

# **REVISTA CIÊNCIAS EM SAÚDE**

HEALTH SCIENCES JOURNAL e-ISSN 2236-3785



## ORIGINAL ARTICLE



### Drug-related female autointoxication registered at a toxicology care center

Autointoxicação feminina por medicamentos registradas em um centro de assistência toxicológica

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Received 29 May 2020, accepted 17 Dec 2020, published 9 Mar 2021

KEYWORDS	ABSTRACT
Psychotropic drugs Drugs Suicide attempt Women	<ul> <li>Objective: To analyze the data on epidemiological records of autointoxication reports registered at a toxicological assistance center.</li> <li>Methods: Exploratory, descriptive, and retrospective study with the analysis of secondary data, conducted from the audit on Toxicological Occurrence Notification and Attendance forms, referring to the period from 2014 to 2018, filed in a toxicological information and assistance center, located in a municipality in southern Brazil. The data obtained were compiled in spreadsheets and analyzed using simple descriptive statistics.</li> <li>Results: 2,942 epidemiological records on women's autointoxication were audited, 72.0% of the total cases in the period studied. The predominant age group was 18 to 29 years old, with 1697 (57.7%) cases. The main toxic agent was medication, and the only agent of intoxication in 2,358 cases (80.1%). Psychotropic drugs accounted for 55.2% (1,593) of the cases, mainly antiepileptic and psychoanalytic drugs. Clonazepam was present in 567 (35.6%) suicide attempts and as the sole agent in 275 (17.3%) of them. In 873 cases (54.8%), mental illness was reported, in 546 (34.3%) previous suicide attempts, and 1,082 (67.9%) continued use of psychotropic medication. The main outcome was hospital discharge in 1,239 cases (77.8%).</li> <li>Conclusion: The study showed an increase in cases of female autointoxication over the period studied. The high percentage of autointoxication with psychotropic medications may be related to the ease of access at home and society's medicalization.</li> </ul>

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This study was carried out at Hospital Universitário Regional de Maringá, Universidade Estadual de Maringá.

https://doi.org/10.21876/rcshci.v11i1.993

How to cite this article: Souza MB, Lini RS, Oliveira MLF, Mossini SAG. Drug-related female autointoxication registered at a toxicology care center. Rev Cienc Saude. 2021;11(1):14-21. https://doi.org/10.21876/rcshci.v11i1.993

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#### PALAVRAS-CHAVE

Drogas psicotrópicas Mulheres Medicamentos Tentativa de suicídio

#### RESUMO

**Objetivo:** Analisar os dados de fichas epidemiológicas de notificações de autointoxicação registradas em um centro de assistência toxicológica.

**Métodos:** Estudo exploratório, descritivo e retrospectivo com análise de dados secundários, realizado a partir da auditoria em fichas de Notificação e de Atendimento de Ocorrências Toxicológicas, referentes ao período de 2014 a 2018, arquivadas em um centro de informação e assistência toxicológica, localizado em um município na região Sul do Brasil. Os dados obtidos foram compilados em planilhas e analisados por estatística descritiva simples.

**Resultados:** Foram auditadas 2.942 fichas epidemiológicas de autointoxicação de mulheres, 72,0% do total de casos do período estudado. A faixa etária predominante foi de menor de 18 a 29 anos com 1697 (57,7%) casos. O principal agente tóxico foi o medicamento, como único agente da intoxicação em 2.358 casos (80,1%). Medicamentos psicotrópicos representaram 55,2% (1.593) dos casos, principalmente os antiepiléticos e psicoanalépticos. O clonazepam esteve presente em 567 (35,6%) tentativas de suicídio e como único agente em 275 (17,3%) delas. Em 873 casos (54,8%) foi informado transtorno mental, em 546 (34,3%) tentativa de suicídio anterior e 1.082 (67,9%) uso contínuo de medicação psicotrópica. O principal desfecho foi alta hospitalar em 1.239 casos (77,8%).

**Conclusão:** O estudo apontou crescimento de casos de autointoxicação feminina ao longo do período estudado. A alta porcentagem de autointoxicação com medicamentos psicotrópicos pode estar relacionada com a facilidade de acesso nos domicílios e à medicalização da sociedade.

#### INTRODUCTION

Expressions of social violence, suicide attempt (SA), and suicide are considered severe global public health problems, as they represent approximately half of all violent deaths registered in the world<sup>1,2</sup>. In 2020, the number of cases was estimated to reach 1.5 million<sup>1,2</sup>. Storino et al.<sup>3</sup> point out that one death by suicide occurs every 40 seconds and one SA every 2 or 3 seconds.

The spectrum of suicidal behavior involves suicide or self-inflicted death, SA as non-lethal self-aggressive behavior, related to an intentional act against one's own life, and suicidal ideation<sup>2,4,5</sup>. The two main risk factors associated with suicide are the history of previous SA and the presence of mental disorders, such as depression and bipolar affective disorder, and injuries associated with alcohol and other the use of psychoactive substances<sup>6</sup>. SA, the result of the interaction of social, economic, and demographic factors, are then considered sentinels at risk of suicide and are frequent causes of driving people to emergency care services<sup>7</sup>.

The high percentage of SA may be the result of unfavorable economic conditions. However, several studies have highlighted social violence as an expressive risk factor and the higher prevalence and chance of SA<sup>1,4-</sup> <sup>6</sup> defined by gender, which is revealed not only in the highest occurrence of cases in women but also in the different motivations and processes that bring men and women together or differ in the act of ending their lives<sup>2</sup>. Suicide corresponds to the second leading cause of death in the world for women between 15 and 29 years of age<sup>8</sup>, and females have more history of SA than men, even with a higher probability of subsequent SA<sup>9</sup>.

Studies have specified autointoxication as the most common SA method in Brazil between 2007 and 2016<sup>10-12</sup>. Santos et al.<sup>7</sup> highlighted intoxication as one of the primary means used in SA and suicides committed

in Brazil, understood as the human act of trying to end one's life by using chemical substances, but without consummation<sup>10</sup>. In this perspective, it is worth mentioning that intoxication is among the three primary means used in SA<sup>13</sup>.

Intoxication is a condition of compulsory notification throughout the national territory, but the underreporting of suicide cases is still a persistent reality, in addition to the failures to report SA occurrences in many urgent and emergency care centers. This fact makes it difficult to not include actions to promote life in public management<sup>10</sup>. In this sense, toxicological information and assistance centers, as sentinel units for epidemiological surveillance of intoxication, are essential for improving the notification system and implementing suicide prevention and surveillance programs<sup>14</sup>.Furthermore, studies related to this theme are of paramount importance to know the local reality and reflect on the information generated, supporting the development of appropriate strategies for promoting life and preventing SA<sup>15</sup>.

Medicines, accompanied by pesticides and rodenticides, were the most frequent SA agents in the scientific literature<sup>16,17</sup>. Drug overdose represents a frequent form of SA, especially among women and the elderly. According to Domingues et al.<sup>18</sup>, more than one-third of the Brazilian population practices self-medication, and one of the major problems of this practice is the possibility of intoxication.

This study analyzed cases of autointoxication, considered the main circumstance for suicide attempts in our country, by collecting data in a sentinel surveillance unit for poisoning, and by the contribution to the planning of actions aimed at coping with behavior suicide and SA practiced by women. Thus, it analyzed data from epidemiological records of autointoxication reports by women registered in a toxicological assistance center.

#### **METHODS**

This is a descriptive and cross-sectional population-based study with a retrospective analysis of secondary data. Toxicological Occurrence Notification and Attendance Forms (TO Sheets) were filed in a toxicological information and assistance center, called Intoxication Control Center - CCI, located in a municipality in the southern region of Brazil (Maringá, Paraná).

The CCI is an academic unit in a teaching hospital. It works as an advisory and consultancy unit for the toxicological urgencies/emergencies area, answering telephone requests from health professionals and the lay population, with clinical-toxicological and toxicovigilance actions, intending to prevent and reduce morbidity and mortality from poisoning<sup>14</sup>.Access to TO files was authorized by the Hospital Management to which the Toxicological Assistance Center is connected.

The study population was composed of women with intoxication due to SA, notified to the CCI from January 2014 to December 2018, and recorded on TO forms, without excluding the age group. The period under study was chosen based on national indicators that showed a tendency toward an increase in autointoxication cases for SA<sup>10</sup>.

The data collection procedure was performed in three phases: retrospective search of all to TO records for the period studied, filed at the CCI (as TO records are stored according to the intoxication circumstance, and it was necessary to consult all TO records and to the separation of female toxicological events); selection of medication autointoxication forms; and compilation of the data from the TO sheets in a spreadsheet. The leading researcher conducted the record's audit from August to December 2019, and the double analysis procedure was carried to verify the records' inconsistency. Ignored or uninformed data were identified and reported in the study.

The data obtained were organized in electronic spreadsheets, developed by the researchers using Microsoft Office Excel 2013, evaluated for duplicate notification, and analyzed using simple descriptive statistics. Analysis of the variables was performed: age and education of the intoxicated person; toxic agent used to self-caused intoxication and the pharmacological class of drugs; causal factors and immediate reason for SA; comorbidities and previous SA; psychological/ psychiatric monitoring and use of continuous psychotropic drugs; and clinical outcome. Variables unfilled in or filled in as 'ignored' were considered incomplete.

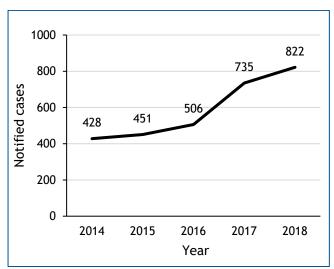
Psychotropic drugs were listed and separated into groups (antiepileptics, antiparkinsonians, psycholeptics, antipsychotics, anxiolytics, hypnotics and sedatives, psychoanaleptics, antidepressants, and psychostimulants), according to the ATCC classification (Anatomical Therapeutic Chemical Code)<sup>19</sup>. The proportions of the variable medicine were described according to the pharmacological class.

The study met the National Health Council's ethical requirements following Resolutions 466/2012-CNS and 510/2016-CNS. Because it is a population-based study and required only publicly-based data, it was not

submitted to approval by the Research Ethics Committee.

#### RESULTS

A total of 8,740 TO files were analyzed; 4,086 (46.7%) were from SA, and 2,942 (72.0%) of those involved women. The temporal analysis of notified cases is shown in Figure 1. There was an increase of 92.1% reported cases over the analyzed period.



**Figure 1** – Evolution of the notification curve for suicide attempts in women, 2014 to 2018 (Maringá, PR, Brazil).

The occurrence of SA was higher in the age group from 18 to 29 years old, representing 57.7% (1,697) of the cases. The education of women, indicated in 1,177 (73.9%) records, was completed high school for 426 (26.7%) and incomplete elementary school for 206 (12.9%). Regarding the causal factors, mental disorder was observed as the main comorbidity. Family conflicts, with the partner or another family member, were the main reasons reported, data filled in half of the forms analyzed. The most listed mental comorbidities were depression (535/33.6%) and other unspecified mental disorders (582/36.5%) (Table 1).

Previous SA occurred in 546 (34.3%) cases, but 690 (43.3%) attempted suicide for the first time. In 357 cases (22.4%), this information was not recorded in the epidemiological record. In 873 (54.8%) of the cases, the woman underwent psychological/ psychiatric follow-up, and in 1,082 (67.9%) of the cases, they used psychotropic medication for continuous use.

The toxic agent used to self-cause intoxication was the drug, being present as the only agent in 2,358 (80.1%) cases. There was also an association with drugs of abuse (4.2%) and rodenticides (0.7%) (Table 2). The predominant class of drugs was of psychotropic drugs, corresponding to 1,593 (55.2%) of the total cases, and this class was found as an isolated

drug in 937 (77.3%) (Table 3). It was observed that, of the total number of notifications for psychotropic drugs, the most used ones belonged to the group of antiepileptics followed by psychoanalytics, with 36.7% and 34.2%, respectively (Figure 2). Since 1,163 (73.0%) women ingested more than one type of drug substance in SA, the 1,593 cases analyzed resulted in a total of 2,100 drug descriptions, combined differently with each other and with the other classes mentioned in Table 3.

**Table 1** — Characteristics of the population of women involved in suicide attempts, 2014 to 2018 (Maringá, PR, Brazil).

Variable	n	%		
Age group (years)				
<18	598	20,3		
18-29	1099	37,4		
30-39	567	19,3		
40-49	429	14,6		
50-59	182	6.2		
60 or +	64	2.2		
Ignored	3	0.1		
Education				
lliterate	8	0.5		
Compl. element. school	131	8.2		
Incompl. element. school	206	12.9		
Compl. high school	426	26.7		
Incompl. high school	137	8.6		
Compl. higher education	124	7.8		
Incompl. higher education	143	9.0		
Technical education	2	0.1		
Ignored	416	26.1		
Reason				
Family discussion	177	11.1		
Discussion with partner	214	13.4		
Psychological disorder	212	13.3		
Family death	20	1.3		
Finantial difficulty	6	0.4		
Postpartum depression	1	0.1		
Other discussions	20	1.3		
Others	173	10.9		
Not informed	845	53.0		
Comorbidities				
Systemic arterial hypertension	63	4.0		
Mental disorder	582	36.5		
Mental disorder (Depression)	535	33.6		
Diabetes	26	1.6		
Respiratory diseases	3	0.2		
Others	112	7.0		
None	179	11.2		
lgnored	210	13.2		

The main medication used to self-cause intoxication was clonazepam, present in 567 (35.6%) cases and as the only agent in 275 (17.3%) cases. A large amount of use of amitriptyline (304 cases), fluoxetine (171 cases), diazepam (133 cases), and lithium (103 cases) were also observed. Table 4 shows the list of all psychotropic drugs used for autointoxication in the period studied, according to class.

The analysis of notifications of self-inflicted intoxication involving psychotropic medication pointed to hospital discharge as the outcome in most cases (77.8%). However, seven cases evolved to death: the majority in the 18 to 49 age group.

*Table 2* – Toxic agent of choice for women attempting suicide, 2014 to 2018 (Maringá, PR, Brazil).

Toxic agent	n	%
Medication	2358	80.1%
Associations involving medication	210	7.1%
Rodenticides	123	4.2%
Household Cleaning Products	67	2.3%
Pesticides for agricultural use	47	1.6%
Household pesticides	51	1.7%
Veterinary products	27	0.9%
Associations between other agents	17	0.6%
Industrial Chemical	16	0.5%
Others	10	0.3%
Plants	2	0.1%
Drug abuse	1	0.03%

#### DISCUSSION

The number of SA in women was higher than that of men throughout the analyzed period, corroborating with data found in DATASUS, referring to the years 2014 to 2018. The data presented are in accordance with the systematic review published by Felix et al.<sup>20</sup>, in which most studies found a higher prevalence of SA in women, adolescents and young people, people living alone, unemployed, and individuals with low education, similar to that described in the epidemiological profile of attempts and deaths by suicide in the country<sup>10</sup>. The prevalence of females can be related to biological, psychological/emotional or social factors, susceptibility to domestic violence, abuse of patriarchy, and problems such as gender equality, hormonal issues, and psychosocial stresses<sup>21</sup>.

The results also point to an increase in the occurrence of female autointoxication over the period studied. Since the toxicological information and assistance center investigated is a sentinel unit for epidemiological surveillance of intoxication, to reduce underreporting, its data may reflect emerging social problems linked to the use of chemical substances centralizing the information on toxicological events<sup>14</sup>. The existence of this situation is a social alert for coping

with the suicide spectrum<sup>1,4</sup>.

The results obtained regarding gender and age range corroborate with other studies, which show women and young people as groups susceptible to SA<sup>22-</sup><sup>26</sup>. Vidal et al.<sup>27</sup> found that the groups that most attempted suicide due to exogenous intoxication were adolescents and young adults, with a more significant number of female cases due to medication ingestion.

Most of the studies that discuss female SA point

to women without schooling or who studied up to elementary school; however, having studied more years did not reveal greater resilience. Similar data were obtained in a study conducted in Turkey, in which young women and women with a higher educational level were at risk of attempt and recurrences<sup>28</sup>. Other studies reported a predominance of elementary education among female victims, suggesting low education as a risk factor in SA<sup>22,23,25,29</sup>.

*Table 3* – Distribution of classes of drugs used in suicide attempts, carried out by women, 2014 to 2018 (Maringá, PR, Brazil). Values in n (%).

Class	Isolated	Associated	Total
Psychotropic	937 (77.3)	656 (39.2)	1593 (55.2)
Anti-infl./pain relievers/antipyr./antiallerg.	124 (10.2)	307 (18.3)	431 (14.9)
Antib./antifung./antivir.	15 (1.2)	324 (19.3)	339 (11.7)
Antihypertensive drugs	20 (1.7)	83 (5.0)	103 (3.6)
Phytotherapics	10 (0.8)	30 (1.8)	40 (1.4)
Others	70 (5.8)	258 (15.4)	328 (11.4)
Not informed	36 (3.0	17 (1.0)	53 (1.8)

Anti-infl. = anti-inflammatory drugs; antipyr. = antipyretic; antiallerg. = antiallergic; antib. = antibiotics; antifung. = antifungals; antivir. = antivirals.

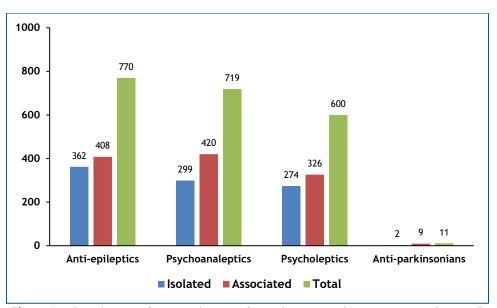


Figure 2 – Distribution of reported cases of suicide attempt by women according to the class of psychotropic drugs, 2014 to 2018 (Maringá, PR, Brazil).

Regarding the autointoxication agent, studies also refer to medication as the leading toxic agent for SA<sup>16,17</sup>. For Ribeiro et al.<sup>29</sup>, it is assumed that there is easy access to medications, rodenticides, pesticides, among others, that facilitate SA, mainly inside the victim's residence. It is necessary to define strategies to restrict the purchase of these potential agents, widely used in attempts at self-poisoning. Among the drugs, there is an emphasis on anxiolytics, especially benzodiazepines, more prescribed to women and the elderly, constituting in many countries the group of drugs most frequently used in SA, alone or in association with alcohol or other agents<sup>30</sup>. It is recognized that national health information systems do not communicate directly, with a lack of integration. This fact requires using probabilistic relationships to identify the same individual in these different sources<sup>7</sup>.

Notably the primary drugs used in SA are widely used to treat depression and anxiety, or the most common toxic agents in social life. The data obtained corroborate with other studies where the percentage participation of SA is significant in drug poisoning<sup>22,25</sup>.

**Table 4** – Psychotropics used for suicide attempt, carried out by women, 2014 to 2018 (Maringá, PR, Brazil). Values in n (%).

Psychotropic	Total	Isolated
Clonazepam	567 (35.6)	275 (17.3)
Amitriptyline	304 (19.1)	76 (4.8)
Fluoxetine	171 (10.7)	60 (3.8)
Diazepam	133 (8.3)	56 (3.5)
Lithium	103 (6.5)	13 (0.8)
Alprazolam	80 (5.0)	33 (2.1)
Velanfaxine	73 (4.6)	16 (1.0)
Sertraline	68 (4.3)	28 (1.8)
Risperidone	64 (4.0)	17 (1.1)
Escitalopram	58 (3.6)	20 (1.3)
Quetiapine	53 (3.3)	16 (1.0)
Bupropion	50 (3.1)	19 (1.2)
Clorpromazine	46 (2.9)	15 (0.9)
Zolpidem	44 (2.8)	19 (1.2)

In other studies, the prevalence of drug associations was observed, directly related to the victims' suicidal intention. This fact shows the victims' perception about associations that may be more effective for consummating  $SA^{31,32}$ .

Experts emphasize the ease in acquiring psychotropic drugs, even though the National Health Surveillance Agency (ANVISA) controls medication prescription and point out the lack of guidance and medical follow-up on the necessary treatment. Indiscriminate use does not concern the patient and the dispensing system exclusively, but several other factors, including the attitudes of health professionals<sup>33</sup>. Another aspect to be analyzed is prescribing this class of medication, which is not exclusive to psychiatrists, a fact that aggravates the scenario of indiscriminate prescription in Brazil. Studies show that physicians of different specialties prescribe psychotropic medications to patients without adequate evaluation and follow-up, showing these professionals' role in the misuse of controlled medications<sup>34,35</sup>.

The need for joint action between health professionals is evident so that the treatment is effective, and the patient is adequately assisted. It is necessary to prioritize educational actions for the correct and rational use of medicines. Prescribing professionals who work in dispensation also need guidance to be aware of the most significant SA risk population.

This panorama of information presented can guide the development of actions capable of perceiving and capturing each local practice's particularities and peculiarities to subsidize new actions to promote health and orient this population. Given the practical importance of suicide prevention strategies, the population's awareness of the rational use of medicines and health professional training is evident.

The results showed that the main drugs used in autointoxication SA in women were clonazepam, amitriptyline, fluoxetine, diazepam, and lithium, all belonging to the group of psychoactive agents. Such findings agree with studies by Nasario et al.<sup>33</sup> and Trevisan et al.<sup>36</sup>, who warn about the predominance of psychoactive drugs and their intensified use in populations, often without proper monitoring in cases of mental disorders. Clonazepam was also the preferred SA drug in a study conducted in a general emergency service in Santa Catarina<sup>37</sup>.

The risk of suicide is higher in people with mental disorders than the psychologically healthy population since international estimates show that people who die by suicide have some mental disorder, emphasizing mood and depression, anxiety disorders, and use of drugs. Also, the risk of suicide increases proportionally to the number of attempts, and the history of SA is the leading risk factor for a new attempt or suicide<sup>4</sup>.

Even considering methodological care, one of the study's limitations is the use of secondary data and the quality of the information in the notification records. The incomplete filling of the forms used by the service to record these events may have hindered the analysis of some data.

#### CONCLUSION

The study pointed to the growth of female autointoxication cases over the study period, corroborating data from the southern region of Brazil, and the higher occurrence of cases in young women, indicating the need for more equitable reception in health services for this age group. The high percentage of autointoxication with psychotropic drugs may be related to the ease of access at home and community medicalization. However, operational actions for strict control over the prescription and dispensing of medications can reduce the current rates of female autointoxication.

The practice of pharmaceutical care has marked differences in traditional practices, as it is configured as a cooperation agreement between the patient and pharmacist, seeking to optimize the therapeutic results. It can be a challenge, or just put into practice what is provided in formal training, but behaviors must be modified, incorporating in professional practice a model that allows the pharmacist to take responsibility for pharmacotherapy and act as a promoter of the rational use of medicines.

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**Conflicts of interest:** No conflicts of interest declared concerning the publication of this article.

Indications about the contributions of each author: Conception and design of the study: MBS, SAGM, MLFO Analysis and interpretation of data: MBS, MLFO, SAGM Data collection: MBS Writing of the manuscript: MBS Critical revision of the article: RSL, MLFO, SAGM Final approval of the manuscript\*: MLFO, SAGM, MBS, RSL Statistical analysis: MBS, RSL Overall responsibility: SAGM \*All authors have read and approved of the final version of the article submitted to Rev Cienc Saude.

Funding information: Not applicable.