

Repetitive suicide attempts by poisoning in Vojvodina, Serbia – Psychotropic drugs as main causes

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Abstract. – **OBJECTIVE:** Repetitive acute self-poisoning takes great part of all admissions at the Emergency Department including self-harm as one of the main reasons. The aim of this study is to analyze the characteristics of the patients treated for repetitive self-poisoning with suicidal intent (RSP-SI) in Vojvodina (Serbia), in order to propose preventative strategy and better management of the issue.

PATIENTS AND METHODS: The retrospective study included data regarding patients treated for RSP-SI during a 5-year period in Vojvodina, Serbia.

RESULTS: Repetitive self-poisoning was determined in 485 patients, of whom 35.05% reported suicidal intention. Mean number of RSP-SI per patient was 3.61±3.08. The mean period between two RSP-SI in group of females and males was 9.69±13.60 and 6.95±11.02 months, respectively. Almost two thirds (65.29%) of them were unemployed. Most of the patients had mental and behavioral disorders due to psychoactive substance use (ICD F10-19; 51.18%) and anxiety, dissociative, stress-related, somatoform and other non-psychotic mental disorders (ICD F40-48; 33.53%). The sole etiological agent was identified in 39.15% attempts. In 58.08% of the attempts more than one substance was detected (2.50±0.73 per attempt). The co-ingestion of alcohol and benzodiazepines was the most common combination (19.41%). Psychiatry intervention was needed in 70.31% of the patients. Five of all patients with RSP-SI (2.94%) committed suicide.

CONCLUSIONS: The recognition and the treatment of mental disorders as well as the control of psychiatric medications prescribing could represent one of the most important preventive strategies for repetitive suicidal behavior.

Key Words:

Self-poisoning, Suicide, Suicide attempt, Benzodiazepines, Alcohol.

Introduction

Acute repetitive self-poisoning (RSP) takes great part of all admissions at the Emergency Department (ED). Main reasons for RSP are substances abuse and attempts of suicide or deliberate self-harm. Self-poisoning is one of the most used methods among suicide attempters¹⁻⁸.

Even though the prevalence of suicide attempts has increased in some countries, the real number of suicide attempts is still underestimated⁹. This is important because the unrecognized suicide attempt is a significant risk factor for subsequent suicidal behavior and negative psycho-social outcome in general¹⁰⁻¹³. The greatest risk-factors for adolescent patients who attempted suicide in the last 12 months were found

to be higher substance scores, depression and anxiety and higher life stress level^{13,14}.

Estimating the risk of suicide and repeated self-harm, Knipe et al¹⁵ have emphasized self-poisoning as the most common method of non-fatal self-harm at first episode (98%). Most of the suicidal attempts by self-poisoning were the result of ingestion of one or more substances. The type of ingested substances varies according to geographical localization factors like accessibility and availability of poisons, socioeconomic status of poisoned patients and cultural and religious influences¹⁶⁻¹⁹. Pesticides are more characteristic for patients from developing countries, while medications are the most frequent cause of deliberate self-poisoning in developed countries^{1,17,20,21}. Moreover, the type of the substance depends on the intent of suicide. Thus, persons with low suicidal intent usually impulsively take pills in order to get the attention from others³. Even they have low intention to commit a suicide – the medical outcome of such attempts can be serious^{3,6}.

Considering the issue of drug interactions, the combination of two or more substances represents a significant medical problem^{22,23} which can provoke real life-threatening condition^{21,24} and result in more severe health damage than the person initially wanted. A non-fatal suicide attempt is a risk factor for the next one. In the 1990s in the United Kingdom, 15% of people who committed suicide were admitted at ED for self-harm in the year before their death²⁵. According to Ardani et al²⁶, up to 15% of all suicide attempts are successful. Therefore, people who are admitted to hospital after self-harm are an important target group for suicide prevention efforts¹³.

Taking into account many research articles regarding repetitive deliberate self-harm by poisoning, the aim of this study is to analyze the characteristics of the patients treated for repetitive self-poisoning with suicidal intent (RSP-SI) at the Clinical Center of Vojvodina, which is University Hospital at the Autonomous Province of Vojvodina, Serbia. This is the first detailed study of this type conducted not just in Serbia, but also in the Balkan region. Evaluating such features, risk factors for this type of behavior will be determined in order to propose preventative strategy and better management of the issue.

Patients and Methods

This retrospective study was conducted at three institutions/departments (Emergency Department

– ED, Center for Forensic Medicine, Toxicology and Molecular Genetics and Psychiatric Clinic) at Clinical Center of Vojvodina, which is the University Hospital of the Autonomous Province of Vojvodina, that covers the population of approximately 2 million at the norther part of Serbia. The study included data regarding patients admitted with RSP-SI in a 5-year period (2012-2016). Repetitive self-poisoning was diagnosed in patients who were admitted at ED due to poisoning more than once during the observed time frame. Poisoning was determined *via* anamnestic and toxicological data. Suicidal intent in those patients was confirmed in anamnestic/hetero-anamnestic data. Every suicidal attempt by other method than poisoning was excluded. The research was approved by the Ethical Committee of the Faculty of Medicine, University of Novi Sad and the Ethical Committee of the Clinical Center of Vojvodina.

The ED record review includes demographic data – age, gender, permanent residence (rural or urban), employment, data regarding RSP-SI like number, date and period between two attempts, substances involved (by category) and medical outcome and healthcare facility level.

Variables like age, gender, date of autopsy, cause of death, drugs detected in postmortem samples of peripheral blood were reviewed at the autopsy record.

The number of admissions at the Clinic of Psychiatry, Clinical Center of Vojvodina and patient's psychiatric diagnoses were collected from its database and were classified according to International Classification of Diseases (ICD).

Statistical Analysis

The data were processed by MS Office Excel 2019. The results were expressed in the form of percentages, mode, median and mean with standard deviation (\pm SD). Chi-square statistics was used in order to see if distributions of categorical variables differ from each other. T-test was used to analyze differences between two means. A probability level of $p < 0.05$ was considered statistically significant.

Results

During the observed period, there were 4886 admissions (3678 patients) at the ED due to self-poisoning where more than a third of them (1693 admissions – 34.65%) were repeated episodes. The RSP was determined in 485 patients, of whom 170 (35.05%) reported suicidal inten-

Table I. Age categories of the patients with repetitive self-poisoning with suicidal intention.

Age	Males	Females	Σ	%
13-19	3	1	4	2.35
20-29	19	27	46	27.06
30-39	20	27	47	27.65
40-49	9	29	38	22.35
50-59	6	19	25	14.71
60-69	2	4	6	3.53
70+	0	4	4	2.35
Total	59	111	170	100.00

tion (RSP-SI). Among them, 59 (34.71%) were males and 111 (65.29%) were females. Total number of suicidal attempts in this group was 613, where the mean of suicide attempts per patient was 3.61 ± 3.08 (mode=2). Taking into account all the patients with RSP, female patients were significantly more prone to suicidal attempt than male ones ($p < 0.001$). However, males had statistically significant more suicidal attempts per person (4.54 ± 3.91 vs. 3.11 ± 2.39 , $p < 0.05$). Almost two thirds of male patients were from urban place (66.10%), while the higher percentage of female patients were from rural environment (52.25%) ($p = 0.022$). The mean age of male and female patients at their first admission was 35.31 ± 11.48 years (mode=29, median=32) and 40.35 ± 14.23 years (mode=22.49, median=40), respectively. The majority of the female patients were in the age group 40-49, while the most common age category in males was 30-39 (Table I).

The unemployed patients with RSP-SI were predominant (65.29%, $p < 0.001$) followed by employed ones (18.24%) and patients in retirement (16.47%). Regarding the gender and employment of those patients, it was shown that the unemployed males (72.88%) were more prone to RSP-SI than unemployed females (61.26%), but also that female patient in retirement (19.82%) had higher chance for RSP-SI than the male patients from the same group (10.17%).

The mean period between two suicidal attempts in the group of females was 9.69 ± 13.60 months,

while in the group of males it was 6.95 ± 11.02 months. However, the most frequent period between 2 suicidal attempts in the group of males was shorter than 30 days (19.91%), while in the group of females that period was between 30 and 60 days (11.59%) (males' mode=0 months, females' mode=1 month).

Taking into account all the RSP-SI (613), the substances remained unknown in 2.77% of patients. There was only one substance identified as etiological agent in more than one third of attempts (39.15%). Among them benzodiazepines were the most commonly determined, followed by alcohol and antiepileptic drugs (Table II).

More than one substance was detected in 58.08% attempts (2.50 ± 0.73 substances per attempt) with predominance of two substances detected (36.38%). The co-ingestion of alcohol and benzodiazepines was the most common combination (19.41%) followed by the combination of benzodiazepines and anticonvulsants (3.59%) and benzodiazepines and atypical antipsychotics (1.47%) (Table III). There were 15.66% admissions with 3 substances combined. Table III shows the top 5 combinations of 3 substances, where alcohol and benzodiazepines are present in all of them.

In our study after the initial ED admission and treatment, most of the patients (70.31%) were directed to the Clinic of Psychiatry for further support. However, as a result of severe poisoning 1.96% patients were treated at the Intensive Care

Table II. Substances in mono-intoxication in the repetitive self-poisoning with suicidal intention.

Substance	No	% of all attempts	% of all mono-intoxication
Benzodiazepines	96	15.66	40.00
Alcohol	88	14.36	36.67
Other type of anticonvulsants †	17	2.77	7.08
Atypical antipsychotics	8	1.31	3.33
Opioids	7	1.14	2.92

†without benzodiazepines

Table III. The most common combinations of substances in the repetitive self-poisoning with suicidal intention.

Number of co-ingested substances	Number of attempts	%
2	223	36.38
3	96	15.66
4	30	4.89
5	7	1.14
Top 5 combinations (2 substances)	Number of attempts	%
Alcohol and benzodiazepines	119	19.41
Benzodiazepines and other anticonvulsants	22	3.59
Benzodiazepines and atypical antipsychotics	9	1.47
Benzodiazepines and antidepressants (except SSRIs)	8	1.31
Benzodiazepines and SSRIs	8	1.31
Top 5 combinations (3 substances)	Number of attempts	%
Alcohol, benzodiazepines and other anticonvulsants	21	3.43
Alcohol, benzodiazepines and opioids	9	1.47
Alcohol, benzodiazepines and SSRIs	6	0.97
Alcohol, benzodiazepines and antidepressants (except SSRIs)	4	0.65
Alcohol, benzodiazepines and NSAIDs	4	0.65

Unit, 0.49% at the Surgery Department and 1.63% at the Institute for Pulmonary and Cardiovascular Diseases. One male patient died after initial management, from complications of acute poisoning. That was his second suicidal attempt by self-poisoning with organic solvent (glue) 30 days since the last attempt (Table IV).

During the observed period the average number (percentage) of RSP-SI admissions at the Clinic of Psychiatry was 7.43 ± 11.14 (91.18%). The most common psychiatric diagnoses of RSP-SI patients were mental and behavioral disorders due to psychoactive substance use (ICD F10-19 – 51.18%), anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (ICD F40-48 – 33.53%) and specific personality disorders (ICD F60-F69 – 20.00%) (Table V). Considering the fact that some patients had more than one psychiatric diagnose, Table V shows percentage of the 7 most frequent group of mental disorders, among RSP-SI patients. In the ICD F10-19 group of patients, alcohol relat-

ed problems (ICD F10.0-10.99) were the most common (54.02%), followed by opioid, cannabis, sedative, hypnotic or anxiolytic related disorders (ICD F11.00-13.99 – 29.89%), and mental and behavioural disorders due to multiple drug use and use of other psychoactive substances (ICD F19.0-19.9 – 16.09%). Among patients with ICD F40-48 diagnoses 96.49% of them had reaction to severe stress and adjustment disorders (ICD F43).

In the Forensic Medicine database, the autopsy records have revealed 2.94% of RSP-SI patients. One of them died in a car accident, and 4 of them committed suicide (Table VI).

Discussion

Repetitive attempt of suicide is a common case all around the world, with self-poisoning as one of the most frequently used method. It has been estimated that there is one fatal suicide among 20 attempts⁸.

Table IV. Outcomes of repetitive self-poisoning with suicidal intention after initial medical treatment.

Outcome	Number of admissions	%
Psychiatry	431	70.31
Heart and lung institute	10	1.63
Otorhinolaryngology	1	0.16
Surgery	3	0.49
ICU	12	1.96
Discharged	39	6.36
Refused medical care	6	0.98
Death	1	0.16
Unknown	110	17.94
Σ	613	100.00%

Table V. Mental disorders in patients with repetitive self-poisoning with suicidal intention.

Diagnosis	ICD code	Number of patients	%
Mental disorders due to known physiological conditions	F01-09	8	4.71
Mental and behavioral disorders due to psychoactive substance use	F10-19	87	51.18
Schizophrenia, schizotypal, delusional and other non-mood psychotic disorders	F20-29	12	7.06
Affective disorders	F30-39	28	16.47
Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders	F40-48	57	33.53
Disorders of adult personality and behavior	F60-69	34	20.00
Intellectual disabilities	F70-79	2	1.18

During the observed 5-year period, 2.94% persons with RSP-SI died of suicide at the end, and 4 out of 5 of self-poisoning. This is in accordance with recently published data by other authors. Thus, Carroll et al²⁷ showed that an estimated 1.6% of those with self-harm would die in the subsequent year, and up to 3.9% in the subsequent 5 years. Moreover, a large prospective study restricted to people who had poisoned themselves in a rural region of Sri Lanka reported that the risk of suicide (including all methods) in 2 years was 0.7%¹⁸. On the other hand, according to Knipe et al¹⁵ only 8.5% of those with self-harm, suitable for suicide prevention, were admitted at hospital. Such findings imply that a lot of suicidal attempts are unnoticed by the health system, and that attempted suicides are more profound problem than we assume.

Female patients were significantly more prone to suicide attempt, which is in accordance with numerous studies conducted worldwide^{2,7,28}. Females had a greater tendency to end their life by suicide by less lethal methods such as poisoning¹⁶. Higher mean number of suicidal attempts in males (4.54) than in females (3.11) can be explained by the results of Nordentoft et al²⁹. In this study lower suicidal intent in males is associated with higher risk of repetition of suicidal attempts. On contrary, the mean number of suicidal attempts (4.54±3.91) in males vs. 3.11±2.39 in females observed in our study is significantly higher than in other investi-

gations. Similar to our findings, in the large cohort study in Sri Lanka the maximum number of suicidal attempts was four¹⁵.

Taking into account the age of the patients, the most susceptible age categories were 20-29, 30-39 and 40-49 years, which is comparable with previous publications^{4,7,15,17,30}.

Most of the patients from our study were unemployed (65.29%), suggesting low socioeconomic position as important risk factor for suicide attempt, which is similar with results from other studies^{13,19}.

Benzodiazepines and alcohol, together with other psychotropic drugs were the most abused etiological agents in all self-poisoning suicidal attempts^{6,7,28,31}. The most frequently abused medications can be issued only after psychiatry or neurological evaluation (prescription is required). This might imply that most of the persons who attempted suicide more than once are psychiatry patients⁴. Despite common assumption that most of the suicides involve underlying mental disorders, according to recent studies – a considerable percentage of suicides occur without preceding symptoms of psychiatric illness^{32,33}. Some authors underlined that the access to psychotropic medication via prescription is associated with choice of psychotropic medication as suicide method^{34,35}. Statistical analysis of the population of Norway indicates drugs, mainly benzodiazepines, as the most common cause of intoxication,

Table VI. Fatal suicide attempts of patients with repetitive self-poisoning with suicidal intention.

Patient	Gender	Method	Number of non-fatal attempts	Period† (months)	Substances
1	m	self-poisoning	4	6	benzodiazepines, SSRIs and atypical anti-psychotics
2	f	hanging	2	10	/
3	f	self-poisoning	5 17		benzodiazepines, SSRIs and opioids
4	f	self-poisoning	2 7		anticonvulsants
5	m	car accident	3 6		/

†period between the last non-fatal attempt and fatal suicidal attempt

with ethanol in the second place³⁰. The most serious effects of poisoning were reported after overdoses of both alcohol and drugs. Reason that benzodiazepines are easily available is based on their usage for a wide spectrum of indications, including anxiety, insomnia and epilepsy. Better control of benzodiazepines prescribing might be one of the measures to decrease prevalence of self-poisoning with these agents.

Usage of new psychoactive substances, such as synthetic cannabinoids, stimulants and hallucinogenic drugs, could still be unrecognized risk factor for RSP-SI and other types of deviant behavior³⁶. New psychoactive substances, usually replace those who have been banned³⁶. This can be unrecognized by medical practitioners due to new combination of symptoms they induce and inadequate drug tests. That may be the reason why only conventional illegal drugs were found in our study as a cause of poisoning in considerable percentage of patients (8.24%) with other psychoactive substance related problems (ICD F19.0-19.9).

In most of the poly-drug combinations the antidepressants were noticed, which is consistent with recently published data³⁷. The authors observed a decrease in the frequency of poisoning with tricyclic antidepressants and a significant increase in drug poisoning with newer generations of antidepressants. Better safety profile of SSRIs in overdose in comparison with tricyclic antidepressants could be the reason for favorable clinical outcome of the patients poisoned with antidepressants in our investigation.

Most of the suicidal attempts in our study were caused by the ingestion of 2 or more agents. However, in a similar study conducted in Poland, single drug-caused intoxication was observed 2.8 times more often than mixed drug poisoning²⁸.

Similar to our study, the one conducted in United Kingdom with participants up to age 16 years showed higher percentage of females reported for self-harm with suicidal intent¹³. The authors also emphasized that patients who were overdosed during the last hospitalization had a higher risk for suicidal attempt¹³. This correlates with high percentage (51.18%) of patients with mental and behavioral disorders due to psychoactive substance use (ICD F10-19) noted in our study. However, previously reported results¹³ have shown that participants with heavy alcohol use were more likely to have non-suicidal self-harm, whereas the highest percentage (54.02%) of patients with ICD diagnosis F10-19 in our research were in fact those with alcohol related disorders (ICD F10.0-10.9).

High percentage (33.53%) of patients with RSP-SI from our study were diagnosed with anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (ICD F40-48). Even though benzodiazepines are the drug of choice in the treatment of those conditions, some studies drew attention on withdrawal symptoms and their potential influence on suicidal attempts³⁸. Results from case study from London suggested that short-acting benzodiazepine (lorazepam) induced withdrawal symptoms that eventually lead to suicide attempt of a patient³⁸. They and authors from other studies emphasized that long-acting benzodiazepine (diazepam) is adequate follow up treatment for withdrawal symptoms, with 10 mg of diazepam being equivalent dose for 1 mg of lorazepam^{38,39}.

Higher anxiety, various stressors and depression as important risk factors for self-harm with suicidal intent were reported in a study conducted at Oxford university¹⁴. This can relate to our study in the terms of patients psychiatric diagnosis; thus, anxiety and stress related disorders (ICD F40-48) and affective disorders (ICD F30-39) were diagnosed in high percentage of patients with RSP-SI (33.53% and 16.47%, respectively).

Studies from South India and California (USA), tried to find correlation between patients' impulsivity and suicidal attempts^{10,40}. Both studies showed that impulsivity as personality trait alone wasn't associated with higher suicidal intent. However, various stressors such as previous painful and provocative events, combined with impulsivity showed higher correlation with suicidal attempt^{10,40}. Reaction to severe stress and adjustment disorders (ICD F43) were diagnosed in almost one third of all patients with RSP-SI in our study, confirming results of cited studies.

We have observed the high risk of RSP-SI in the initial post event period. The period between 2 suicidal attempts in the majority of males (19.91%) was shorter than 30 days. In a recent prospective study of RSP-SI, the median time between repetitions within 1 year and 2 years were around 3 and 6 months, respectively¹⁸. Similarly, the median time between 2 attempts in Taiwan was 105 days⁴¹. Such findings emphasize the importance of longer inpatient stays which can help individuals to get through the period of the greatest risk of repeat self-harm. Most of the patients in our study were hospitalized at the Psychiatry Clinic after the initial treatment of acute poisoning. In England, half of self-harmed patients admitted to the emergency department were discharged without being admitted to the hospital⁴². A short hospital stay

may allow the patient to be discharged back into the same environment that has contributed to the suicidal behavior¹⁸.

Evaluating general hospital costs of medical and psychiatric care for self-harmed patients in England, Tsiachristas et al⁴³ have reported the mean cost of 809 pounds per self-harm episode and highlighted the need for effective methods of preventing of self-harm and reducing the extent to which it was repeated.

Conclusions

The early recognition and treatment of mental disorders and a control of prescribing of psychiatric medications could represent important preventive strategies for RSP-SI. Even though the mean number of RSP-SI per person was 3.61, the suicide rate was low. This suggests that RSP-SI is call for help so it is highly advisable to implement compulsory in-patient psychiatric consultation as an integral part of the management of self-poisoning in order to prevent further suicidal behavior.

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Authors' Contributions

Conceptualization and study design: VMJ, DP, GVE, NPV; Literature review: VMJ, DP, AMV; Supervision: IS, SP, NG, AD; Definition of conclusions: VMJ, DP, IS, SP, AD, GVE; Article writing (first draft): DP, VMJ, AMV; Criticism and review: VMJ, IS, GVE, NPV; Article writing (definitive version): All authors.

Ethical Committee Approval

The research was approved by the Ethical Committee of the Faculty of Medicine, University of Novi Sad and the Ethical Committee of the Clinical Center of Vojvodina.

Conflict of Interest

The authors declare that they have no conflict of interest.

Data Availability Statement

All data generated or analyzed during this study are included in this published article.

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