

CLINICAL PATTERN OF PSYCHOTROPIC MEDICATIONS INTOXICATION AT NATIONAL CENTRE FOR CLINICAL AND ENVIRONMENTAL TOXICOLOGY RESEARCH, CAIRO UNIVERSITY HOSPITALS

Ahmed Fathy Hussein Awad¹, Eman Abdel-Fattah El-Zohairy¹, Nevine Khairy El-Kady¹, Eman Abdel-Moneim Abel- Rasheed² and Amani Abdel-Fattah Bayoumy¹

Author Details

¹Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Cairo University, Cairo, Egypt. ²Department of Medical Pharmacology, Faculty of Medicine, Cairo University, Cairo, Egypt.

Corresponding Author: Nevine Khairy El Kady

e-mail: nevinelkady@kasralainy.edu.eg

Submit Date 2021-11-09

Revise Date 2022-12-17

Accept Date 2022-12-28

ABSTRACT

Background: In recent years, patterns of the use of psychotropic drugs have varied, with increasing rates of psychiatric presentation and diagnosis in children and adolescents (Altay A et al., 2019). Psychotropic substances intoxications are an important problem in forensic medicine and clinical toxicology. **Objectives:** This study aimed to assess clinical patterns of psychotropic medication overdose in Egypt regarding different socio-demographic factors and the most common drug category used. **Methodology:** From April to September 2018, 110 cases were submitted to the National Environmental and Clinical Toxicology Research Center at the university hospitals in Cairo. They were divided into three age groups based on their ages: group A (under 18 years old), group B (18–40 years old), and group C (beyond 40 years old). Data were examined in light of socio-demographic information, medication categories, and clinical manifestations. **Results:** The most common age group was age group B (18-40 y) (55.5%). Females were more common than males (65.5% and 34.5%, respectively). The most common manner of toxicity was suicide (39.1%). Antipsychotics represented the highest percentage of cases at 68.2%. The most common clinical manifestation was altered conscious level (91%), and the common ECG changes were sinus tachycardia (73.6%). **Conclusion:** Most cases were from age group A (18-40 years), female, single, from an urban area, without work, presenting in the first 6 hours from drug intake. The most common manner of toxicity was suicide due to social problems. The most common drug category was atypical antipsychotics, presenting with altered consciousness levels and sinus tachycardia.

KEYWORDS

Psychotropic Medications, Manners, Toxicity, Toxicology center

INTRODUCTION

Psychotropic medications are among the most widely prescribed drugs worldwide. These drugs can be subdivided into antidepressants, sedatives, antipsychotics, mood stabilizers and attention-deficit

hyperactivity disorder medications (Stephenson et al., 2013).

Suicidal attempts with psychotropic medications are common. Simply having access to these medications by prescription or prescribed access could be an important risk

factor for using these medications in overdose (Kim, J et al., 2018).

Although psychotropic medicines have been used to treat mental problems, there is a correlation between rising prescription rates and rising rates of drug overdoses committed intentionally. Different prescription practices and availability of these medicines from illicit sources account for variances in the frequency of psychiatric medications used in suicide across different nations (Corcoran et al., 2013).

Tricyclic antidepressant poisoning is a significant drug-related self-poisoning cause in affluent nations and a major source of poisoning and fatality in developing nations (Meigh, M. & Fong, J 2018). Sedative hypnotics, antipsychotics, and antidepressants are among the drugs with the highest rise in reported exposures to poison control centers between 2000 and 2015, according to the National Poison Data System in the United States (Gummin et al., 2017).

Toxicological exposures and fatalities associated with antipsychotics continued to increase in the past ten years; for example, the USA with 43,540 exposures and six deaths in 2008. Consequently, the clinician needs to be familiar with the pharmacology and toxicology of these medications (Hammad et al., 2016).

SUBJECTS AND METHODS

In this descriptive prospective study, 110 patients brought to Cairo University Hospitals' National Environmental and Clinical Toxicology Research Center between April 2018 and September 2018 were included. Data were examined in light of socio-demographic information, medication categories, and clinical manifestations. The cases were divided into accidental and suicidal exposure to sedative-hypnotics, antipsychotics, antidepressants, and mood stabilizers. A coding system was used to maintain the privacy and confidentiality of data and records.

Inclusion criteria:

This study covered the period from April 1, 2018, to September 30, 2018, and included patients of all ages hospitalized at the National Environmental and Clinical Toxicology Research Centre with a history of psychotropic drug toxicity and/or signs of such toxicity.

Exclusion criteria:

Patients with any pre-existing chronic diseases such as cardiac, hepatic and diabetes, patients who received any medical treatment before admission and patients of mixed drug ingestion were excluded.

Diagnosis:

Diagnosis of psychotropic medication poisoning was based on history and/or manifestations of toxicity. A standard sheet was conducted to record the complete clinical assessment of each patient. The following data were recorded for each patient; Socio-demographic data including age, sex, residence, marital state, date and time of admission. Past medical history, including chronic systemic illness, history of psychiatric illness or receiving any psychiatric treatment, was recorded. Toxicological data including type of drug, dose taken, manner of poisoning, and time passed from drug intake to hospital admission (delay time). Complete clinical examination was performed for all patients, including assessment of the level of consciousness by Glasgow coma scale (GCS), vital signs, general examination and systemic examination. Laboratory investigations, including sodium (Na) and potassium (K) levels and arterial blood gas analysis (ABG), were measured for all patients at admission and before treatment.

RESULTS

One hundred ten recorded psychotropic drug use, including overdoses, medical mistakes like extra doses, unintentional medication use, particularly in minors, and cases of suicide were included in the present research. The mean age group was 20.6 ± 13.4 y. The socio-demographic characteristics of the studied cases are shown in **Table 1**.

Table 1. Socio-demographic data of the studied group:

		n	%
Age groups	Group A	39	35.5
	Group B	61	55.5
	Group C	10	9.1
Gender	Female	72	65.5
	Male	38	34.5
Marital status	Married	22	20
	Unmarried	88	80
Residence	Urban	92	83.64
	Rural	18	16.36
Occupation	No	99	90
	Yes	11	10

*n: number

As shown in **Table 2**, the most common drug category was antipsychotics. Most drugs belonged to patients; most cases presented in

the first 6 hours from drug intake, The most common manner of toxicity was suicidal. Most individuals had no prior history of suicide attempts, and social issues were the most frequent triggers.

Table 2. Types of drugs and conditions of intake:

		n	%
Type of Drugs	Antipsychotics	75	68.2
	Typical antipsychotics	14	18.7
	Atypical antipsychotics	61	81.3
	Antidepressants	22	20
	Tricyclic antidepressants	10	45.45
	Selective reuptake inhibitors	10	45.45
	Others	2	9
Drug accessibility	Sedative hypnotics	12	10.9
	Mood stabilizers	1	0.9
	Family Member treatment	29	26.4
	Own (Self) treatment	48	43.6
	From Pharmacy	32	29.1
Time delay	Unknown	1	0.9
	less than 6 hours	85	77.3
	6-24 hours	16	14.5
	>24 hours	3	2.7
Previous Attempts	Unknown	6	5.5
	None	97	88.2
	Once	8	7.3
Manner Of Toxicity	More than one time	5	4.5
	Accidental	33	29.9
	Suicidal	76	69.1
Cause of intake	Social	52	47.3
	Psychological	26	23.6
	Negligence from parents	19	17.3
	Medication errors	13	11.8

*n: number

Tables 3 and 4 show that the most common manifestation was an altered consciousness level. The most common ECG

changes were sinus tachycardia. Most cases present with normal ABG and negative drug screening.

Table 3. Clinical manifestations among studied cases:

Systems	Clinical manifestations	n	%
CNS	Conscious	10	9
	Drowsy	50	45.5
	Comatose	50	45.5
	Acute Extrapyramidal Manifestations	25	22.7
Pulse	Convulsions	2	1.8
	Normal	21	19.1
Blood Pressure	Tachycardia	89	80.9
	Hypotension	27	24.5
Temperature	Normal	83	75.5
	Fever	7	6.4
Pupil	Normal	103	93.6
	Constricted	42	38.2
GIT manifestation	Normal	68	61.8
	No	104	94.5
Respiration	Yes	6	5.5
	Normal	101	91.8
Others	Abnormal	9	8.2
	Salivation	4	3.6

*n: number

*CNS: cerebral nervous system

*GIT: gastrointestinal tract

Table 4. Investigations of studied cases:

		n	%
Arterial blood gas	Normal	101	91.8
	Metabolic acidosis	3	2.7
	Respiratory acidosis	6	5.5
ECG	Normal	26	23.7
	Sinus tachycardia	81	73.6
	Wide QRS	3	2.7
Drug screening	Yes	12	10.9
	No	98	89.1

*n: number

*ECG: electrocardiogram

As shown in **Table 5**, there were a highly statistically significant relation of age regarding the manner of toxicity ($p < 0.001$), cause of

intake ($p < 0.001$) and drug accessibility ($p < 0.001$) and types of drugs ($p < 0.025$).

Table 5. Relation of age groups regarding the manner of toxicity, cause of intake, drug accessibility and types of drugs.

Manner of toxicity	Age						<i>p</i> -value
	Group A		Group B		group C		
	n	%	n	%	n	%	
Suicidal	12	30.8	56	93.3	8	80	<0.001*
Accidental	27	69.2	4	6.7	2	2	
Cause of intake	n	%	n	%	n	%	
Social	11	28.2	37	60.6	3	30	
Psychological	0	0	21	34.4	6	60	
Medication errors	9	23.1	3	5	1	10	<0.001*
Negligence	19	48.7	0	0	0	0	
Drug accessibility	n	%	n	%	n	%	
Family treatment	21	53.8	8	13.3	0	0	
His/ her treatment	11	28.2	30	50	7	70	<0.001*
From pharmacy	7	17.9	22	36.7	3	30	
Types of drugs	n	%	n	%	n	%	
Antipsychotics	33	44	34	45.3	8	10.7	
Antidepressants	5	22.7	15	68.2	2	9.1	
Sedative hypnotics	1	8.3	11	91.7	0	0	<0.025*

p < 0.05 is statistically significant

Also, there were a highly statistically significant relation of gender regarding the manner of toxicity ($p < 0.001$), cause of intake

($p < 0.001$) and drug accessibility ($p < 0.009$), as shown in **Table 6**.

Table 6. Relation of sex regarding the manner of toxicity, cause of intake and drug accessibility.

Manner of toxicity	Sex				<i>p</i> -value
	Females		Males		
	n	%	n	%	
Suicidal	60	83.3	16	43.2	
Accidental	12	16.7	21	56.8	<0.001*
Cause of intake	n	%	n	%	
Social	43	59.7	16	43.2	
Psychological	17	23.6	9	24.3	
Medication errors	3	4.2	10	27	<0.001*
Negligence	9	12.5	10	27	
Drug accessibility	n	%	n	%	
Family treatment	17	23.6	12	32.4	
His/ her treatment	27	37.5	21	56.8	
From pharmacy	28	38.9	4	10.8	<0.009*

p < 0.05 is statistically significant.

DISCUSSION

The National Centre for Clinical & Environmental Toxicology Research, Cairo University Hospital, received reports of overdoses from psychiatric drugs throughout six months from the start of April to the end of September 2018. The research included 110 instances (72 females and 38 males). Regarding gender distribution in the present study, female cases (65.5%) represented the majority of studied cases compared to male cases, which represented (34.5%). In agreement with our findings, the result from *Shahid Beheshti Drug and Poison Information Centre (DPIC), Iran*, from 2010 to 2012 where female cases were (68%), and male cases were (32%) (**Esmaily et al., 2016**). This is also approved by **Okumura, (2015)**.

Regarding residency distribution in the present study, cases from urban areas represented (84.4%), while cases from rural (20%) of cases were antidepressants, (10.9%) were sedative-hypnotics

areas represented (15.6%). This is consistent with research by **Hammad et al. (2016)** that found instances from urban regions outnumbered those from rural areas. This might be attributed to the fact that the NECTR is located in Greater Cairo, which is closer to most metropolitan regions and where many patients can go for medical guidance, as well as stigmatizing beliefs in rural areas.

Regarding marital status among cases in the present study, 80% of cases were unmarried, and 20% were married. This was consistent with research carried out at Ain Shams University Hospitals (PCCA) between June 2007 and the end of July 2008, which found that the majority of cases were single (58%) in nature (**Ghanem et al., 2013**).

Regarding types of drugs in the present study, *according* to drug categories, (68.2%) of cases were antipsychotics,

and the last category was mood stabilizers (0.9%). This disagrees with a study by **Okumura, (2015)**, who stated that the most frequent drug category was sedative-hypnotics, followed by antidepressants, then antipsychotics.

Regarding drug accessibility among cases in the current study, (44%) was belong to cases (own treatment), (29.4%) were from the pharmacy, while (and 26.6%) were belong to one family member. Medication errors in children and psychological illness in adolescents and adults may explain this. This agrees with a study conducted by **Corcoran et al., (2013)**, who stated that most suicidal cases were by their treatment (68.1%).

Regarding the manner of toxicity of cases in the current study, most cases were suicidal toxicity (69.1%), while accidental cases were (30.9%). This agrees with a study conducted by **Borg et al., (2016)**, who stated that the majority of cases were suicidal (95%) while accidental cases were (5%). This disagrees with a study conducted by **Esmaily et al (2016)**, who stated that the majority of cases were accidental toxicity (60%) while suicidal cases were (40%). Regarding the cause of intake in the current study, the most common cause of intake was social (47.3%). This may be explained as the predominance of social problems may be due to love troubles, family troubles, emotional stress or educational problems.

Regarding vital signs of cases in the present study, (80.9%) of cases presented with tachycardia, (24.5%) of cases presented with hypotension and (6.4%) of cases presented with fever. This agrees with a study conducted by **Borg et al., (2016)**, who stated that tachycardia was the most frequently noted abnormality. This was also explained by a study conducted by **Yanagawa (2010)**, who stated that the greater severity of a psychotropic drug overdose leads to either an excessive peripheral vascular dilatation or a mal-distribution of the cardiac output, and these phenomena are followed by an increased heart rate and a decreased blood pressure because of the associated circulatory insufficiency. Thus, tachycardia and/or shock also reflect the existence of circulatory insufficiency. α 1-receptor antagonism and muscarinic receptor antagonism may also contribute to tachycardia.

Peripheral vasodilatation with reflex tachycardia is commonly encountered in the resultant orthostatic hypotension (**Tan, 2009**).

Regarding CNS manifestations in the present study, the affected conscious level was the most clinical manifestation (91%) , explained by **Yanagawa, (2007)**, who stated that an overdose of psychotropic drugs usually induces an inhibitory action on the central nervous system. In our study, (22.7%) of cases were with extrapyramidal manifestations.

Regarding pupil size in the present study, (38.2%) of cases presented with abnormal pupils. This result agrees with a study by (**Yanagawa, et al., 2010**). He claimed that (16.4%) of instances had aberrant pupil size and explained this by noting that the latency of the light reflex response has previously been shown to be extended in the presence of antidepressants. Citalopram, a selective serotonin reuptake inhibitor, may cause fixed pupils by partly preventing norepinephrine reuptake and suppressing the Edinger-Westphal nucleus as a result via an action on the 2 adrenergic receptors. Antipsychotics have a 2-adrenergic antagonistic effect. Additionally, they could lessen the pupillary light reaction. The aberrant pupil responsiveness brought on by a chemical overdose might cause severe drowsiness.

Regarding additional signs in the research, salivation was evident in (3.6%) of the patients. According to research by Godoy (2012), clozapine (a typical APS) stimulates muscarinic acetylcholine receptors of subtype M1 to cause a long-lasting, low-level discharge of saliva from the parotid and submandibular glands. The secretory response to the two medications is additive when administered together. Additionally, clozapine increases saliva production via the glands' B-adrenergic receptors. On the other hand, the antagonistic effect on glandular muscarinic M3 receptors and 1- adrenergic receptors, respectively, reduces saliva flow in response to the activation of the parasympathetic and sympathetic innervations.

CONCLUSION

Most cases were from age group A (18-40 years), female, single, from an urban area,

without work, presenting in the first 6 hours from drug intake. The most common manner of toxicity was suicide due to social problems. The most common drug category was atypical antipsychotics, presenting with altered conscious levels and sinus tachycardia.

RECOMMENDATIONS

We should implement an education program for patients, parents, and healthcare professionals who work with psychiatric patients to lower the risk of poisoning from these medications. For example, we should limit the number of medications prescribed for short periods and implement strong patient monitoring to lower the risk of hospital admission, mortality, and morbidity.

CONFLICTS OF INTEREST

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

REFERENCES

- Altay A, M., Bozatlı, L., Demirci Şipka, B., & Görker, I. (2019): Current Pattern of Psychiatric Comorbidity and Psychotropic Drug Prescription in Child and Adolescent Patients. *Medicina*, 55(5): 159.
- Borg, L., Julkunen, A., Rørbaek Madsen, K., Strøm, T. & Toft, P. (2016): Antidepressant or Antipsychotic Overdose in the Intensive Care Unit - Identification of Patients at Risk. *Basic & clinical pharmacology & toxicology*, 119(1): 110-4.
- Corcoran, P., Heavey, B., Griffin, E., Perry, I.J. & Arensman, E. (2013): Psychotropic medication involved in intentional drug overdose: implications for treatment. *Neuropsychiatry*, 3(3): 285.
- Esmaily, A., Alavian, G., Afzal, G., & Ghane, T. (2016): Psychotropic Agents Poisoning: Analysis of Cases Reported to Shahid Beheshti Drug and Poison Information Center. *International Journal of Medical Toxicology and Forensic Medicine*, 6(1): 7-11.
- Godoy, T., Riva, A., & Ekström, J. (2012): Atypical antipsychotics—effects of amisulpride on salivary secretion and on clozapine- induced sialorrhea. *Oral diseases*, 18(7): 680-691.
- Gummin, D. D., Mowry, J. B., Spyker, D. A., Brooks, D. E., Fraser, M. O., & Banner, W. (2017): Annual report of the american association of poison control centers' national poison data system (NPDS): 34th annual report. *Clinical toxicology*, 55(10): 1072-1254.
- Hammad, S.A.E.H., Girgis, N.F., Amin, S.A.Z., Zanaty, A.W. & Hatab, H. M.E.K.A., (2016): Evaluation of acute antipsychotic poisoned cases. *Menoufia Medical Journal*, 29(4): 1116.
- Kim, J., Kim, M., Kim, Y.R., Choi, K.H., & Lee, K.U. (2015): High prevalence of psychotropics overdose among suicide attempters in Korea. *Clinical psychopharmacology and neuroscience*, 13(3): 302.
- Meigh, M. & Fong, J. (2018): Amitriptyline overdose in an unconsciousness patient with QRS widening on EKG. *Visual Journal of Emergency Medicine*, 10: 106-107.
- Okumura, Y., Tachimori, H., Matsumoto, T., & Nishi, D. (2015): Exposure to psychotropic medications prior to overdose: a case-control study. *Psychopharmacology*, 232(16): 3101-3109.
- Stephenson, C.P., Karanges, E. & McGregor, I.S. (2013): Trends in the utilisation of psychotropic medications in Australia from

2000 to 2011. Australian & New Zealand Journal of Psychiatry, 47(1): 74-87.

Tan, H.H., Hoppe, J. & Heard, K. (2009): A systematic review of cardiovascular effects after atypical antipsychotic medication overdose. The American Journal of Emergency Medicine, 27(5): 607–616.

Yanagawa, Y., Miyazaki, M., & Sakamoto, T. (2010): Relationship between abnormal pupillary reactivity and the outcome of a psychotropic drug overdose. The American

journal of emergency medicine, 28(6): 703-707.

Yanagawa, Y., Sakamoto, T. & Okada, Y. (2007): Recovery from a psychotropic drug overdose tends to depend on the time from ingestion to arrival, the Glasgow Coma Scale, and a sign of circulatory insufficiency on arrival. The American journal of emergency medicine, 25(7): 757-761.

الملخص العربي

النمط الإكلينيكي للتسمم بجرعات زائدة من الأدوية النفسية في المركز القومي للسموم ال كلينيكية والبيئية بمستشفيات جامعة القاهرة

د/ أحمد فتحي حسين عوض^١ ، أ.د./ ايمان عبد الفتاح محمد الزهيري^١، د/نيفين خيرى القاضي^١، أ.د./ ايمان عبد المنعم عبد
الرشيد^٢، د/ أماني عبد الفتاح بيومي^١

^١ قسم الطب الشرعي والسموم الاكلينيكية كلية الطب جامعة القاهرة

^٢ قسم الفارماكولوجي كلية الطب جامعة القاهرة

يمكن أن تكون الجرعات الزائدة من الادوية متعمدة (انتحارة) أو غير مقصودة ، و كلاهما يمثل جزءاً متامياً من العبء العالمي للإصابات. الأدوية النفسية هي الأكثر شيوعاً. بسبب اختلاف توافر الأدوية ، تختلف هذه الأنماط وأسباب الجرعة الزائدة من الأدوية حسب الموقع والفترة الزمنية. الأدوية النفسية هي من بين الأدوية الموصوفة على نطاق واسع في جميع أنحاء العالم. يمكن تقسيم هذه الأدوية إلى مضادات الاكتئاب ومزيلات القلق، والمهدئات، ومضادات الذهان، ومثبتات المزاج، وأعراض اضطراب نقص الانتباه وفرط الحركة.

تهدف الدراسة الحالية إلى تقييم نمط حالات الجرعات الزائدة من الادوية ذات المؤثرات النفسية التي تم إدخالها إلى المركز القومي للسموم الإكلينيكية والبيئية خلال فترة ستة أشهر من بداية أبريل وحتى نهاية سبتمبر 2018 فيما يتعلق بالعقار الأكثر شيوعاً والعوامل الاجتماعية والديموغرافية المختلفة في محاولة لتحديد الافراد الاكثر عرضة للمخاطر في مجتمعنا.

أجرت هذه الدراسة المستقبلية على مائة وعشرة حالات من كلا الجنسين شملت جميع الفئات العمرية. وقد حضر مركز السموم بكلية الطب جامعة القاهرة خلال الفترة من 2018/4/1 إلى 2018/9/30. تم تصنيفهم إلى ٣ فئات عمرية ؛ الفئة العمرية (أ) (اقل من ١٨ سنة) و كانت نسبتها (٣٥,٥٪) والفئة العمرية ب (١٨ - ٤٠ سنة) و كانت نسبتها (٥٥,٥٪) والفئة العمرية ج (اكثر من ٤٠ سنة) نسبتها (٠,٩٪). معظم الحالات إناث (٦٥,٥٪)، من المناطق الحضرية (٨٤,٤٪)، حالات فردية (٧٠٪)، ولم يكن لديها عمل (٩٠٪).

معظم الحالات التي تم عرضها خلال الساعات الست الأولى من تناول الأدوية (٧٧,٣٪)، وكانت منتحرة (٣٩,١٪)، و غالبية الأدوية كانت تخص الحالات (٤٠٪). كانت فئة الأدوية الأكثر شيوعاً هي مضادات الذهان بنسبة (٦٨,٢٪) يليها مضادات الاكتئاب بنسبة (٢٠٪) ثم المنومات المهدئة بنسبة (١٠,٩٪) وأقلها مثبتات المزاج بنسبة (٠,٩٪).

كان الاضطراب في درجة الوعي هو الاكثر شيوعا بين الحالات بنسبة (٩١٪). و كانت تغيرات رسم القلب الأكثر شيوعا هي عدم انتظام دقات القلب الجيبي بنسبة (٦٣,٧٪).