdose. A sample of 729 opiate and cocaine users completed a cross-sectional survey. Of the sample, 65% reported never having overdosed, 31% had overdosed longer than 12 months before the interview, and 4% had overdosed within the past 12 months. Results indicate that a high score on the Center for Epidemiological Studies Depression Scale (CES-D), a measure of depressive symptoms, was associated with having overdosed within the past 12 months (relative risk ratio [RRR] = 3.06; 95% confidence interval [CI], 1.33 to 7.05) after adjusting for age, gender, injection frequency, and physical health impairment. These results suggest that drug users with depressive symptoms should be targeted for overdose prevention programs.*

KEYWORDS   *Cocaine, Depression, Heroin, Injection drug users, Overdose.*

INTRODUCTION

Drug overdose is a leading cause of death among opiate users,[1] and the experience of nonfatal overdose is common.[2] Epidemiologic studies have identified several factors that increase the risk of overdose, including (1) concomitant use of other drugs, such as benzodiazepines and alcohol; (2) low tolerance level; and (3) impaired physical health status of the user.[3] Warner-Smith et al.[4] documented that drug users who have experienced a nonfatal overdose suffer from peripheral neuropathy, lung infections, cardiac complications, and cognitive impairment.

The role of mental health status as a risk factor for overdose has not been examined in detail. Rates of comorbid depression are consistently higher in drug-using populations.[5] Although depressive symptoms are strong predictors of suicide and attempted suicide,[6,7] most drug overdoses do not appear to be suicide attempts.[8–10] It has been hypothesized that some individuals use illicit drugs to self-medicate for dysphoria and other mental conditions.[11] Depressed drug users are more likely to use more of their drug to alleviate their symptoms and improve their mood.[12] However, in one retrospective study of heroin overdoses, Zador and colleagues[13] found that users reported use of multiple drugs to enhance pleasurable

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drug effects rather than to treat physical withdrawal symptoms or depression. Such polydrug use increases the likelihood of overdose.

The purpose of this study was to examine the association between depressive symptoms and nonfatal overdose experience among a sample of opiate and cocaine users in Baltimore, Maryland. We hypothesized that there would be a positive association between the presence of depressive symptoms and recency of overdose.

METHODS

Data for this study came from a cross-sectional survey administered from March 2001 through October 2002 as part of a follow-up of the Self-Help in Eliminating Life-Threatening Diseases (SHIELD) study, an experimental human immunodeficiency virus (HIV) prevention intervention targeting current and former drug users. Details of this study are described elsewhere.[14] In summary, participants for the study were recruited using street-based techniques and through participant word of mouth. Inclusion criteria were age 18 years old or older, having daily contact with people who use drugs, willingness to bring in three network members, and willingness to conduct outreach activities. A total of 1,637 participants were eligible and completed a baseline interview.

Participants were included in the current study if they reported a history of opiate and cocaine use. All participants provided written informed consent that was approved by the Johns Hopkins Bloomberg School of Public Health. Trained interviewers administered the survey face to face. Participants were paid $25 for their time.

Measures

Outcome: Overdose Recency An ordinal outcome variable was created to describe the recency of the participant's most recent overdose. This variable was based on the date of the most recently reported drug overdose. Categories for the outcome variable were coded 0 for having never overdosed, 1 for having last overdosed more than 12 months from the time of the interview, and 2 for having overdosed within 12 months of the interview.

Depressive Symptoms: Center for Epidemiological Studies Depression Scale Depressive symptoms were assessed using the Center for Epidemiological Studies Depression Scale (CES-D),[15] a 20-item, 4-point scale developed for use in the general population. The scale has high validity and reliability.[16] The CES-D has been shown to have a high sensitivity for *DSM-II* (*Diagnostic and Statistical Manual of Mental Disorders, 2nd Edition*) major depression and an adequate specificity as a screening instrument for depression.[17] This scale has been used with drug-using samples[18] and had high internal reliability (Cronbach α = .89). A summed score ranging from 0 to 60 was created for each participant. A cutoff score above 16 has been validated as an indication of probable clinical depression.[19]

Overdose Characteristics Participants were asked specific questions about their most recent overdose, such as the drug they used, whether they had been using alcohol at the same time, where the overdose occurred, and whether they were alone. To assess intentionality of overdose, participants were asked, "How intentional

was the last overdose: definitely intentional (wanted to die), not really sure, and not intentional at all." Participants were also asked to report whether they had used more, less, or the same amount during their last overdose.

Drug Use Characteristics   Participants reported the frequency that they drank alcohol, injected or snorted heroin, and injected cocaine within the past 6 months. Ordinal variables were created for each drug to describe frequency of use in the past 6 months (no use, less than daily use, and daily use). Given the high correlation between the injection drug variables, an index was created to describe the frequency of injection within the past 6 months: 0 indicated no injection of heroin, cocaine, or speedball in the past 6 months; 1 indicated less than daily use of any injection drug; and 2 indicated daily use of any injection drug.

Other Sample Characteristics   Participants were asked if they had been homeless, unemployed, incarcerated, and on methadone or at a detoxification center at any time in the past 6 months (yes vs. no). Based on the SF-36, participants rated their current health status using a 5-point response category (excellent, very good, good, fair, and poor).[20] They also rated how much their health limits function in domains of dressing, bending, walking a mile, and vigorous activities. This question used a 3-point response category (a lot of limitation, some limitation, and no limitation). An ordinal variable was created, and a score of 0 indicated no limitation, scores ranging from 1 to 7 indicated some limitation, and scores 8 or above indicated a lot of limitation.

Analysis

Participants were categorized and compared by recency of overdose (never, more than 12 months prior to the interview, within 12 months of the interview) using chi-square, *t*-test, and analysis of variance (ANOVA) statistics. The main independent variable of interest, depressive symptoms, was examined using the continuous score on the CES-D and a dichotomous variable cut at the median 12 and at the commonly accepted level of 16. Using Akaike's information criterion (AIC) for assessing model fit,[21] the CES-D score cut at 16 was chosen for the final analyses.

Multinomial regression modeling was used to assess independent associations between independent variables and overdose recency. Multinomial regression models compare each level of the outcome variable to a base category (e.g., never overdose) using relative risk ratios (RRRs). Relative risk ratios approximate the odds ratios and can be interpreted in a similar manner. Therefore, a RRR above 1.00 indicates an increase in the odds of the outcome for each unit increase of the independent variable, holding other variables in the model constant.

Final multivariate models were constructed to examine the association between a high score on the CES-D and overdose recency while controlling for other factors, such as frequency of injection, age, alcohol use, and physical health status, which have been identified as overdose risk factors. Frequency of alcohol use was not significant and did not change the coefficients of the other covariates in the model when removed. Therefore, this variable was not included in the final model. Given the low number of cases of those who reported purposely intending to overdose, this variable was excluded from the multivariate model. All analyses were conducted using Stata (version 6.0).[22]

RESULTS

General Sample Characteristics and Center for Epidemiological Studies Depression Scale

A total of 769 participants completed the survey. Of these, 39 did not report a history of heroin, cocaine, or crack use and were excluded from the analyses. An additional case (n = 1) with missing data on overdose history was excluded. Approximately one third of the remaining sample reported having ever overdosed (Table 1), with 4% having experienced their most recent overdose within the past 12 months. Comparisons between the three groups revealed statistically significant differences between groups. The mean age of participants who had never overdosed was younger than those who had overdosed more than 12 months ago (post hoc Bonferonni correction $P < .001$), but there was no age difference between those who had overdosed within the past 12 months and the other two groups. A greater proportion of participants who overdosed more than 12 months ago were male ($P < .001$).

One quarter of those who had overdosed within the past 12 months reported having been in a detoxification center in the past 6 months compared to 10% of those who had never overdosed and 13% of those who had overdosed more than 12 months ago ($P = .02$). However, 33% of participants who had overdosed more than 12 months ago received methadone compared to 23% of those who never overdosed and 13% of those who had overdosed recently ($P < .001$).

One third (34%) of the participants who had never overdosed rated their health as fair to poor compared to those who had overdosed more than 12 months ago (22%) and those who had overdosed within the past 12 months (13%, $P < .01$). However, a greater proportion of participants who overdosed within the past 12 months (88%) reported some to a lot of health impairment ($P < .01$) compared to the other two groups (62% and 74%, respectively).

There was a marked difference in mean CES-D score. Those who had experienced an overdose within the past 12 months scored significantly higher than those who had never overdosed and those who had overdosed more than 12 months ago (scores of 22 versus 14 and versus 14, respectively).

Overdose Characteristics

The number of total overdoses experienced differed significantly by overdose recency (Table 2). Those participants who had overdosed within the past 12 months reported an average of five lifetime overdoses compared to the two ($P < .001$) reported by those who had overdosed more than 12 months ago. Circumstances of the most recent overdose appeared similar across groups. Intention to overdose was uncommon, with 91% reporting not intending to die. Heroin was the most commonly reported drug used. Participants reported using heroin alone 58% of the time. Use of heroin in combination with other drugs, such as cocaine, other prescription drugs, and alcohol, was reported as polydrug use. During their most recent overdose, the majority of participants reported using more drugs than usual (57%) and drinking alcohol (49%), and they were not alone (79%).

Drug Use Characteristics

Participants who overdosed within the past 12 months reported greater use of heroin, cocaine, and alcohol compared to the other two groups (Table 3). They were more likely to be daily heroin ($P < .001$), speedball ($P < .001$), and cocaine injectors

TABLE 1. Characteristics of drug users (N = 729) by overdose recency, SHIELD study, Baltimore, Maryland

Variables	Never overdose [N = 510 (70)], N (%)	Overdose more than 12 months ago [N = 187 (26)] N (%)	Overdose within past 12 months [N = 32 (4)] N (%)	Chi-square P value
Age in years, mean (SD)	42 (7.25)	45 (6.72)	43 (5.67)	<.001*
Gender				
Male	279 (55)	133 (71)	19 (59)	
Female	231 (45)	54 (29)	13 (41)	<.001
Homeless				
No	462 (91)	166 (89)	26 (81)	
Yes	48 (9)	21 (11)	6 (19)	.21
Incarcerated				
No	446 (87)	165 (88)	25 (78)	
Yes	64 (13)	22 (12)	7 (22)	.28
Employed				
No	97 (19)	36 (19)	3 (9)	
Yes	413 (81)	151 (81)	29 (91)	.39
Detox†				
No	457 (90)	162 (87)	24 (75)	
Yes	53 (10)	25 (13)	8 (25)	<.001
Methadone†				
No	392 (77)	126 (67)	28 (88)	
Yes	118 (23)	61 (33)	4 (13)	.02
Heath status				
Excellent	24 (5)	14 (7)	5 (16)	
Very good	158 (31)	65 (35)	15 (48)	
Good	153 (30)	68 (36)	7 (23)	
Fair	129 (25)	24 (13)	3 (10)	
Poor	46 (9)	16 (9)	1 (3)	.001
Health impairment				
Not at all	193 (38)	47 (25)	4 (13)	
Some	208 (41)	85 (45)	16 (50)	
A lot	107 (21)	55 (29)	12 (38)	.001
CES-D score, mean (SD)	14 (10.8)	14 (11.5)	22 (11.0)	<.001*

CES-D, Center for Epidemiological Studies Depression Scale.
*Based on one-way analysis of variance.
†Missing 40 cases.

($P < .001$). Among those who had overdosed within the past 12 months, no one reported daily snorting of heroin.

Multivariate Models

Comparing Correlates of Overdose Within the Past 12 Months to Never Overdosing   Individuals who scored above 16 on the CES-D were more than three times more likely to report having an overdose within the past 12 months compared to those who scored at or below 16 (RRR = 3.06; 95% CI, 1.33 to 7.05) after adjusting

TABLE 2. Overdose characteristics of drug users by overdose recency, SHIELD study, Baltimore, Maryland

Variables	Overdose more than 12 months ago (N = 187), N (%)	Overdose within past 12 months (N = 32), N (%)	Chi-square P value
Median number of overdoses (range)	2 (1–10)	3 (1–20)	
Mean number of overdoses (SD)	2 (1.73)	5 (4.53)	<.001*
Drug used†			
Heroin only	111 (63)	15 (52)	
Cocaine only	9 (6)	1 (3)	
Polydrug	55 (31)	13 (45)	.04
Drinking alcohol at the time‡			
No	92 (49)	15 (47)	
Yes	91 (49)	17 (53)	.66
Amount of drug used§			
More	105 (56)	19 (59)	
Less	6 (3)	0 (0)	
Same	74 (40)	13 (41)	.70
Was the overdose intentional?			
No	173 (93)	27 (84)	
Not sure/Yes	14 (7)	5 (16)	.13
Were you alone?			
No	148 (79)	24 (75)	
Yes	38 (20)	8 (25)	.77

*Based on a two-sample t test.
†Missing 14 cases.
‡Missing 4 cases.
§Missing 2 cases.

for age, gender, injection frequency, and physical health status (Table 4). In the multivariate analyses, we examined additional covariates, including alcohol and sedative use, and found that these variables were neither statistically significant nor did they alter the magnitudes of the associations. We examined this model using CES-D as a continuous score and found that these covariates did not change appreciably in magnitude or significance. The RRR of the CES-D as a continuous independent variable was 1.04 (95%CI, 1.01 to 1.08) For every standard deviation increase in CES-D score, the odds of a recent overdose increased by 44%. Consistent with our expectations, injection frequency was linearly associated with recent overdose. Surprisingly, age and gender were not significant in this multivariate model.

Comparing Correlates of Overdose More Than 12 Months Ago to Never Overdosing   In contrast to the multivariate model, current levels of depressive symptoms were not associated with having overdosed more than 12 months prior to the interview. Older age, male sex, injection in the past 6 months, and current health impairment were statistically significant in predicting having overdosed more than 12 months prior to the interview. These findings are similar to those of previous studies examining risk factors for overdose.[23–25]

TABLE 3.   Drug use characteristics by overdose recency, SHIELD study, Baltimore, Maryland

Variables	Never overdosed (N = 510), N (%)	Overdose more than 12 months ago (N = 187), N (%)	Overdose within past 12 months (N = 32), N (%)	Chi-square P value
Speedball*				
None	417 (82)	112 (60)	10 (31)	
<Daily	70 (14)	62 (33)	16 (50)	
≥Daily	22 (4)	13 (7)	6 (19)	<.001
Inject heroin*				
None	412 (81)	117 (63)	10 (31)	
<Daily	60 (12)	45 (24)	14 (44)	
≥Daily	37 (7)	25 (13)	8 (25)	<.001
Inject cocaine				
None	431 (85)	126 (67)	13 (41)	
<Daily	65 (13)	54 (29)	16 (50)	
≥Daily	13 (3)	7 (4)	3 (9)	<.001
Snort heroin†				
None	326 (64)	145 (78)	21 (66)	
<Daily	113 (22)	33 (18)	11 (34)	
≥Daily	69 (14)	9 (5)	0 (0)	.001
Smoke crack†				
None	325 (64)	138 (74)	16 (50)	
<Daily	159 (31)	42 (22)	15 (47)	
≥Daily	24 (5)	4 (4)	1 (3)	.07
Alcohol use				
None	166 (33)	62 (33)	7 (22)	
<Daily	306 (60)	97 (52)	17 (53)	
≥Daily	38 (7)	28 (15)	8 (25)	.001

*Missing 1 case.
†Missing 2 cases.

DISCUSSION

The main finding of this study is that among drug users, the presence of more depressive symptoms was strongly associated with recent overdose (within the past 12 months). Those who overdosed within the prior year were more than three times more likely to score above the 16-point cutoff on the CES-D compared to those who had never overdosed even after controlling for frequency of injecting, health impairment, age, and gender. Previous studies have focused on identifying physical health and physiological causes and risk factors for overdose, but have seldom examined the role of mental health factors. With overdose contributing to premature mortality and excessive morbidity among drug users, it is critical to expand investigation to examine potential psychosocial risk factors.

One explanation of the results presented may be that people who suffer from depressive symptoms may increase the amount of drugs that they use to improve mood or enhance intoxication.[26] Their drug tolerance may not be concomitantly elevated, which may lead to a drug overdose. Overdose education is needed for

TABLE 4. Multinomial regression predicting recency of overdose among drug users (N = 729) in Baltimore, Maryland

Variables	Overdosed more than 12 months ago compared to never overdosed, RRR (95% CI)	Overdosed within the past 12 months compared to never overdosed, RRR (95% CI)
CES-D score		
≤16	1.00	1.00
>16	0.89 (0.60, 1.32)	3.06 (1.33, 7.05)
Age, years (continuous)	1.04 (1.01, 1.07)	1.00 (0.95, 1.06)
Gender		
Male	1.00	1.00
Female	0.53 (0.36, 0.78)	0.69 (0.31, 1.53)
Injection frequency		
None	1.00	1.00
<Daily	2.42 (1.57, 3.71)	7.85 (3.12, 19.8)
≥Daily	2.60 (1.56, 4.31)	9.52 (3.51, 25.8)
Health impairment		
None	1.00	1.00
Some	1.69 (1.10, 2.60)	2.77 (0.86, 8.95)
A lot	2.06 (1.24, 3.44)	3.24 (0.92, 11.4)

CES-D, Center for Epidemiological Studies Depression Scale; CI, confidence interval; RRR, relative risk ratio.

drug users who are inclined to mix drugs and use more drugs when feeling depressed.

An alternative explanation for these findings may be that people who experience a stressful event such as a nonfatal overdose may experience elevated symptoms of depression. Providing referrals to counseling or mental health services to people who have overdosed could address this and present opportunities for referrals to drug treatment. Finally, it has been suggested that a high correlation between depression and suicide may help explain these results. However, over 90% of the participants who overdosed within the past 12 months reported not intending to die when they overdosed.

The comorbidity of depression and mood disorders among substance abusers has been well documented in national studies[27–29] and in samples of opiate abusers[30,31] and injection drug users.[32] Coordination among medical, substance abuse treatment, and mental health services in assessing depressive symptoms and making appropriate referrals may reduce rates of overdose. In one retrospective study of fatal overdose, the majority of cases had sought and received services from a general medical practitioner within the past year.[33] Furthermore, the individuals in approximately one quarter of the cases had seen a psychiatrist or substance abuse treatment service prior to death. These findings suggest the importance of screening for depression by these types of providers.

Certain limitations to this study should be acknowledged. All data were self-reported and subject to sampling biases. The cross-sectional nature of the survey limits our ability to establish chronological events. The time frame for assessing

depressive symptoms (within the past week) was inconsistent with the time for assessing recency of overdose (within the past 12 months). We cannot determine whether depression causes overdose or the reverse. It is possible that drug users who have experienced an overdose recently may have had greater depressive symptoms because of feelings of shame and hopelessness, lack of control of their drug use, or an increased physical impairment due to the overdose. However, as individuals who had overdosed more than a year prior to the survey did not report more depressive symptoms than individuals who had never overdosed, it is less likely that drug overdoses led to sustained depression.

These findings suggest that drug users who are experiencing high levels of depressive symptoms may be at increased risk for drug overdose. Screening and treating drug users for depression may reduce not only depressive symptoms, but also risk of drug overdose. Moreover, prevention efforts should address the importance of poor mental health as a possible risk factor for overdose.

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