



Non-Opioid Substances Acute Poisonings with Suicidal Intent in Patients with Opioid Use Disorder

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Abstract

Introduction: Several epidemiological studies have evaluated the role of illicit drug use in suicide behaviour.

Aim: To assess patients with opioid use disorder and suicidal intent related to behavior, severity of acute poisoning and the most commonly used non-opioid substances.

Materials and methods: This cross sectional study included 67 patients diagnosed with opioid use disorder. The study was conducted at the University Clinic of Toxicology in Skopje over a 5-year period (2013-2017). The following variables were examined: gender, age, duration and route of opioid administration, duration of hospitalization, and types of substances used in acute poisoning. Assessment of patients' behavior and severity of poisoning was made by using the Suicide Behaviours Questionnaire-Revised and the Poison severity score.

Results: The majority of patients were male (88.1%). The mean age of patients was 30±6.1 years. The average duration of opioid use disorder was 8.5±3.9. A single poisoning was found in 62.7%, double poisoning in 25.4%, and triple poisoning in 11.9% of participants. Benzodiazepines were most commonly used by the patients (55.2%). The largest number of patients (32.8%) had minor Poison severity score (PSS), and only 17.9% had severe PSS. None of the patients had a fatal suicide attempt. 86.6% of patients had a score of ≥7 indicating a high risk of repeat suicide attempts.

Conclusion: Benzodiazepines were most commonly used as a single or combined substance in patients with opioid use disorder. PSS indicated that most of the participants were with minor PSS and with high risk of a repeat suicide attempt.

Keywords:

acute poisoning, opioid use disorder, suicide attempt

INTRODUCTION

Several epidemiological studies have evaluated the role of illicit drug use in suicide behaviours. However, the results of these studies are generally inconsistent. On the other hand, several reviews¹⁻³ and a few meta-analyses⁴ have ad-

ressed this issue, but they are either out-of-date or limited to suicide death or investigated the relationship between suicide and co-occurring mental disorders and illicit drug misuse.^{3,4} The prevalence of attempted suicide among heroin users stands in sharp contrast to those reported in the

general community. A history of attempted suicide has been shown to be a predictor of subsequent attempts.⁵

The proportion of suicides that were opioid overdoses rose from 2.2% to 4.3% between 1999 and 2014, with the highest increases occurring among people 45 to 64 years of age. On the other hand, 17% of drug-related deaths (all drugs, not only opioids) in 2010 were classified as suicides. People using opioids regularly were at highest risk: they were about 75% more likely to make suicide plans and twice as likely to attempt suicide as people who did not report any opioid use. Though suicidal ideation and attempts are not the same as suicide deaths, they are predictors of eventual suicide. Together, these data suggest that the true proportion of suicides among opioid-overdose deaths is somewhere between 20% and 30%, but it could be even higher.⁶

In most cases, drug addicts attempt suicide by overuse of drugs, that is an overdose, or a combination of drugs and tablets, while in a few cases the manner in which the suicide is attempted is not directly related to drugs.^{7,8} Although there is a correlation between the disorder caused by the use of substances and suicidal behaviour, a large number of addicts will never attempt suicide. It is therefore important to identify those individuals with the disorder caused by the use of substances that may be at higher risk of suicide.^{1,8,9} Many risk factors for suicide in the general population also apply to drug addicts. The older drug addicts are at a higher risk of attempts and suicides than younger addicts.^{5,8} Previous suicide attempts represent a strong risk factor for repeat suicidal attempts. Affective disorders in general, and particularly depressed mood is a risk factor for suicidal behavior in the general population and among addicts. Another very important fact when it comes to suicide attempts is the drug used. It is known that heroin and sedatives are substances with which suicide attempts are most often made, while other drugs are less characteristic.^{1,8} Suicidal addicts tend to have certain emotional problems and behavioural problems that strongly affect their activities, primarily as impulsive reactions and the inability to control behavior.⁸

The aim of the study was to assess patients with opioid use disorder and suicidal intent related to behavior, severity of acute poisoning and the most commonly used non-opioid substances.

MATERIALS AND METHODS

Study design

This was a cross sectional study conducted at the University Clinic of Toxicology in Skopje over a 5-year period.

Data source

Data about the total number of poisonings with suicide attempt were taken from the Poison Control Center that was

established in 2007 at the University Clinic of Toxicology, and we analyzed them for the period between 2013 and 2017. We examined the following variables: gender, age, duration and route of opioid administration, duration of hospitalization, and types of substances used in acute poisoning. Each participant was interviewed and underwent clinical and psychiatric examinations. Assessment of patients' behaviour and severity of poisoning were made by using: a) The Suicide Behaviours Questionnaire-Revised (SBQ-R) by Osman et al, 1999) with the following questions: 1. Have you ever thought about or attempted to kill yourself? 2. How often have you thought about killing yourself in the past year? 3. Have you ever told someone that you are going to commit suicide, or that you might do it? 4. How likely is it that you will attempt suicide some day? b) The Poison severity score (PSS, Persson H et al., 1998) with the following coding: none - 0 (no symptoms or signs related to poisoning); minor - 1 (mild, transient and spontaneously resolving symptoms); moderate - 2 (pronounced or prolonged symptoms); severe - 3 (severe or life-threatening symptoms); fatal - 4 (death).

Study population

The analysis included 67 patients diagnosed with opioid use disorder following the criteria of the Diagnostic and Statistical Manual of Mental Disorders - 4th ed. (DSM-IV). All patients had an acute poisoning as a suicide attempt using non-opioid substances and were treated at the University Clinic of Toxicology in Skopje. Exclusion criteria were other kind of suicide intent or overdose with opioid substances.

Statistical analysis

All tests were performed with the statistical package SPSS 20.0. Continuous variables were described using mean and standard deviation or median and interquartile range. Categorical variables were described using frequencies and percentages. Data were tested for normality by Shapiro-Wilk test and graphically checked for symmetry. Differences between groups were assessed by Mann-Whitney U-test. Correlations were assessed by Spearman's Rank Order correlation and expressed by Spearman's correlation coefficient. P value <0.05 was set as the threshold for statistical significance.

RESULTS

Study population

Between 2013 and 2017, a total of 67 patients with opioid use disorder and suicide attempts with non-opioid substances were registered at the University Clinic of Toxicology in Skopje (**Table 1**). The majority of patients were male

(n=59, 88.1%). The mean age of patients was 30±6.1 years, with median IQR = 30 (25-33). The youngest patient was 17 and the oldest 49 years old. The mean age of male patients was 30.8±5.9, with median IQR = 30 (27- 33), and of female patients 24.9±5.6, with median IQR = 23.5 (22-28.5) with a significant difference between genders (Mann-Whitney U Test: Z=2.427; p=0.015). The average duration of opioid use disorder was 8.5±3.9 with median IQR = 8 (6-10) years. The duration of the opioid use disorder in male patients was 8.9±3.8 with median IQR = 9 (6-11) and was significantly longer compared to females (5.2±2.2), with median IQR = 5 (3.5- 6) years (Mann-Whitney U Test: Z=2.881; p=0.004). Of 67 patients, 35 (52.24%) were on substitution therapy. Thirty patients (85.7%) were on methadone substitution therapy with average daily use of 90 mg. Intravenous abuse of methadone substitute was registered in 17 patients (56.7%). Five (14.3%) patients were on buprenorphine substitution therapy with average daily use of 12 mg. Heroin was used by 10 patients (14.9%). Intravenous route of administration was registered in 4 patients (40%). Tramadol was used orally by 9 patients (13.4%) with average daily dose of 700 mg. Methadone from “black market” was used by 13 patients (19.4%) and 12 (92.3%) of them were intravenous drug users. Twenty-five (37.3%) patients, all of them male, gave a statement that they were in prison.

Acute poisonings with non-opioid substances in patients with opioid use disorder

A single poisoning was found in 42 (62.7%), double in 17 (25.4%) and triple in 8 (11.9%) of the participants. There was a non-significant linear negative correlation between age and number of substances used for poisoning (Spearman's Rank Order Correlation: R =-0.104; p>0.05). Benzodiazepines were most commonly used by 37 (55.2%) patients as a single or combined substance in acute poisoning (Fig. 1). Of all benzodiazepines, the most frequently used were diazepam and alprazolam, of antidepressants amitriptyline and venlafaxine, and of neuroleptic drugs olanzapine was the most frequently used. Sixteen patients were with corrosive poisonings. The most commonly used corrosive substance was hydrochloric acid (n = 11, 68.8%). Six (37.5%) of them developed strictures of the gastrointestinal tract.

The largest number of patients - 22 (32.8%) had minor PSS, and only 12 (17.9%) had severe PSS (Table 2). None of the patients had a fatal suicide attempt. There was no significant association between PSS and gender of the participants (Spearman's Rank Order Correlation: R = 0.104, p>0.05).

Forty-nine (73.1%) participants were treated as inpatients. The average hospitalization duration was 5.5±5.2 days with median IQR= 4 (3-5) and min/max 2-29 days. A total of 58 (86.6%) patients had a score of ≥7 indicating a high risk of a repeat suicide attempt (Table 3).

There was no significant gender difference related to SBQ-R-scoring. No significant difference was found between SBQ-R-scoring and age of the participants (Spearman's Rank Order Correlation: R=0.106, p>0.05).

All patients underwent a psychiatric examination. The most frequent diagnoses were depression in 33 (49.25%), emotionally unstable personality disorder in 23 (34.33%), psychotic disorders in 7 (10.45%), paranoia in 2 (2.98%), and schizophrenia in 2 (2.98%) patients.

DISCUSSION

Suicide is closely linked to the substance use. Therefore, it is very important to confirm the factors that influence on the possibility of suicidal behavior. In the literature, older men who use drugs are considered to be at a higher risk of suicide attempts than younger addicts. Addiction characteristics are significant in terms of duration of substance use and duration of intravenous use. This way of use is the most invasive and inherently carries the risk of suicide. The question is whether suicidal people are more prone to intravenous injection of entering into such a state of “protracted suicide” or that the existing manner of use carries higher risk also for completed suicidal attempts. The tendency toward criminal behavior that is often associated with addicts with violent behavior is potentially a significant risk factor for suicide among drug users. Up to 75% of drug users are involved in violent behavior (e.g. physical assault, robbery, assault with weapons).⁸

Suicide is a multifactorial phenomenon with several psychological, social, biological, cultural and environmental factors. Psychiatric disorders, history of previous suicide and alcohol use disorder are among the major risk factors for suicide. Several epidemiological studies have investigat-

Table 1. Total number of patients with non-opioid substance acute poisonings with suicide intent versus patients with opioid use disorder

Year	2013	2014	2015	2016	2017
Total number of patients (N)	680	565	730	611	556
Patients with opioid use disorder (N/%)	8 (1.18%)	21 (3.72%)	18 (2.47%)	12 (1.96%)	8 (1.44%)

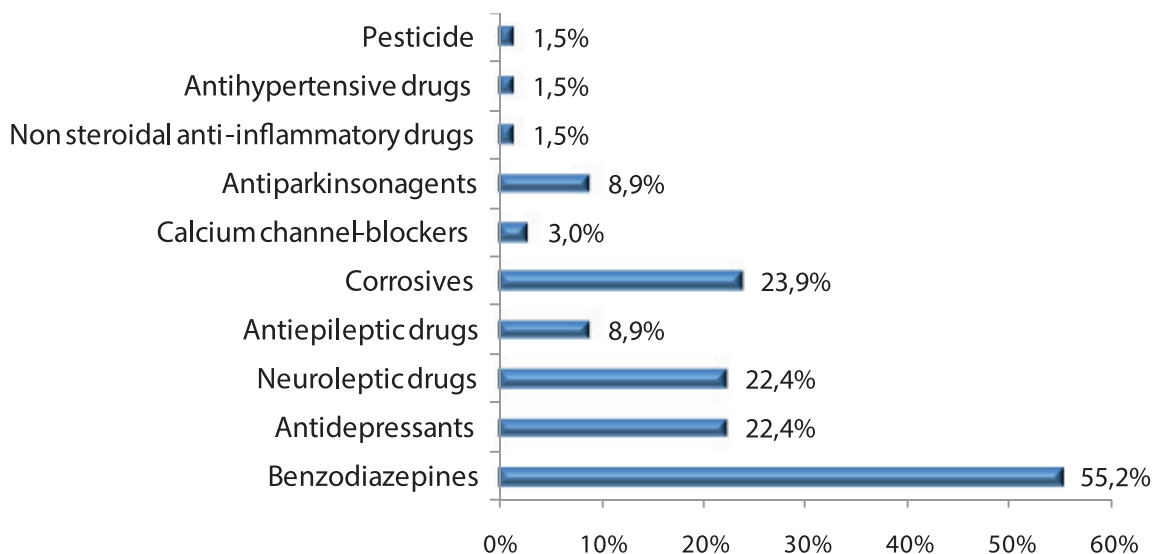


Figure 1. Distribution according to substance used for poisoning.

Table 2. Distribution of Poison Severity Score (PSS) by gender

PSS	Male (N/%)	Female (N/%)
none ⁰	15 (25.4%)	3 (37.5%)
minor ¹	19 (32.2%)	3 (37.5%)
moderate ²	15 (25.4%)	/
severe ³	10 (16.9%)	2 (25%)

⁰ no symptoms or signs related to poisoning; ¹ mild, transient and spontaneously resolving symptoms; ² pronounced or prolonged symptoms; ³ severe or life-threatening symptoms

Table 3. Distribution by gender and Suicide Behaviors Questionnaire-Revised (SBQ-R)- scoring

Gender	Mean	N	Standard Deviation	Min	Max	Percentiles			p
						25 th	50 th (Median)	75 th	
Male	10.8	59	3.4	5	17	8	10	14	Mann-Whitney U Test: Z=0.8314; p=0.4057
Female	10.0	8	5.0	5	17	6.5	7	15.5	
Total	10.7	67	3.6	5	17	7	10	14	

ed the effect of illicit drugs on suicide outcomes, but the results are generally inconsistent. To date, a few meta-analyses have been performed to estimate the overall association between substance abuse and suicide behaviours, but these meta-analyses were associated with some limitations and biases. The main limitation of these studies was that they did not explore the effect of substance use disorder (SUD) on different types of suicide outcomes. An old em-

pirical review of cohort studies was conducted by Wilcox et al. on English language reports indexed in Medline before 2002 to explore the association between SUD and suicide death. They reported that standardized mortality ratio for suicide was 1351 (95% CI: 1047, 1715) among opioid users, 1373 (95% CI: 1029, 1796) among intravenous drug users and 1685 (95% CI: 1473, 1920) among mixed drug users. This review revealed that not only the type of substance,

but also the ways they are used have an impact on suicide outcomes.³

Heroin users have a death rate 13 times higher than that of their peers, and deaths among heroin users attributed to suicide range from 3%-35%. Overall, heroin users are 14 times more likely than peers to die from suicide. The prevalence of attempted suicide is also many orders of magnitude greater than that of community samples. The major general population risk factors for suicide also apply to heroin users (gender, psychopathology, family dysfunction and social isolation). Heroin users, however, have extremely wide exposure to these factors. They also carry additional risks specifically associated with heroin and other drug use. Drugs as a method of suicide play a larger role in suicide among heroin users than in the general population. Heroin, however, appears to play a relatively small role in suicide among this group. Overall, suicide is a major clinical issue among heroin users. It is concluded that suicide is a major problem that treatment agencies face, and which requires targeted intervention if the rates of suicide among this group are to decline.⁵

Histories of self-harm and suicide attempts are common among people in prison in Australia, and substance dependence is an established risk factor for these lifetime experiences. Rates of completed suicide among men in prison in Australia have been reported at almost 4 times the rate seen in the general population, while almost one quarter of Australian prisoners report a history of self-harm, compared to approximately 8% of the general population. A key contributor to this disproportionate rate of suicide and self-harm in prisoner populations is the strong association among people with a history of injecting drug use (IDU), a characteristic disproportionately represented among people in prison. Almost half of Australian prisoners reported a history of IDU (Australian Institute of Health and Welfare, 2015). Suicide rates among people who inject drugs (PWID) have been estimated at 14 times that seen in the general population, while the major risk factors associated with self-harm and suicide including psychological distress, family conflict and social isolation are over-represented among PWID.¹⁰

In one study, 43.8% of participants reported histories of suicidal ideation, and 75% of this sample also reported suicide attempts. These striking statistics confirm that suicidal behaviours among people with long-term opioid dependence remain a significant public health concern. Histories of depression, anxiety, and adverse life events (including childhood emotional neglect) were independently associated with an increased probability of lifetime suicidal ideation. Additionally, the gender-based analysis in the present study suggests that the relationship between these factors and suicidal ideation may be unique for women and men. Together, these findings may inform the development of additional domains of suicide risk assessment for people with opioid dependence.¹¹

Strengths and limitations

This study provides insight into the type of the most abused non-opioid drugs by patients with opioid use disorder, severity of the poisoning and risk of suicide attempt in this population.

The following limitations should be considered when interpreting our findings. The study included only persons who came to the clinic, and thus the generalizability of the results may be limited. Further studies are necessary/ further research is needed about the frequency of suicide attempts and assessment of the most commonly used non-opioid substances in acute poisonings among population with opioid use disorder in comparison with other population. It is also necessary to assess the frequency of suicide attempts in patients with opioid use disorder on methadone substitution therapy in comparison with patients who are on Buprenorphine substitution therapy.

Implications for practice

Our findings underline the importance of monitoring patients with opioid use disorder for a) better motivation to start with treatment; b) more control in their substitution therapy c) more control in prescription of opioid and non-opioid drugs; d) greater control over the availability of toxic chemicals.

CONCLUSION

Benzodiazepines were most commonly used as a single or combined substance in patients with opioid use disorder. PSS indicated that most of the participants were with minor PSS and with high risk of repeated suicide attempt.

ETHICS STATEMENT

The authors state that no ethical approval was needed.

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Острые отравления неопиоидными веществами с суицидальным намерением у пациентов с расстройствами, вызванными употреблением опиоидов

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Абстракт

Введение: В нескольких эпидемиологических исследованиях была оценена роль запрещённых наркотиков при суицидальном поведении.

Цель: Оценить состояние пациентов с расстройством, вызванным употреблением опиоидов и намерением совершить самоубийство, поведение, степень тяжести острого отравления и часто используемых неопиоидных веществ.

Материалы и методы: В этом перекрёстном исследовании приняли участие 67 пациентов с диагнозом расстройств, вызванных употреблением опиоидов. Исследование проводилось в Университетской токсикологической клинике в Скопье в течение пятилетнего периода (2013–2017 годы). Были рассмотрены следующие переменные: пол, возраст, продолжительность и путь введения опиоида, продолжительность госпитализации и типы веществ, используемых при остром отравлении. Оценка поведения пациентов и тяжести отравления проводилась с помощью переработанной анкеты для оценки суицидального поведения и для оценки тяжести отравления (Poison severity score).

Результаты: Большинство пациентов составляли мужчины (88,1%). Средний возраст пациентов составил 30 ± 6,1 года, а средняя продолжительность расстройства, связанного с употреблением опиоидов - 8,5 ± 3,9. Одинокое отравление было обнаружено у 62,7%, двойное у 25,4% и тройное у 11,9% участников. Бензидиазепины были наиболее часто используемыми пациентами вещества (55,2%). Наибольшая доля пациентов (32,8%) имела показатель тяжести отравления (PSS) «умеренный», и

только 17,9% имели «тяжелый» PSS. Ни у одного из пациентов не было смертельной попытки самоубийства. 86,6% пациентов имели оценку ≥ 7 , что является показателем высокого риска рецидива самоубийства.

Выводы: Бензодиазепины чаще всего использовали в качестве чистого или комбинированного средства у пациентов с расстройством, вызванным употреблением опиоидов. PSS показал, что у большинства участников был лёгкий PSS и с высоким риском рецидива самоубийства.

Ключевые слова:

Острое отравление, расстройство, вызванное употреблением опиоидов, суицидальная попытка
