THERAPEUTIC DRUG INTOXICATION PATTERN IN THE FEMALE POPULATION DURING THE COVID-19 PANDEMIC IN THE SOUTHEAST SERBIA

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Drugs are the second cause of human intoxication-related mortality and the first in intoxication records. About 1 in 4 individuals around the world will develop mental illness at some point in their lifetimes. Viral outbreaks, such as the coronavirus disease (COVID-19) pandemic, are associated with short-term and long-term psychological and societal distress. The current review of poisoning patterns in southeast Serbia is imperative. A retrospective cross-sectional study was carried out for two years, from March 2020 to March 2022, to evaluate the prevalence and trends of pharmaceutical drug poisonings. Retrospective data on poisoning cases was collected from the medical records section of the Toxicological Laboratory of the Institute of Forensic Medicine in Niš. Of the 310 cases, 59.35% of intoxications were observed in the female population. The most significant female predominance was observed in the age category 12–19 years (75%). In all age groups over 51, there are more female intoxications than male intoxications by a factor of more than 2.17. In age category 12–19, the most commonly detected drug class was sedatives, followed by analgesics and antiepileptics. In the population over 51, the most frequently detected drug classes in intoxication were sedatives (32.67%), followed by drugs for cardiovascular diseases (15.84%), antiepileptics (13.86%), and antidepressants (11.88%). Women over 51 and in the adolescent age category should be the target group for education and raising awareness about mental health. The prescription of sedatives should always be carefully considered, as this class of drugs is the most common in poisoning.

Acta Medica Medianae 2024;63(3):42–47.

Key words: *drugs, intoxication, COVID-19, female*

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Introduction

Drugs are the second cause of human intoxication-related mortality and the first in intoxication records. Additionally, the years of life that could be lost due to drug intoxication point to significant social and financial costs. National public health data raise awareness the rate of drug poisoning mortality is increasing in many countries (Japan, Australia, England etc.) (1–3).

Drug intoxication can be classified according to intention into intentional (self-harm, suicidal) and unintentional (accidental) intoxications. Intentional intoxication can be a consequence of poor mental health. Drugs are mostly available substances, which is why they are high on the list of substances for self-harm. On the other hand, improper drug storage, a lack of awareness of drug toxicity, and drug interactions are common reasons for unintentional poisoning (4).

About 1 in 4 individuals around the world will develop mental illness at some point in their lifetimes. Women are impacted at a higher rate than men, with 1 in 5 women experiencing a prevalent mental illness (e.g., anxiety, depression) versus only 1 in 8 men (5, 6).

More than 1 in 5 women in the United States experienced a mental health condition in the past year, such as depression or anxiety. Many mental health conditions, such as depression and bipolar disorder, affect more women than men or affect women in different ways than men (7).

Three-quarters (75%) of mental health issues are established before the age of 24, and

young women have emerged as the highest-risk group for mental ill health (8).

Viral outbreaks, such as the COVID-19 pandemic, are associated with short-term and long-term psychological and societal distress (9).

The COVID-19 pandemic has resulted in an unprecedented societal burden, from a burden on health systems, inevitable deterioration of the economy, higher rates of unemployment, global social restrictions, lockdowns, and disturbing news stories that impose considerable stress. These factors could trigger a new onset of mental health disorders or worsen previously developed mental health disorders (10).

Among many studies conducted worldwide, Kiang et al. observed an increase of 44% in the period between January 2020 and December 2020 over the same period of the previous year in California (11).

Recent research estimates that 1 in 8 children and young people experience mental health problems in England, and this record went up to 1 in 6 during the COVID-19 pandemic (12).

Epidemiological data on this important health issue are, however, scarce in Serbia. Therefore, the need for a current review of poisoning patterns in southeast Serbia is imperative. This study sought to characterize poisoning in the female population and common pharmaceutical drugs as toxic agents.

Material and Methods

The study was conducted in Niš, city in southeast Serbia which has a total population of about 2 million inhabitants. To assess the prevalence and patterns of poisonings with pharmaceutical drugs, a retrospective cross-sectional study was conducted for two years, from March 2020 to March 2022. Retrospective data on poisoning cases was collected from the medical records section of the Toxicological Laboratory of the Institute of Forensic Medicine in Niš. All cases of poisoning available in the medical records departments were included in the study. The cases were reviewed for gender, age, and identified substances. Results were statistically evaluated using Microsoft Excel.

Results

Number of Poisoning Cases

Among 510 samples sent to the toxicological laboratory of the Institute of Forensic Medicine from the University Clinical Centre of Niš, intoxications with different agents were proven in 435 cases (85.30%). Prescribed and over-the-counter (OTC) drug poisonings were reported in 323 cases (74.25%).

Age Categorization

Of 323 cases, 13 had no information on age or gender. Of the 310 cases, 59.35% of intoxications were observed in the female population, with a female-over-male ratio of 1:1.5. All cases were categorized into age and gender categories, which are presented in Figure 1.

An increased incidence of female cases was reported in all age categories, except in categories 28–35 and 36–43 years, but the most significant female predominance was observed in the age category 12–19 years (75%). In all age categories over 51 years, the ratio of intoxications in the female category and the male category is more than 2.17.
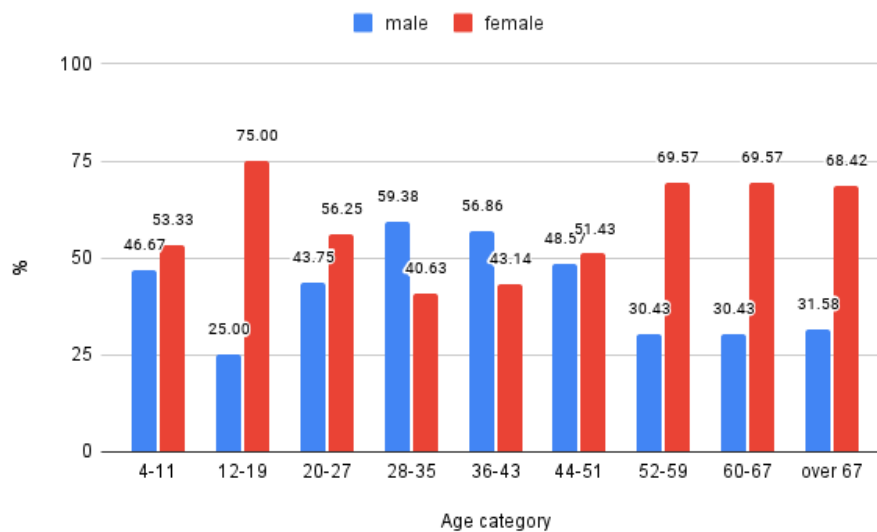

Figure 1. Distribution of intoxications among age and gender categories

Adolescent category

In age category 12–19, the most commonly detected drug class was sedatives, followed by analgesics and antiepileptics. It is presented in Figure 2. Among antidepressants, sertraline (77.78%) was proven in the highest number of cases, while in the class of sedatives, diazepam and bromazepam predominance was observed, as expected.

Multi-drug poisoning was reported in 56.67% of cases. Alcohol was detected in 4 patients, in 2 of whom it was combined with sedatives.
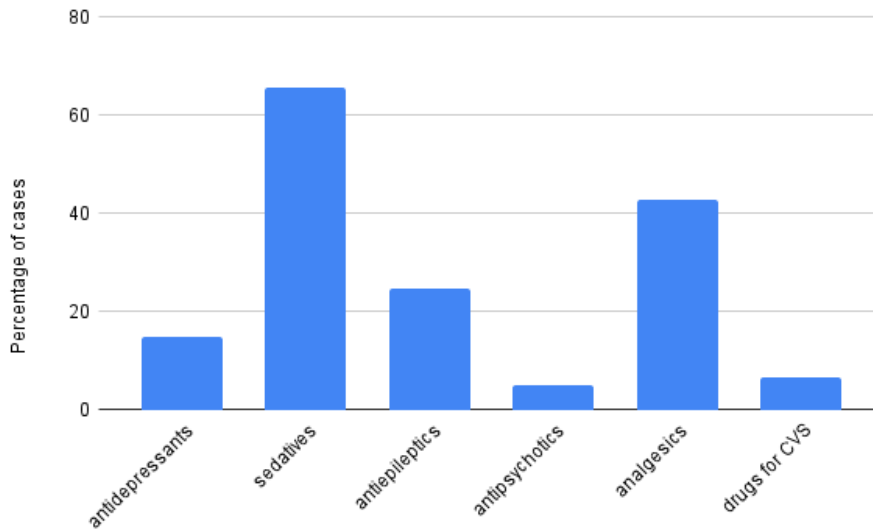

Figure 2. Distribution of drug classes in intoxications among female adolescents

Females over 51 years

Twenty point ninety-six percent of drug intoxications were observed in females older than 51 (Figure 3). The largest incidence (42.22%) was seen in age groups between 51 and 60, followed by those between 61 and 70 (33.33%). Multidrug intoxications were reported in 80% of cases, with polypsychotic drug intoxications in 37.78% of these cases. Regarding therapeutic classes, the most frequently detected drug classes in intoxication were sedatives (32.67%), followed by drugs for cardiovascular diseases (15.84%), antiepileptics (13.86%), and antidepressants (11.88%). Bromazepam and diazepam were
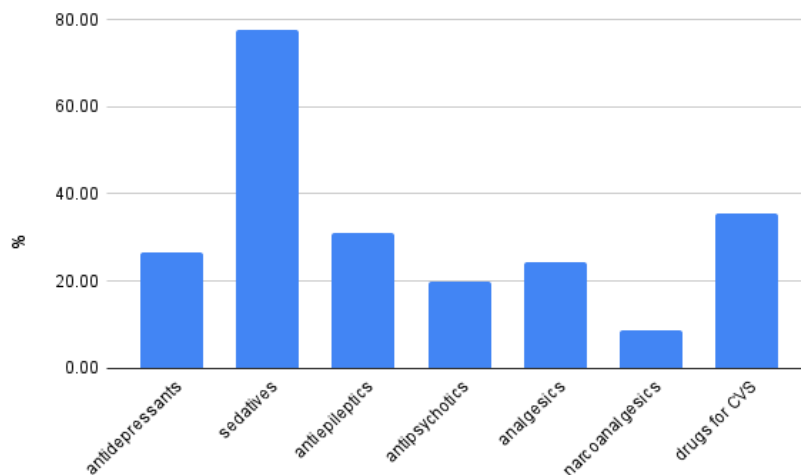

Figure 3. Distribution of drug classes in intoxications among women over 51 years

detected in 13.86% and 10.89% of all cases, respectively. Traditionally, paracetamol and ibuprofen were the most frequently detected from the group of analgesics. In all cases of ethanol intoxication, benzodiazepines were also identified.

Discussion

Many studies on this important topic are conducted worldwide. Increased incidences in the female population in age categories 12–19 and older than 51 years show an urgent situation regarding female mental health to health professionals. Drug overdoses can affect people of any age. Most childhood poisonings are accidental while poisoning in adolescents is mainly intentional (self-harm) (13).

The highest prevalence in the category 12–19 years can possibly be explained by the COVID-19 pandemic, when pupils and students were not allowed to go to school and they used to finish all their obligations online. The negative effect of COVID-19 on social life and, consequently, on the mental health of the teenage population is obvious, according to the results of this study. In a study conducted in Belgium before COVID-19, the highest prevalence of poisonings was observed in the age group 21–40 years (43.0%). These results are different from the ones that we have obtained, which can be explained by the previously mentioned COVID-19 lockdown (14).

In a study regarding acute intentional poisonings in children in Romania during the COVID-19 pandemic, a higher frequency of acute intentional poisonings was noticed in girls (65.49%) as compared to boys (34.50%), as well as in our research (15).

A high frequency of sedatives detected in samples indicates a high prevalence of usage of sedatives in Serbia. The reason for this has to be carefully considered, as this class of drugs is very often abused. Prescription and availability of sedatives should be evaluated to avoid misuse and abuse. It is essential to raise awareness about the rational prescription of sedatives in our country. The second most commonly detected group is antiepileptics. Similar results were published by the National Center for Poisoning Control at the Military Medical Academy in Belgrade: 61.7% of sedative intoxications and 19.5% of antiepileptic intoxications, compared to 30.63% of sedative intoxications and 19.97% of antiepileptic intoxications in our study. The percentage of sedative intoxications in our study is much lower than the percentage of intoxications in the evaluation of the National Poisoning Center.

Analgesics are high on the list of drugs most commonly abused, as expected, with paracetamol and ibuprofen predominating in both observed categories. It is expected, as this is an OTC drug class that is available to obtain without a prescription. Also, these drugs are present in almost all homes, so it was expected that they would be abused by adolescents. Adults have to keep drugs away from children and adolescents.

A low number of intoxications with drugs for cardiovascular diseases can be explained by the high compliance and adherence of these patients. These patients are possibly better educated about proper drug use.

In the adolescent population, fewer drug classes are noted than in the overall population. The most commonly detected drug class was also sedatives. In the study conducted by Jonassen et al. in Norway, OTC analgesics in adolescents were evaluated. They concluded that depression and anxiety are the strongest psychological predictors of weekly OTC analgesic use. Higher symptom levels and being female increase the strength of this association. Depression and anxiety also predict weekly OTC analgesic use after controlling for physiological pain (16).

In England, studies have shown in recent years, that medically attended poisonings among preschool children have reduced, but those among adolescents appear to have increased (17, 18).

Althobaiti et al. have monitored intoxication in children during the COVID-19 pandemic. They have mostly documented carbamazepine, methanol, risperidone, propranolol, and olanzapine intoxications. Benzodiazepines were the most commonly used drug (18%), which is in accordance with our results (19).

Polysubstance intoxications are very difficult for clinicians, as symptoms can be altered due to substance-drug interactions (20). An especially dangerous combination is alcohol and psychopharmaceuticals with sedative effects, which can lead to depression of the CNS and consequently be lethal (21). Also, polysubstance poisoning is demanding and time-consuming for toxicology analysts (22).

Conclusion

Our results draw attention to women's mental health. Women over 51 and in the adolescent age category should be the target group for education and raising awareness about mental health. The prescription of sedatives should always be carefully considered, as this class of drugs is the most common in poisoning. The general population must be informed about drug interactions with other substances, such as other drugs, ethanol, and illicit drugs. An important concern should be raised about the availability of prescription medications within the reach of children. This research can be used as a basis for future research and comparison to evaluate changes in patterns of intoxication in southeast Serbia.

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TROVANJA ŽENA LEKOVIMA U TOKU PANDEMIJE COVID-19 U **JUGOISTOČNOJ SRBIJI**

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     Lekovi su drugi na listi uzročnika smrtnosti povezane sa trovanjima i prvi na listi uzročnika trovanja. U proseku, jedna od četiri osobe na svetu razvije neki oblik mentalne bolesti u toku života. Pandemije, poput pandemije virusa korona 2019 (COVID-19), imaju kratkoročne, ali i dugoročne efekte na mentalno zdravlje i važan uticaj na društveni život. Trenutno nema podataka o trovanjima lekovima u toku pandemije COVID-19 na jugoistoku Srbije, pa je analiza ovog fenomena bila neophodna. U te svrhe sprovedena je retrospektivna studija preseka za period od marta 2020. do marta 2022. godine. Korišćeni su podaci toksikološke laboratorije Zavoda za sudsku medicinu u Nišu. Od 310 slučajeva intoksikacije bilo je 59,35% zabeleženih u ženskoj populaciji. Najveći broj slučajeva u ženskoj populaciji primećen je u kategoriji žena starih od 12 do 19 godina (75%). Među onima koji su imali više od 51 godine broj trovanja bio je 2,17 puta veći kod žena. Prilikom posmatranja kategorije osoba starih od 12 do 19 godina primećen je najveći broj trovanja sedativima, analgeticima i antiepilepticima. Najčešći uzročnici trovanja u populaciji koja ima više od 51 godine bili su sedativi, lekovi za lečenje kardiovaskularnih bolesti, antiepileptici i antidepresivi. S obzirom na ove rezultate, može se reći da žene u periodu adolescencije i žene starije od 51 godine treba da budu ciljna grupa prilikom edukacija i podizanja svesti o mentalnom zdravlju.

     Propisivanje sedativa uvek treba pažljivo razmotriti budući da se ova grupa lekova najčešće koristi za trovanje.

Acta Medica Medianae 2024; 63(3):42−47.

Ključne reči: *lekovi, trovanje, COVID-19, žene*