Acute Substance Use as a Warning Sign for Suicide Attempts: A Case-Crossover Examination of the 48 Hours Prior to a Recent Suicide Attempt

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ABSTRACT

Objective: The extent to which specific categories of acute substance use are short-term risk factors, or warning signs, for suicide attempts is unknown. The aim of the current study was to quantify the near-term effects of sole use and co-use of substances on medically attended suicide attempts.

Methods: The current study used a case-crossover design, comparing substance use within the 24 hours prior to a suicide attempt (case day) to the control day, the matched 24 hours the day prior to the case day. Participants were 363 recent suicide attempters presenting to a Level 1 trauma hospital between October 2008 and April 2014. A timeline follow-back methodology was used to assess acute exposures within the 48 hours before the suicide attempt. Conditional logistic regression was used to report odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Results indicated that patients were at increased odds of attempting suicide after drinking alcohol within a 24-hour period (OR = 4.40; 95% CI, 2.31–8.40) and using a drug from another class of substances with central nervous system (CNS) depressant characteristics (sedatives/anxiolytics and opioids; OR = 2.82; 95% CI, 1.13–7.01), after adjustment for other acute substance use. The acute use of cannabis and CNS stimulants (stimulants/amphetamines and cocaine) was not uniquely associated with suicide attempt. Co-use of alcohol synergized effects of other CNS depressants (OR = 8.76; 95% CI, 1.02–75.44).

Conclusions: Findings suggest the importance of considering acute alcohol use and use of CNS depressants, and the concurrent use of both substances, when evaluating short-term risk for suicide attempts in clinical settings.

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Worldwide, suicidal behavior (suicide attempts and death by suicide) is an important cause of death and disability.[1] Given the significant public health impact and potential for attempts to become fatal[2] (ie, suicide attempts are one of the strongest predictors of suicide), it is crucial for research to identify risk factors for suicide attempts. One modifiable key risk factor for suicidal behavior is substance use. It is accepted that both proximal (acute) and chronic (ie, distal habitual or problematic) use of substances play an important role in suicidal behavior.[3] Notably, the vast majority of investigations of substance-related suicidal behavior have focused on the more chronic pathway: the role of distal patterns of substance use and substance use disorders. This research is impressive and educates clinicians as to *who* is at greater risk for suicidal behavior.[3,4] Research on warning signs, or the acute short-term risk pathway to suicidal behavior (substance use in the hours, or day, before the attempt[5–7]), has received much less empirical attention. Such research can help identify *when* a patient is at imminent risk for suicidal behavior, a key determination for providers. Not surprisingly, the US National Action Alliance for Suicide Prevention's Research Prioritization Task Force[8] identified the study of short-term risk factors (acute substance use[7]) as an important component in their priority list.

To most adequately answer the ultimate question—"Why did a patient attempt suicide *today*, compared to a previous day when he/she was also at high risk but did not attempt suicide?"—a within-subjects design is necessary. The case-crossover design is a within-subjects technique that uses each patient as his or her own control.[9] Initially developed to detect triggers for myocardial infarction, this design measures factors that change from day to day (eg, use of specific substances). For each individual, use of substances on the day of the target event (suicide attempt) would be compared to use on a day more distant from the target event (a day when he or she did not attempt suicide). This design is advantageous because it (1) provides the most conservative control—the same individual across acute time periods; (2) controls for all stable risk factors (eg, age, sex, chronic substance use, childhood abuse), which do not change daily; and (3) allows for a controlled examination of substance use as an acute trigger of the suicide attempt. Therefore, the case-crossover methodology is ideally suited to estimate the possible acute effects of substance use over and above the chronic effects.

Case-crossover research on acute substance use and suicidal behavior is in a nascent stage. To date, such studies have demonstrated that acute alcohol use confers increased risk for attempts, with point estimates between 6- and 10-fold.[10,11] Further, only 2 controlled studies have looked at any non-alcohol drug use as a warning sign for suicide attempts. One study[10] found no effect, and the other[12] found that any acute drug use increased risk for suicide attempt. The latter study assessed acute drug use only in the context of acute alcohol use, so it is uncertain whether the drug effect is due to alcohol's acute effect on suicide attempt.

Clinical Points

- Clinicians should educate vulnerable patients on the increased risk for attempts within 24 hours of drinking and provide education to all suicidal patients and not only to those patients with suspected problematic alcohol use.
- Clinicians should also document a pro versus con analysis before prescribing or continuing sedative, anxiolytic, or opioid medications among suicidal patients and educate patients about increased short-term risk of suicide attempt with these medications, especially in combination with alcohol.

Importantly, no controlled studies exist to provide estimates of the acute impact of specific types of non-alcohol substances on suicidal behavior.[3] This is a serious limitation to the literature, given that specific substances have different acute depressant and stimulant effects on the central nervous system (CNS). Further, it is essential to understand whether acute use of drugs from specific categories uniquely relates to suicide attempts after adjustment for other acute substance use categories and other acute risk factors for suicidal behavior (eg, negative life events[10,13]).

Finally, given that multiple substances are often used concurrently, it is important to explicate patterns of co-use prior to a suicide attempt and to determine whether the effect of acute use of a specific type of drug on suicide attempts is increased or negated when combined with alcohol (the most prevalent substance used worldwide[14]). Understanding the magnitude of suicide risk for different types of acute substance categories, as well as co-use, will help to inform prevention and treatment efforts and explicate potential mechanisms of action. The current study employs a case-crossover design among medically attended suicide attempters presenting to the only Level 1 trauma hospital in the state of Mississippi. The goal of the current report is to provide the most temporally sensitive estimates to date on the short-term risk for suicide attempts by acute use of specific types of substances.

METHODS

Participants

Patients between the ages of 18 and 64 years were recruited from a Level 1 trauma hospital within 24 hours after a suicide attempt (ie, a self-inflicted behavior with some intent to die[15,16]). A consecutive sample of 416 suicide attempt patients was enrolled across a 5.5-year period (October 2008 to April 2014). Beginning with participant 121, subjects received $35 for their time and interviews were audiotaped.[10,16] To ensure that the presence of financial compensation did not influence results, we first tested whether the effects of acute factors (ie, categories of substance use and a negative life event) on suicide attempt were moderated by whether financial compensation was received. All interactions were nonsignificant (P values > .05) and thus both subsamples were combined. The present study uses data from participants with complete data (N = 363; 87.3%), which included 62% women; the mean (SD) age was 36.58 (11.75) years, and the sample was 63% white and 37% minority (black or other race or ethnicity).

Procedure

This study was approved by the hospital's institutional review board, and written informed consent was obtained. Participants were assessed during their hospitalization, after their attending physician deemed them medically and psychologically stable, and within 7 days of their suicide attempt (the mean [SD] overall length of stay was 5.34 [5.01] days). The 2.5-hour assessment session included a battery of questionnaires and semistructured interviews with their sequence counterbalanced to control for possible order effects. For the Timeline Follow-Back Interview for Suicide Attempts (described in the next section), interviewers included the Principal Investigator (C.L.B.) and advanced students trained to reliability by the Principal Investigator.

Measures and Data Analytic Plan

The Timeline Follow-Back Interview for Suicide Attempts (TLFB-SA)[10,13,16] uses a TLFB methodology[17] focusing on precursors of suicide attempts. This interview was used to gather retrospective information on the timing of substance use and negative life events during the 48 hours prior to the attempt. First, basic information was gathered (eg, periods of sleep, activities, location) to serve as anchors for recall. Next, participants were presented with lists of (1) types of alcoholic beverages, (2) types of other drugs (medications not as prescribed and illicit drugs[10,18]), and (3) 33 negative life events.[10,13] Participants were then asked whether they used any type of substance or experienced any of the listed negative life events during the specified time period. Then, data on the exact timing (ie, start- and stop-times) of behaviors and events were collected. The TLFB-SA demonstrates high interrater reliability, with kappa values ranging from 0.79 to 1.00 for acute exposures.[10,16]

Illicit drugs and medications not as prescribed were placed in the following drug domain categories: (1) cannabis (marijuana, hashish, tetrahydrocannabinol [THC]); (2) CNS depressants (sedatives/anxiolytics, opioids); and (3) CNS stimulants (stimulants/amphetamines or cocaine). Alcohol use was rated as present if any amount of alcohol use was endorsed. Drug domain categories were rated as present if any item within a drug subcategory was endorsed.

A series of conditional logistic regression (CLR) analyses[19] was conducted; CLR analysis is similar to traditional logistic regression except that the case period (24 hours prior to the attempt) and control period (the matching 24 hours the day before) are pair-matched within individuals. The dependent variable was the presence or absence of a suicide attempt in these periods.

First, we estimated the crude odds ratios (ORs) for alcohol (yes/no), cannabis (yes/no), CNS depressants (yes/no), CNS stimulants (yes/no), and a negative life event (yes/no) on suicide attempt (see Table 1). Second, we adjusted these estimates by fitting a single CLR equation in which we

Table 1. Results From Conditional Logistic Regression Analyses Predicting Suicide Attempt From Alcohol Use, Other Drug Use, and a Negative Life Event[a]

Independent Variable[b]	Exposed Day Before Attempt, n (%)	Case: Exposed Day of Attempt, n (%)	OR (95% CI)	AOR (95% CI)
Any alcohol use	77 (21.21)	120 (33.06)	3.87 (2.19–6.82)***	4.40 (2.31–8.40)***
Any cannabis use	48 (13.22)	37 (10.19)	0.39 (0.16–0.93)*	0.43 (0.16–1.19)
Any other CNS depressant drug use (sedatives/anxiolytics/hypnotics, opioids)	29 (7.99)	45 (12.40)	3.29 (1.41–7.66)**	2.82 (1.13–7.01)*
Any other CNS stimulant drug use (stimulants, cocaine)	27 (7.44)	17 (4.68)	0.29 (0.09–0.87)*	0.51 (0.15–1.68)
Any negative life event	137 (37.74)	234 (64.46)	3.69 (2.56–5.34)***	3.50 (2.37–5.16)***

[a]N = 363.
[b]Acute exposure to these variables. All independent variables coded 1 (present) or 0 (absent).
*P < .05. **P < .01. ***P < .001.
Abbreviations: AOR = adjusted odds ratio (indicates that the effect of an exposure is adjusted for other exposures [rows] simultaneously), CI = confidence interval, CNS = central nervous system, OR = odds ratio (indicates that only 1 exposure [row] is included within each analysis).

entered all 4 substance categories and presence of a negative life event simultaneously (see Table 1).

Third, since the adjusted ORs from the model described in the previous paragraph do not take into account the common practice of patients' using particular combinations of multiple substances, we further estimated crude effects (ORs) for specific subgroups. To examine the effect of specific subgroups using only 1 type of substance (and having no other substance use), we estimated the effect of sole use of alcohol, cannabis, CNS depressants, and CNS stimulants, all compared to those who used none of the substances (see Table 3). To examine the effect of specific subgroups using alcohol in combination with only 1 other type of substance use, we estimated the joint (combined) effect of alcohol with cannabis, CNS depressants, and CNS stimulants (see Table 3), all compared with those who used none of the substances. Although other combinations of substances could be of interest, our limited sample size precluded those inquires. No correction for multiple testing was used because the majority of analyses examine effects for specific subgroups and the aim of this preliminary report is to provide initial estimates for such subgroups (sole use and co-use of specific substance categories). Descriptive information regarding co-occurrence of substance use is also presented.

RESULTS

General Descriptives

The majority had a history of prior suicide attempts (63%; mean [SD] = 7.00 [13.57] attempts). The most common index suicide attempt methods were poisoning (77%), sharp instrument (17%), gun (4%), hanging (3%), and other methods (4%) including jumping from high places, motor vehicle crash, drowning, or immolation. Most participants (84%) used only 1 method.

Exposed Cases

During the control and case periods, the following were reported: alcohol use (control: n = 77 [21.2%], case: n = 120 [33.1%]), drug use (control: n = 90 [24.8%], case: n = 80 [22.0%]), and negative life event (control: n = 137 [37.7%], case: n = 234 [64.5%]). In terms of drug use within the specific drug domain categories (see Table 1), the rates for control versus case day, respectively, were as follows: any cannabis use (13.2% vs 10.2%), any CNS depressant use (8.0% vs 12.4%), and any CNS stimulant use (7.4% vs 4.7%).

Acute Risk for Suicide Attempt

Unadjusted results (see Table 1) revealed that the exposures (presence vs absence) of any acute alcohol use (OR = 3.87; 95% CI, 2.19–6.82), CNS depressant use (OR = 3.29; 95% CI, 1.41–7.66), and negative life event (OR = 3.69; 95% CI, 2.56–5.34) were associated with increased odds of attempting suicide, while the exposures of any cannabis use (OR = 0.39; 95% CI, 0.16–0.93) and CNS stimulant use (OR = 0.29; 95% CI, 0.09–0.87) were associated with decreased odds of attempting suicide. Presence of each substance use exposure was compared to no use of a specific substance, and the presence of the negative life event exposure was compared to absence of a negative life event. Adjusted results, ie, simultaneous inclusion of these exposures (see Table 1), revealed that any acute alcohol use, CNS depressant use, and negative life event were uniquely associated with attempting suicide, while any cannabis use and CNS stimulant use were no longer associated with attempting suicide after simultaneous adjustment of exposures.

Descriptive information regarding co-occurrence of substance use is presented in Table 2. On the control day, the majority of individuals solely used 1 type of substance (see Table 2) within each category: alcohol: 62.3%; cannabis: 47.9%; CNS depressants: 58.6%; and CNS stimulants: 48.2%. However, on the case day, there was generally greater co-occurrence of use of different types of substances, and thus reduced rates of sole use, compared to the control day. For instance, the percent solely using only 1 type of substance within each category included the following: cannabis: 29.7%; CNS depressants: 48.9%; and CNS stimulants: 11.8%. Approximately 68% of those who used alcohol on the case day solely used alcohol, which is a similar percentage to sole alcohol users on the control day. Alcohol was the substance most commonly used with another type of substance on both control and case days, respectively (of those who used

Table 2. Descriptive Data on the Co-Use of Substances Within the Control Day (day before the suicide attempt) and the Case Day (day of the attempt)[a,b]

Variable	Used Alcohol, n (%)	Used Cannabis, n (%)	Used CNS Depressants, n (%)	Used CNS Stimulants, n (%)
Day before attempt[c] (control day)				
Any alcohol use (n = 77)	48 (62.34)[d]	18 (23.38)	8 (10.39)	9 (11.69)
Any cannabis use (n = 48)	18 (37.50)	23 (47.92)[e]	5 (10.42)	8 (16.67)
Any other CNS depressant drug use (n = 29)	8 (27.59)	5 (17.24)	17 (58.62)[f]	2 (6.90)
Any other CNS stimulant drug use (n = 27)	9 (33.33)	8 (29.63)	2 (7.41)	13 (48.15)[g]
Day of attempt[h] (case day)				
Any alcohol use (n = 120)	81 (67.5)[d]	22 (18.33)	18 (15.00)	12 (10.00)
Any cannabis use (n = 37)	22 (59.46)	11 (29.73)[e]	9 (24.32)	7 (18.92)
Any CNS depressant drug use (n = 45)	18 (40.00)	9 (20.00)	22 (48.89)[f]	5 (11.11)
Any CNS stimulant drug use (n = 17)	12 (70.59)	7 (41.18)	5 (29.41)	2 (11.77)[g]

[a]N = 363.
[b]Parentheses (in columns) indicate the percentage of individuals who used a specific category within a row solely or who also used another type of substance.
[c]"Day before attempt" indicates substance use in the matched 24 hours the day before the attempt.
[d]Solely used alcohol.
[e]Solely used cannabis.
[f]Solely used CNS depressants.
[g]Solely used CNS stimulants.
[h]"Day of attempt" indicates substance use within 24 hours of the suicide attempt.
Abbreviation: CNS = central nervous system.

Table 3. Results From Conditional Logistic Regression Analyses Predicting Suicide Attempt From Sole Use of a Substance and Co-Use of Alcohol With Only 1 Other Type of Substance[a]

Independent Variable[b]	Exposed Day Before Attempt, n (%)	Case: Exposed Day of Attempt, n (%)	OR (95% CI)
Users of a substance solely[c]			
No substances used (reference)	225 (61.98)	202 (55.65)	NA
Sole users of alcohol	48 (13.22)	81 (22.31)	4.07 (2.06–8.02)***
Sole users of cannabis	23 (6.34)	11 (3.03)	0.31 (0.09–0.98)*
Sole users of CNS depressants	17 (4.68)	22 (6.06)	3.01 (1.09–8.31)*
Sole users of CNS stimulants	13 (3.58)	2 (0.55)	0.19 (0.04–0.96)*
Co-use of alcohol[d] with only 1 other type of substance			
No substances used (reference)	225 (61.98)	202 (55.65)	NA
Alcohol and CNS depressant use	6 (1.65)	11 (3.03)	8.76 (1.02–75.44)*
Alcohol and cannabis use	13 (3.58)	12 (3.31)	1.68 (0.46–6.15)
Alcohol and CNS stimulant use	5 (1.38)	5 (1.38)	2.32 (0.41–13.17)

[a]N = 363.
[b]All independent variables coded 1 (present) or (0) absent.
[c]"Co-use of alcohol" indicates that alcohol was used in combination with only 1 other type of substance.
[d]"Sole users" indicates that only 1 type of substance was used (and no other types of substances).
*$P < .05$. ***$P < .001$.
Abbreviations: CI = confidence interval, CNS = central nervous system, NA = not applicable, OR = odds ratio (indicates that only 1 exposure [row] is included within each analysis).

cannabis: 37.5% and 59.5%; CNS depressants: 27.6% and 40.0%; and CNS stimulants: 33.3% and 70.6%).

Table 3 presents results from analyses performed to determine the effect of sole use of a specific type of substance (ie, no other use from another substance category) on suicide attempt (reference = no substances used). Notably, the same pattern of results was obtained as those displayed in Table 1. Table 3 also presents results from analyses performed to determine the effect of co-acute use of alcohol with only 1 other type of substance on suicide attempt (reference = no substances used). Only the co-acute use of alcohol and CNS depressants posed increased risk (8.76-fold increased odds) of attempting suicide (95% CI, 1.02–75.44).

DISCUSSION

The current study provides, for the first time, OR estimates for specific categories of acute drug use on suicide attempt. In our study of medically attended suicide attempt patients, we found that the acute use of alcohol and a drug from a class of substances with CNS depressant characteristics was associated with an increased risk for a suicide attempt. Further, the co-occurrence of alcohol and CNS depressants, with an OR of 8.76, posed additional risk for a suicide attempt beyond the simple summation of the risk for each substance separately.[20] The acute use of cannabis and CNS stimulants was not associated with risk for a suicide attempt after adjustment. However, for the small number of individuals who were sole users of cannabis or sole users of stimulants, their drug use may have decreased the risk of a suicide attempt (see Table 3). Importantly, for all analyses conducted, given our within-person design, factors such as problematic substance use, which do not vary day-do-day, are held constant within individuals by design.[9] Thus, our estimates of acute substance use on suicide attempts are over and above those associated with the baseline risk of long-term or problematic substance use.

While our results on the impact of alcohol as a warning sign for suicide attempt are in concordance with prior case-control[12,21] and case-crossover[10,11] studies, we were able to demonstrate that this relation was totally independent from the effects of other substances used concurrently (see Table 3). The CNS depressant properties of alcohol are likely mechanisms to explain acute alcohol-related risk for suicide attempts.[6] This conjecture is strengthened by the fact that only 1 other substance class, other CNS depressant drugs, was a warning sign for suicide attempt, a novel finding of this study.

Our findings that acute use of neither cannabis nor stimulants was associated with suicide attempt and that sole use of these substances was associated with a reduction of risk are intriguing and subject to several interpretations. For instance, results from a

case-crossover study[22] involving injury broadly suggest that acute cannabis use is associated with a decreased risk for injury. Interestingly, when examining substance-specific symptoms of intoxication,[23] mood lability/dysphoria and impairment in attention/memory are present with alcohol and CNS depressants and are not listed as symptoms with cannabis or CNS stimulants. Conversely, euphoria is an intoxication symptom of the latter categories, but not the former.[23] In terms of cannabis and CNS stimulants, it is possible that their shared acute intoxication effect of euphoria may decrease risk for a suicide attempt. Conversely, withdrawal symptoms of both cannabis and CNS stimulants (eg, irritability/agitation, anger or aggression, anxiety, depressed mood, restlessness, sleep difficulty[23]), which are also broadly considered imminent warning signs for suicidal behavior,[24] could conceivably lead to self-harm.

Importantly, across substance categories, we observed very high rates of co-use with alcohol on the day of the suicide attempt (40%–71%; see Table 2). Acute use of cannabis or CNS stimulants in combination with alcohol led to the disappearance of any prior observed protective effects, while co-use of alcohol synergized effects of other CNS depressants. These findings highlight the importance of the assessment of sole use and co-use of substances to determine accurate estimates of short-term risk for suicide attempt.

There are limitations to this study. Clearly, our results are preliminary, based on a small number of patients for a specific substance category (particularly for sole users of a drug category), and thus need replication. However, this study is the first to provide controlled estimates of the effects of acute sole and co-use of specific substances on suicide attempt. Further, our design used a retrospective methodology, which is vulnerable to biases in recall. However, the TLFB methodology provided continuous hourly snapshots before the suicide attempt. The low incidence rate of attempts makes it difficult to prospectively study the fine-grained topography of acute sole use and co-use of specific substances within the hours of the attempt. Future studies with larger sample sizes should also examine whether effects differ by sex. Despite these limitations, our study is the first to use state-of-the-art epidemiologic methods to provide comprehensive estimates on the role of sole use and co-acute use of several substances as immediate risks factors (triggers) for medically attended suicide attempts.

CONCLUSION

Clinicians should educate suicidal patients on the increased risk for attempts within 24 hours of drinking alcohol and provide this education to all suicidal patients and not only to those patients with suspected problematic alcohol use. It is recommended that providers offer to construct suicide and distress safety plans,[16,25] which provide adaptive strategies to cope with negative life events, urges to use alcohol or illicit drugs, and the emergence or increase in distress or suicidal thoughts, in order to prevent future suicidal behavior. Further, clinicians should conduct and document a pro versus con analysis before prescribing or continuing sedative, anxiolytic, or opioid medications among suicidal patients and should educate patients about increased short-term risk of suicide attempt after use of such medications, especially in combination with alcohol. Of course, this recommendation generalizes to clinicians who are treating, or who are aware of, use of illicit CNS depressant drugs (such as heroin), and recommendations to stop such use is of utmost importance to decrease short-term risk for suicide. Determination of the presence and nature of triggers or warning signs for suicidal behavior is necessary to help clinicians gauge imminent risk for suicidal behavior among their patients.

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