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Intervention in an Opioid Overdose Event Increases Interest in Treatment Among Individuals with Opioid Use Disorder

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Abstract

Background: This study sought to explore whether intervening in suspected cases of opioid overdose alters interest in treatment for opioid use disorder (OUD). Data were collected as a part of a trial comparing the effects of different overdose education and naloxone distribution (OEND) training curricula on overdose outcomes.

Methods: Following OEND training, participants completed four in-person follow-up visits at 1-, 3-, 6- and 12-months. Participants were also regularly contacted to inquire about overdose events they responded to, witnessed, or experienced themselves. Other assessments included the Addiction Severity Index that queries participants' perceived importance of drug treatment on a scale of: 0 (Not at All) to 4 (Extremely). For the current secondary data analysis, treatment importance was assessed at the time points most immediately preceding and following participant intervention in an overdose event using naloxone.

Results: The sample reported a mean duration of opioid use of 14.9 (± 11.5) years, with 67% having witnessed an overdose event prior to the study. Of the 321 enrolled, 92 participants used naloxone in response to 166 suspected cases of an opioid overdose. For the entire sample, mean treatment importance did not significantly change throughout the study. Among participants who utilized naloxone, treatment importance increased following the event (Before: 3.03, After: 3.39, p=0.02). Due to the amount of time between the overdose event and assessment of post-event treatment importance (40.5 days, ±40.2), the current study most likely underestimates this effect.

Conclusions: The current study suggests that responding to an overdose event increases interest in OUD treatment. Currently only considered an acute intervention to reduce overdose morbidity

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and mortality, OEND may have the potential to increase enrollment in medications to treat OUD. However, a prospective investigation needs to determine if the impact of an overdose event could be utilized to increase treatment engagement.

Keywords

Overdose; Naloxone; Opioid Use Disorder; Heroin

Introduction

The United States has borne the brunt of the morbidity and mortality related to the recent opioid overdose epidemic. Though only 4.7% of the global population, the U.S., accounts for approximately one-third of opioid-related overdose deaths worldwide.[1,2,3] The dire need for overdose harm reduction led to the wide-spread adoption of community-level overdose education and naloxone distribution (OEND). OEND programs seek to increase overdose knowledge and access to the opioid antagonist, naloxone, among people who use opioids, family and friends of people with OUD, and community members who may come into contact with people at risk for opioid overdose. Take-home naloxone has become a widely used overdose harm reduction practice in the U.S.[4,5] Though these programs are available worldwide, they have particular importance in the U.S., which lacks other overdose harm-reduction services for active drug users, such as safe consumption facilities .[6,7,8]

Several studies suggest that expanded access to naloxone has a measurable effect on overall opioid overdose death rates.[9,10,11] While emergency interventions like naloxone are critical, long-term effective treatment solutions are also key to managing the opioid epidemic. Increasing treatment with medications for opioid use disorder (MOUD) is a major objective of the U.S. Department of Health and Human Services (DHHS) comprehensive strategy to combat the opioid crisis.[12] Methadone, buprenorphine, and naltrexone have been shown to significantly increase quality of life and decrease overdose mortality among individuals with OUD.[13] Yet, ambivalence is a significant barrier to treatment initiation among individuals with OUD.[14,15,16,17]

The period following an overdose reversal may be a unique opportunity to address and potentially resolve treatment ambivalence and initiate treatment among a particularly high-risk population. In June 2017 the New York City Department of Health and Mental Hygiene launched its Relay program, which attempts to connect opioid overdose victims with supportive services – including MOUD– while in the emergency department.[18] This program is based on the idea that surviving an overdose event may be a sufficient motivator to initiate OUD treatment. Similarly, the current investigation sought to explore if intervening in suspected cases of opioid overdose may also increase interest in treatment. Individuals with OUD are the target demographic of naloxone distribution programs.[4,19] Utilizing the impact of personally responding to an overdose event to promote treatment could be a means to optimize the impact of OEND on the opioid crisis.

Methods

Participant Recruitment and Selection:

The current data were collected as part of a trial investigating the risks and benefits of overdose education and distribution of naloxone to individuals with OUD (ClinicalTrials.gov Identifier: NCT02535494). All procedures were approved by the New York State Psychiatric Institute (NYSPI) Institutional Review Board. Individuals with OUD were recruited from the New York City (NYC) metropolitan area through various print media formats (e.g., newspaper and transit advisements). Following a brief telephone interview, prospective participants who met provisional inclusion criteria were scheduled for in-person screening at NYSPI. In-person screening consisted of various self-report and clinician-administered inventories. To be enrolled, participants must have met OUD criteria within the past 6 months, be between the ages of 21-65, and be able to provide informed consent and comply with study procedures. Participants were excluded from participation if they had an active psychiatric disorder that might interfere with participation or make participation hazardous (e.g., psychotic disorder, or bipolar disorder with mania), or had received formal opioid overdose prevention training from a New York State Department of Health-authorized naloxone provider within the past 2 years.

Study Procedures and Data Collection:

Individuals who qualified received overdose prevention training by study staff, along with an overdose response kit containing two doses of naloxone for intranasal or intramuscular use. The participant was provided with the naloxone formulation of their choice. The training curriculum covered the following topics:

- risks factors for opioid overdose,
- how to recognize an opioid overdose, and
- how to intervene during an overdose, including how to use naloxone.

As a part of the larger trial, participants were randomized to basic training (~20 minutes) or a more in-depth didactic (~90 minutes). All study participants completed in-person follow-up visits for one year after OEND training (baseline): 1-, 3-, 6- and 12-months post-training. Opioid use disorder treatment status was reassessed at each follow-up visit and each overdose-reporting visit. At each post-training follow-up visit, the study team inquired about overdose events the participant may have witnessed or experienced themselves. Participants were strongly encouraged to return to NYSPI to complete the follow-up assessments, however, some were completed over the telephone. Throughout their period of enrollment, participants were also asked to immediately notify the study team if they witnessed or responded to a suspected opioid overdose. The Addiction Severity Index[20] was used to evaluate changes in the severity of drug use over the year-long duration of the study. Among its 36-questions, the ASI asks participants to rate “How important to you now is treatment for these drug problems?” on a 5-point scale:

- 0 – Not at all,
- 1 – Slightly,

- 2 – Moderately,
- 3 – Considerably,
- 4 – Extremely.

Statistical Analyses:

The current analysis sought to assess whether intervention in an overdose event led to changes in the "importance" of substance use treatment. For the current analysis, overdose "intervention" was defined as the administration of naloxone. Data were analyzed for all participants who reported intervention in an overdose event, regardless of their duration of participation in the trial. For participants who intervened in multiple overdoses, investigators only assessed change in treatment importance following their first overdose intervention, while enrolled in the trial. The Shapiro–Wilk test was used to determine if the data were normally distributed.[21] In cases where parametric tests were appropriate, t-tests were used to compare mean ratings at the time point most immediately before and after participants intervened in an overdose event. In cases of a significant Shapiro-Wilkes test, the non-parametric Sign Test was used.[22] Repeated-measures analysis of variance (ANOVA) or the non-parametric Friedman test was used to compare treatment importance at each of the follow-up visits. All hypothesis tests were two-sided and the significance level was set at $p < .05$. Analyses were performed in SAS® 9.4 (SAS Institute Inc.) and SPSS Version 25 (IBM).[23, 24]

Results

Participants:

Over the 5-year trial, 321 persons with OUD were enrolled. Participants reported a mean duration of OUD of 14.9 (± 11.5) years. Nearly three-quarters of participants (72%) reported that they had personally experienced an opioid overdose prior to study enrollment [mean = 2.4 (± 2.1) events]. Meanwhile, 67% had witnessed another individual overdose [mean = 3.9 (± 7.9) events]. Throughout the year-long duration of the study, 89 participants intervened in 166 overdose events. Approximately 97% of interventions by study participants were successful (i.e., the overdose victim was revived or regained consciousness). Baseline demographics as a function of participants who would eventually use naloxone throughout the trial, and those who did not, are presented in Table 1.

Overdose Intervention and Treatment Importance:

Among the entire sample, treatment importance did not significantly change throughout the course of the study (baseline: 1.71, 1-month: 1.86: 3-month: 1.75, 6-month: 1.99 and 12-month: 1.88; $p = .35$). Among all participants who intervened in an overdose event, self-reported treatment importance increased following overdose intervention ($Z = 1.97$, $p = 0.02$). An average of 40.5 (±40.2) days separated the OD event from the post-event assessment. There was no significant difference ($p = 0.21$) in the mean change in score between participants receiving opioid agonist therapy (+0.36) and those not seeking OUD treatment (+0.32). For this comparison, participants were categorized by their treatment status immediately before the time point preceding their first overdose intervention. No

significant difference in the effect of an overdose event was found between participants who intervened in a single overdose event vs multiple overdose events.

Discussion

The current analysis found that intervention in an opioid overdose was associated with a small but statistically significant increase in the perceived importance of treatment for their drug use among individuals with OUD. The positive impact of overdose intervention was observed among participants who were not currently seeking treatment and those prescribed MOUD. The fact that this effect was found in both OUD samples indicates that overdose intervention could prove to be an important time to introduce discussions of treatment initiation or encourage continued treatment engagement and/or better adherence. Ongoing heroin use is common among those receiving medications for OUD, and retention rates at six months are typically below 50%.[25,26,27] Thus, ways to reinforce the commitment to treatment are potentially impactful.

The clinical significance of our observation remains to be determined. If, as this study suggests, intervention in an overdose event decreases ambivalence about drug use, it may represent an opportunity for those who provide services to drug users. For example, many OEND programs require participants to complete overdose reporting prior to receiving additional doses of naloxone.[4,5] As a matter of protocol, OEND programs could easily incorporate an assessment of treatment interest when participants report an overdose event and provide appropriate treatment referrals as needed. This practice could also be integrated into pharmacies, who are becoming increasingly engaged in naloxone distribution nationwide. Therefore, whether the impact of overdose intervention can be effectively utilized as a window of opportunity to engage individuals with OUD to initiate treatment or change drug use behavior (e.g., safer use practices), warrants further investigation.

Other findings from the current trial also deserve further study. Baseline differences between participants who would go on to use naloxone over the course of the trial, versus those who did not, may offer insight into the ability of these characteristics to predict those most likely to intervene in response to an overdose event. For example, participants who witnessed an overdose event prior to study enrollment were less likely to intervene using naloxone in the current trial. However, those who had personally experienced an overdose event before the trial were more likely to administer naloxone. This difference may be reflective of the various risks and benefits that drug users must balance when deciding to administer naloxone (i.e., potential harms such as naloxone-precipitated withdrawal vs potentially saving a life). These are discussed more extensively in qualitative analyses conducted by the current research team and our collaborators.[28]

There are limitations to the current study that should be noted. Most notably, though the change in treatment interest following intervention in an overdose event was statistically significant, it may not be clinically significant. Additionally, given that the participants reported intervention in an opioid-related overdose, they may have felt pressured to express greater interest in OUD treatment. Finally, as this study was limited to the assessment time points of the main trial, on average, a substantial amount of time elapsed between the

occurrence of the overdose event and our assessment of post-event treatment importance. As has been shown to occur with emotional events, the impact of intervening in an overdose event may have diminished.[29] Thus, the current results may be an underestimation of the effect on the perception of treatment need following administration of naloxone.

In sum, combatting the opioid crisis requires a multifaceted approach that includes reducing the risk of developing OUD, increasing treatment enrollment, and reducing morbidity and mortality among opioid users not in treatment. This and other studies have shown that individuals with OUD can be trained to respond appropriately to overdose events and save lives. [30,31] However, there may be additional benefits of engaging persons with OUD in the fight against overdose mortality. The current study suggests that responding to an overdose event may offer a critical moment for engagement and initiation into treatment. Given the growing prevalence of OEND programs, finding ways in which they may benefit opioid users outside of the acute context of an overdose event, could improve how we support individuals suffering from substance use disorders.[1,32]

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Table 1:

Participant Demographics at Baseline

	Intervened In An Overdose Event		
	No	**Yes**	**p-value**
Sex (Male)	77%	80%	0.92
Race/Ethnicity			
Non-Hispanic White	19%	18%	0.98
Non-Hispanic Black	42%	43%	
Hispanic/LatinX	30%	33%	
Other/Multiracial	6%	6%	
Unreported	3%	0%	
Addiction Severity Index: Drug Use Composite Score (range: 0-1)			
Severe >.4	25%	31%	0.28
Non-Severe <.4	75%	69%	
Opioid Use Disorder Treatment Status			
Prescribed MOUD	47%	43%	0.80
Not Prescribed MOUD	42%	46%	
Recently Detoxed	11%	11%	
Ever Witnessed an Opioid Overdose (Prior to Study Enrollment)			
Yes	35%	23%	**0.02**
No	60%	73%	
Don't Know/Refused to Answer	5%	4%	
Ever Experienced an Opioid Overdose (Prior to Study Enrollment)			
Yes	21%	38%	**0.002**
No	73%	57%	
Don't Know/Refused to Answer	6%	5%	
Retention Rate			
Completed 12-Month Follow-up	67%	84%	**0.03**
Importance of Treatment			
0-Not At All	51%	42%	0.21
1-Slightly	3%	8%	

	Intervened In An Overdose Event		
	No	**Yes**	**p-value**
2-Moderately	5%	8%	
3-Considerably	14%	10%	
4-Extremely	27%	32%	