OXFORD Toxicology Research

Toxicology Research, 2024, **13**, 1–8
https://doi.org/10.1093/toxres/tfae193
Paper

Assessment of the pattern, severity, and outcomes of acute mood stabilizer drug poisoning

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Background: Mood-stabilizer drugs are associated with a considerable incidence of morbidity and mortality.
Aim: This study aimed to assess the pattern, severity, and outcomes of poisoning with acute mood stabilizer drugs among admitted patients to Tanta University Poison Control Center, Egypt between January 2021 and September 2023.
Patients and methods: This cross-sectional study was conducted in patients with acute mood stabilizer drug poisoning. Data from electronic medical records were observed. The poison severity score (PSS) assessed the severity of the patients. Primary outcomes were the pattern and severity assessment. Secondary outcomes included the incidence of mortality, the need for intensive care unit (ICU) admission, the need for intubation and mechanical ventilation, the incidence of complications, and the duration of hospital stay.
Results: A total of 67 patients with acute poisoning of mood stabilizers were included. Poisoning with carbamazepine accounted for 58.2% of all mood stabilizers, followed by valproic acid (29.8%), lithium (7.5%), and lamotrigine (4.5%). The highest proportion of patients were young, females, with intentional poisoning and were classified as mild to moderate poisoning based on PSS. There were significant statistical associations between PSS and the need for ICU admission, development of complications, and length of hospital stay among poisoned patients with carbamazepine or valproic acid.
Conclusions: Carbamazepine poisoning and valproic acid poisoning were the most common mood stabilizers compared to lithium and lamotrigine poisoning. In acute carbamazepine and valproic acid poisoning, the PSS is a relevant score that could predict the need for ICU admission, the development of complications, and the duration of hospital stays.

Key words: Mood stabilizer drug poisoning; Carbamazepine poisoning; Valproic acid poisoning; Lithium poisoning; Lamotrigine poisoning; Poisoning severity score.

Introduction

Mood stabilizers are typically used to treat bipolar and schizoaffective disorders. However, these medications are also used as adjunctive therapies for schizophrenia, depression, and several other psychiatric disorders[1,2] They are used to achieve and maintain euthymia, which is a state of no mania and no depression (euthymia).[2]

Mood stabilizer drugs are various groups of medications including antiepileptic medications. In the 1960s and 1970s, the first generation of mood stabilizer drugs were introduced. These included lithium, valproate, and carbamazepine.[3] Lithium has been a cornerstone in the treatment of bipolar disorder for more than 50 years. Second-generation mood-stabilizing drugs include a novel anticonvulsant and lamotrigine.[3] Carbamazepine, valproic acid, lithium, and lamotrigine are the most used drugs to stabilize mood and prevent recurrences of suicidal attempts.[4,5]

More than 90% of individuals who commit suicide have psychiatric diseases.[6] The most common psychiatric diseases related to suicide or serious suicide attempts are mood disorders.[7] Most psychiatric patients usually use their prescribed psychiatric medication for suicidal attempts by intentional oral intake, which is the commonest mode and route of poisoning.[8,9]

Mood stabilizers possess intricate pharmacodynamic profiles that engage many receptors, ion channels, and secondary messenger systems. Carbamazepine is an autoinducer during the first month of treatment and is a recognized inducer of hepatic cytochrome oxidase (CYP) enzymes. Valproic acid metabolism is mainly by glucuronide conjugation by UGT and mitochondrial β-oxidation. CYP metabolism accounts for 10% of valproic acid metabolism, mainly via CYP2C9. Lamotrigine is mainly degraded by glucuronidation to three primary metabolites. A low autoinduction of 17% has been observed with lamotrigine serum concentrations considered clinically negligible.[10]

The poisoning with mood stabilizing drugs is associated with marked morbidity and mortality.[11] A paucity of research has examined the extent of the poisoning of these substances and their probable consequences. Furthermore, the exact total number and severity of mood stabilizer drug poisoning that occurs in Egypt are not known. Recognition of the nature, severity, and outcome of acute mood stabilizer drug poisoning for each country is necessary to determine the characteristics and magnitude of the problem according to which adequate preventive measures and management techniques can be taken.[12]

Poisoning Severity Score (PSS) is a scoring system developed in Europe in the 1990s to identify the most severe symptomatology and grade the severity of poisoning. Thus, the severity grade is determined by the most serious symptoms or signs.[13] The PSS has been used to assess the severity and outcomes of various poisons[14–17] Nevertheless, few studies evaluated the

Received on 4 July 2024; revised on 30 October 2024; accepted on 12 November 2024

relation between the severity of mood stabilizers by PSS and the outcomes. It is therefore essential that both clinical practitioners and regulatory authorities assess the severity of mood stabilizer poisoning. Thus, this study aimed to assess the pattern, severity, and outcomes of acute mood stabilizer drug poisoning by using PSS among admitted patients at Tanta University Poison Control Center.

Patients and methods

Study design, setting, and date

This cross-section study was carried out on the admitted patients at Tanta University Poison Control Center (TUPCC), Emergency Hospital, between the start of January 2021 and the end of September 2023.

Participants

All patients of both sexes and different ages with acute poisoning of carbamazepine, valproic acid, lithium, and lamotrigine were included in this study. Poisoned patients with co-ingestion, missing clinical data, referred patients with previous medical intervention, patients with accompanying chronic diseases, such as hepatic, cardiac, and renal diseases, and patients with head trauma were excluded.

Data collection

Acutely poisoned patients were managed by the attending clinical toxicologist. This included diagnosis, rescue, and supportive therapy as well as appropriate decontamination procedures. The intensive care physician decided to admit the patients to the intensive care unit (ICU), primarily for hemodynamic stabilization, respiratory support, mechanical ventilation, and meticulous care of comatose patients.

Patient data were obtained from the electronic records of the TUPCC archives, which are part of the hospital's medical records. We extracted data based on accessible, clinical, and laboratory-relevant characteristics. Comprehensive demographic and toxicologic data including age and sex, type of poison, route, amount, mode, past medical diseases, and delay time from exposure to hospitalization were collected for all enrolled patients. Diagnosis of acute poisoning of carbamazepine,[18] valproic acid,[19] lithium[20] and lamotrigine[21] was based mainly on the history and clinical manifestations.

Vital signs, including arterial blood pressure, pulse rate, respiration rate, and body temperature, were evaluated in accordance with reference ranges.[22] The attending clinical toxicologists, trained in Glasgow Coma Scale (GCS) assessment, evaluated the consciousness level. We obtained the first reported assessment of the vital signs and the GCS or modified GCS for children[23] at the time of hospital admission.

The initial values from the routine laboratory studies upon admission were extracted. The parameters assessed included the arterial blood's acid–base balance (pH: reference range 7.35–7.45), calculated bicarbonate concentration in arterial blood (HCO3: reference range 22–26 mEq/L), measured partial pressure of carbon dioxide in arterial blood (PaCO2: reference range 35–45 mmHg), arterial oxygen saturation (SaO2: reference range 95%–100%), serum sodium concentrations (reference range 135 to 145 mmol/L), serum potassium concentrations (reference range 3.5 to 5.5 mmol/L), serum magnesium concentrations (reference range 1.7 to 2.2 mg/dL) and random blood glucose test (reference range 80 to 140 mg/dL). Coagulation profile, alanine transaminase (ALT), aspartate transferase (AST), serum blood urea, creatinine, and complete blood count were assessed according to reference ranges.[24] In addition, data from an electrocardiogram (ECG) was assessed. The incidence of mortality, the need for intensive care unit (ICU) admission, the need for intubation and mechanical ventilation, the incidence of complications, and the duration of hospital stay were also extracted.

Calculation of poison severity score

The severity of the poisoning was assessed on admission and 24 h later using the Poison Severity Score (PSS). The highest score recorded was designated as the final PSS. The severity of poisoning was classified into five levels. The first level had no symptoms and signs of poisoning (none), while the second level had mild, transient, and spontaneously resolving symptoms (mild). The third level had prolonged symptoms (moderate), while the fourth level had life-threatening symptoms (severe); the fifth level had fatal symptoms, wherein death occurred.[25]

Outcomes

The main measures were assessment of the pattern and severity using PSS. Secondary outcomes included the incidence of mortality, the need for intensive care unit (ICU) admission, the need for intubation and mechanical ventilation, the incidence of complications, and the duration of hospital stay.

Ethical consideration

The present study was carried out following approval of the medical research ethics committee of the Tanta Faculty of Medicine (Approval code: 36264MS97/3/23). We protected patients' privacy and anonymity, and data were allowed only for the investigators. Written informed consent was not required as the study was retrospective.

Statistical analysis

The collected data were organized, entered on an Excel sheet, and statistically analyzed using SPSS software statistical computer package for Windows, version 25 (IBM Corp., Armonk, N.Y., USA). The Shapiro–Wilk for normality test was performed to assess the distribution of the quantitative data. Normally distributed quantitative data were represented by mean, Standard deviation, and range. Abnormally distributed quantitative data were represented by mean, Standard deviation, range, median and interquartile ranges (IQR) (25th–75th percentiles). Qualitative data were presented by number and percent. The Pearson chi-square test (χ^2) and Kruskal-Wallis test were used to determine whether there was a significant association between different variables.

Results

During the study period, 74 patients with acute mood stabilizer drug poisoning were admitted to the TUPCC. Two patients were excluded due to co-ingestion of other xenobiotics, two patients had chronic liver failure, two patients were referred from other hospitals with previous treatment before hospitalization, and one patient had chronic kidney disease. Sixty-seven patients were included in the current study. Patients with carbamazepine poisoning represented 58.2% of the patients. In comparison, valproic acid poisoning represented 29.8% of the patients, followed by lithium poisoning, which represented 7.5% of the patients, and lamotrigine poisoning, which represented 4.5% of the patients (Fig. 1).

Table 1 shows the highest percentage of poisoned patients with carbamazepine or valproic acid aged under 20 years, while

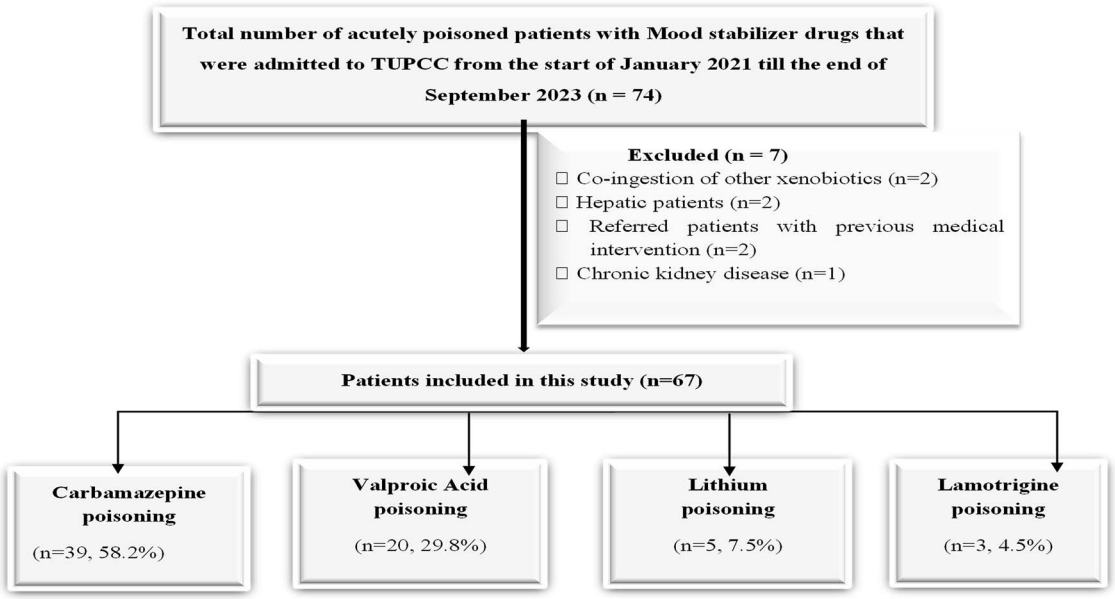

Fig. 1. Flow chart of the acutely poisoned patients with mood stabilizer drugs.

lithium poisoning was common among patients over 30 years and lamotrigine was common among patients aged between 21–30 years. In all groups, most of the patients were females with intentional poisoning with an early arrival to the hospital within the first 5 h post-ingestion and were vitally stable. According to the GCS, about a third of the patients with carbamazepine poisoning (33.3%) and valproic acid poisoning (30.0%) were severely impaired consciousness meanwhile all lithium-poisoned patients had mildly disturbed consciousness, and two-thirds of lamotrigine were moderately disturbed consciousness. Based on PSS, severely poisoned patients accounted for 7.7% of carbamazepine poisoning and 40.0% of valproic acid poisoning. No severe patients with lithium and lamotrigine poisoning were reported (Table 1).

Arterial blood gases showed that the majority of patients with carbamazepine and valproic acid poisoning had different types of acid–base disturbances. In contrast, the majority of lithium and lamotrigine had normal acid–base balance. All poisoned patients with mood stabilizer drugs had normal serum sodium, magnesium, urea, and creatinine. Hypokalemia was the only electrolyte disturbance that occurred in 20.0% of carbamazepine poisoning, 20.5% of valproic acid poisoning, and 40.0% of lithium poisoning. Complete blood counts were normal in most of the carbamazepine and valproic acid poisoning and all poisoned patients with lithium and lamotrigine. Most poisoned patients with mood stabilizer drugs had normal ECG but hyperacute T wave occurred in 12.8% of carbamazepine, 15.0% of valproic acid, and 33.3% of lamotrigine poisoning (Table 2).

In terms of outcomes, no deaths from carbamazepine, lithium, and lamotrigine poisoning were reported. Three patients with valproic acid poisoning (15.0%) died after initial assessment in the wards and before ICU admission. The ICU admission was required in 30.8% of carbamazepine-poisoned patients and 30.0% of valproic acid-poisoned patients. Meanwhile, all patients with lithium and lamotrigine poisoning did not require ICU admission, urgent endotracheal intubation, or mechanical ventilation. Chest infections complicated 17.9% of patients with carbamazepine poisoning and 29.4% of patients with valproic acid poisoning. The median hospital stays were less than 12 h among carbamazepine, valproic acid, and lithium poisoning while nearly 24 h were in poisoned patients with lamotrigine poisoning (Table 3).

In patients with carbamazepine or valproic acid poisoning, PSS was statistically associated with the need for ICU admission, the development of chest complications, and the duration of hospital stays (Table 4).

Discussion

Mood stabilizer drugs are commonly utilized in the treatment of various epileptic and psychiatric disorders. Investigating the patterns, characteristics, and outcomes of mood stabilizer drug poisoning is important for physicians and healthcare professionals to make informed decisions.[3] However, there has been a paucity of research in this area. So, this study aimed to assess the pattern, severity, and outcomes of acute poisoning with mood stabilizer drugs among admitted patients to the Tanta University Poison Control Center, Egypt.

Our main findings revealed that carbamazepine and valproic acid poisoning were the most frequent mood stabilizer drugs followed by lithium and lamotrigine. According to PSS, most patients were classified as mild and moderate poisoning with favorable outcomes. Similarly, Basyoni and colleagues[26] reported that carbamazepine was the most commonly ingested antiepileptic drug (73.2%), followed by valproic acid (14.2%), and only one reported patient with lamotrigine poisoning. Another report from Ain Shams University Poison Control Center in Egypt documented that carbamazepine poisoning accounted for 1.7% of all poisoned patients, and lithium poisoning accounted for 0.03%.[27] In Turkey, Günaydın and colleagues reported that the prevalence of carbamazepine was 40% of patients, and valproic acid was 27.4% of antiepileptic-poisoned patients.[28]

The present study indicates that the elevated incidence of carbamazepine and valproic acid overdoses in comparison to other mood stabilizers is attributable to its extensive range of indications, particularly for patients with epilepsy. Furthermore, lithium poisoning is not a common prescription due to concerns

Table 1. Socio-demographic, toxicological, vital data, Glasgow coma score, and poison severity score among acutely poisoned patients with mood stabilizer drugs (Total $n = 67$ patients).

		Carbamazepine ($n = 39$)	Valproic acid ($n = 20$)	Lithium ($n = 5$)	Lamotrigine ($n = 3$)
Age, years, n (%)	0–20	29 (74.4%)	11 (55%)	1 (20.0%)	1 (33.3%)
	21–30	3 (7.7%)	4 (20.0%)	1 (20.0%)	2 (66.7%)
	> 30	7 (17.9%)	5 (25.0%)	3 (60.0%)	0 (0.0%)
	Min. - Max.	1.5–50	0.5–42	17–54	18–25
Sex, n (%)	Male	16 (41.0%)	8 (40.0%)	1 (20.0%)	0 (0.0%)
	Female	23 (59.0%)	12 (60.0%)	4 (80.0%)	3 (100.0%)
Mode of poisoning, n (%)	Intentional	23 (59.0%)	12 (60.0%)	4 (80.0%)	3 (100.0%)
	Unintentional	16 (41.0%)	8 (40.0%)	1 (20.0%)	0 (0.0%)
Medical disease, n (%)	No	24 (61.5%)	8 (40.0%)	1 (20.0%)	0 (0.0%)
	Epilepsy	7 (17.9%)	8 (40.0%)	0 (0.0%)	0 (0.0%)
	Psychiatric disorders	4 (10.3%)	2 (10.0%)	3 (60.0%)	1 (33.3%)
	Combined epileptic and psychiatric disorders	4 (10.3%)	2 (10.0%)	1 (20.0%)	2 (66.7%)
Amount of drug exposure, mg	Min. – Max.	80.0–80000.0	40.0–30000.0	1600.0–4800.0	1000.0–3000.0
	Median (IQR)	1600.0 (400.0–2000.0)	1200.0 (375.0–6000.0)	2000.0 (1600.0–4000.0)	2000.0 (1000.0–3000.0)
Delay time, hours, n (%)	1–5 hours	25 (64.1%)	14 (70.0%)	3 (60.0%)	3 (100.0%)
	>5–20 hours	13 (33.3%)	4 (20.0%)	1 (20.0%)	0 (0.0%)
	>20 hours	1 (2.6%)	2 (10.0%)	1 (20.0%)	0 (0.0%)
Pulse rate, n (%)	Normal	32 (82.1%)	11 (55.0%)	2 (40.0%)	1 (33.3%)
	Tachycardia	6 (15.4%)	8 (40.0%)	2 (40.0%)	2 (66.7%)
	Bradycardia	1 (2.6%)	1 (5.0%)	1 (20.0%)	0 (0.0%)
Blood pressure, n (%)	Normal	36 (92.3%)	15 (75.0%)	4 (80.0%)	3 (100.0%)
	Hypotensive	2 (5.1%)	3 (15.0%)	1 (20.0%)	0 (0.0%)
	Hypertensive	1 (2.6%)	2 (10.0%)	0 (0.0%)	0 (0.0%)
Respiratory rate, n (%)	Normal	38 (97.4%)	15 (75.0%)	5 (100.0%)	3 (100.0%)
	Tachypnea	1 (2.6%)	4 (20.0%)	0 (0.0%)	0 (0.0%)
	Bradypnea	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
Temperature, n (%)	Normal	37 (94.9%)	17 (85.0%)	5 (100.0%)	3 (100.0%)
	Hypothermia	2 (5.1%)	3 (15.0%)	0 (0.0%)	0 (0.0%)
Oxygen saturation by pulse oximeter, n (%)	Normal	35 (89.7%)	18 (90.0%)	5 (100.0%)	3 (100.0%)
	Low	4 (10.3%)	2 (10.0%)	0 (0.0%)	0 (0.0%)
Glasgow Coma Score, n (%)	Mild (13–14)	21 (53.8%)	13 (65.0%)	5 (100.0%)	1 (33.3%)
	Moderate (9–12)	5 (12.8%)	1 (5.0%)	0 (0.0%)	2 (66.7%)
	Severe (3–8)	13 (33.3%)	6 (30.0%)	0 (0.0%)	0 (0.0%)
Poison Severity Scores, n (%)	Mild	21 (53.8%)	10 (50.0%)	4 (80.0%)	1 (33.3%)
	Moderate	15 (38.5%)	2 (10.0%)	1 (20.0%)	2 (66.7%)
	Severe	3 (7.7%)	8 (40.0%)	0 (0.0%)	0 (0.0%)

n: Number; Min. – Max.: Minimum – Maximum; IQR: interquartile range.

about its potential adverse effects and having a narrow therapeutic index[29,30] On the contrary, the 40th annual report of the American Association of Poison Control Centers reported that lamotrigine was the most common drug, representing 0.5% of patients. Carbamazepine and valproic acid poisoning each represented 0.3%, while lithium poisoning was reported in 0.2% of all poisoned patients.[12] The incidence of poisoning varies between poison control centers, with socioeconomic factors and drug availability influencing the observed patterns. In Egypt, the mean annual cost of carbamazepine is less than that of valproic acid and lamotrigine.[31]

In the present study, the majority of mood stabilizer drug-poisoned patients were young females with oral intentional poisoning. Females are more vulnerable to suicidal behavior due to gender-related vulnerability to psychopathology and psychosocial stressors.[32] Meanwhile, males tend to prefer violent methods of suicide.[33] Additionally, the World Health Organization (WHO) has indicated that approximately 50% of all mental health disorders manifest before the age of 14. Moreover, the prevalence of mental disorders may be attributed to the mounting stressors of the modern era, particularly among young adults.[34] Contrary, the American Poison Control Center's 40th annual report showed that the majority of carbamazepine, valproic acid, and lamotrigine poisoned patients aged above 20 years old and were unintentionally poisoned.[12]

In the present study, epileptic and psychiatric patients represented notable proportions. This lends support to the proposition that the increased prescriptions of carbamazepine and valproate have resulted in a rise in poisonings due to the drugs becoming more readily accessible to a population at elevated risk of self-harm.[35] Where, Farghaly and colleagues[36] estimated the prevalence of epilepsy in children and adolescents in Upper Egypt to be 9.7 per 1,000. A significant proportion of individuals with epilepsy also experience comorbid psychiatric disorders, such as depression. These individuals are at an increased risk of suicidal ideation and self-poisoning.[37] Moreover, although mood stabilizers are efficacious in preventing suicidal behavior in patients with bipolar disorders, it may take several weeks to months for the

Table 2. Laboratory investigations and electrocardiogram (ECG) among acutely poisoned patients with mood stabilizer drugs (Total $n = 67$ patients).

Variable, n (%)		Carbamazepine ($n = 39$)	Valproic acid ($n = 20$)	Lithium ($n = 5$)	Lamotrigine ($n = 3$)
Arterial Blood gases	Normal	18 (46.2%)	6 (30.0%)	3 (60.0%)	2 (66.7%)
	Respiratory alkalosis	7 (17.9%)	2 (10.0%)	0 (0.0%)	1 (33.3%)
	Metabolic acidosis	2 (5.1%)	4 (20.0%)	2 (40.0%)	0 (0.0%)
	Metabolic alkalosis	1 (2.6%)	4 (20.0%)	0 (0.0%)	0 (0.0%)
	Mixed disorder	11 (28.2%)	4 (20.0%)	0 (0.0%)	0 (0.0%)
Serum Potassium	Normal	31 (79.5%)	16 (80.0%)	3 (60.0%)	3 (100.0%)
	Hypokalemia	8 (20.5%)	4 (20.0%)	2 (40.0%)	0 (0.0%)
Liver enzymes	Normal	38 (97.4%)	13 (65.0%)	4 (80.0%)	3 (100.0%)
	Increased ALT	1 (2.6%)	2 (10.0%)	1 (20.0%)	0 (0.0%)
	Increased AST	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
	Increased both ALT and AST	0 (0.0%)	4 (20.0%)	0 (0.0%)	0 (0.0%)
Random blood sugar	Normal	38 (97.4%)	18 (90.0%)	5 (100.0%)	3 (100.0%)
	Hyperglycemia	1 (2.6%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
	Hypoglycemia	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
Hb	Normal	23 (59.0%)	13 (65.0%)	5 (100.0%)	3 (100.0%)
	Low	16 (41.0%)	7 (35.0%)	0 (0.0%)	0 (0.0%)
RBCs	Normal	37 (94.9%)	20 (100.0%)	5 (100.0%)	3 (100.0%)
	Low	2 (5.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
WBCs	Normal	35 (89.7%)	17 (85.0%)	5 (100.0%)	3 (100.0%)
	High	4 (10.3%)	3 (15.0%)	0 (0.0%)	0 (0.0%)
Platelets	Normal	38 (97.4%)	20 (100.0%)	5 (100.0%)	3 (100.0%)
	Low	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Electrocardiogram (ECG)	Normal	31 (79.5%)	15 (75.0%)	5 (100.0%)	2 (66.7%)
	Hyperacute T	5 (12.8%)	3 (15.0%)	0 (0.0%)	1 (33.3%)
	Sinus bradycardia, hyperacute T	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
	Sinus tachycardia	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
	Elevated ST segment, hyperacute T	2 (5.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Sinus tachycardia, hyperacute T	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

ALT: Alanine transaminase; AST: Aspartate transaminase; n: Number; Hb: hemoglobin; RBCs: Red blood cells; WBCs: White blood cells.

Table 3. Outcomes among acutely poisoned patients with mood stabilizer drugs (Total $n = 67$ patients).

Variable		Carbamazepine poisoning ($n = 39$)	Valproic acid poisoning ($n = 20$)	Lithium ($n = 5$)	Lamotrigine ($n = 3$)
Death, n (%)	No	39 (100.0%)	17 (85.0%)	5 (100.0%)	3 (100.0%)
	Yes	0 (0.0%)	3 (15.0%)	0 (0.0%)	0 (0.0%)
Need for ICU admission, n (%)	No	27 (69.2%)	14 (70.0%)	5 (100.0%)	3 (100.0%)
	Yes	12 (30.8%)	6 (30.0%)	0 (0.0%)	0 (0.0%)
Need for Endotracheal intubation, n (%)	No	37 (94.9%)	17 (85.0%)	5 (100.0%)	3 (100.0%)
	Yes	2 (5.1%)	3 (15.0%)	0 (0.0%)	0 (0.0%)
Need for Mechanical ventilation, n (%)	No	38 (97.4%)	19 (95.0%)	5 (100.0%)	3 (100.0%)
	Yes	1 (2.6%)	1 (5.0%)	0 (0.0%)	0 (0.0%)
Survivor with complications, n (%)	No	32 (82.1%)	12 (70.6%)	4 (80.0%)	3 (100.0%)
	Yes	7 (17.9%)	5 (29.4%)	1 (20.0%)	0 (0.0%)
Length of hospital stay, hours	Median (IQR)	7.8 (3.3–13.8)	6.1 (2.7–35.9)	9.5 (3.5–33.9)	24.2 (4.8–44.2)

ICU: Intensive care unit; n: Number; IQR: Interquartile range.

drugs to become effective.[38] Consequently, despite the administration of pharmacotherapy, patients may still engage in suicidal behavior.

Regarding the ingested dose, the median ingested dose was 1,600 mg for carbamazepine, 1,200 mg for valproic acid, and 2,000 mg for each of lithium and lamotrigine. As it is reported, carbamazepine poisoning occurs if the oral dose exceeds 50 mg/kg. Furthermore, children can experience severe poisoning by ingesting as little as one 400 mg tablet.[18] Patients are liable for poisoning with massive valproic acid doses >200 mg/kg[35] while acute lithium poisoning typically occurs with doses >40 mg/kg.[39] In addition, valproic acid and lithium have a narrow therapeutic index. Concerning lamotrigine poisoning, a systematic review reported 2 deaths with ingested doses of 4 g and 7,5 g.[40]

Table 4. Relationship between poison severity score, and outcomes among acutely poisoned patients with carbamazepine ($n = 39$ patients) and valproic acid ($n = 20$ patients).

Carbamazepine poisoning, ($n = 39$)		**Poison severity score**			**Name of test**	**p**
		Mild ($n = 21$)	**Moderate ($n = 15$)**	**Severe ($n = 3$)**		
The need for ICU admission, n (%)	No	21 (100.0%)	6 (40.0%)	0 (0.0%)	χ^2 22.100	< 0.001*
	Yes	0 (0.0%)	9 (60.0%)	3 (100.0%)		
Survivors with complications, n (%)	No	21 (100.0%)	11 (73.3%)	0 (0.0%)	χ^2 19.082	< 0.001*
	Yes	0 (0.0%)	4 (26.7%)	3 (100.0%)		
Length of hospital stay, hours	Median (IQR)	5.0 (2.5–7.8)	9.25 (8.3–30.5)	56.3 (6.6–80.5)	Kruskal Wallis test 8.264	0.016*
Valproic acid poisoning, ($n = 20$)		**Poison severity score**			**Name of test**	**p**
		Mild ($n = 10$)	**Moderate ($n = 2$)**	**Severe ($n = 8$)**		
Death, n (%)	No	10 (100.0%)	2 (100.0%)	5 (62.5%)	χ^2 5.294	0.067
	Yes	0 (0.0%)	0 (0.0%)	3 (37.5%)		
The need for ICU admission, n (%)	No	10 (100.0%)	1 (50.0%)	3 (37.5%)	χ^2 8.691	0.013*
	Yes	0 (0.0%)	1 (50.0%)	5 (62.5%)		
Survivors with complications, n (%)	No	9 (90.0%)	2 (100.0%)	1 (20.0%)	χ^2 8.812	0.009*
	Yes	1 (10.0%)	0 (0.0%)	4 (80.0%)		
Length of hospital stay, hours	Median (IQR)	2.9 (1.3–5.9)	12.7 (11.30–13.0)	42.1 (10.5–243.9)	Kruskal Wallis test 11.211	0.004*

n: Number; ICU: Intensive care unit; Min. – Max.: Minimum – Maximum; IQR: interquartile range; χ^2: the Chi-square test; ∗: Statistically significant as $P \leq 0.05$.

Furthermore, the majority of the studied patients were classified as mild to moderate poisoning based on GCS and PSS. Similarly, Abdelhamid,[27] Basyoni et al.,[26] and the American Poison Centers reported that most carbamazepine, valproic acid, and lamotrigine patients had minor and moderate poisoning.[12] Al Khalili et al.[41] have indicated that the symptoms of an acute carbamazepine overdose typically manifest with a delay, due to the slow and unpredictable absorption of carbamazepine in the gastrointestinal tract. An alternative hypothesis is that the lethal effects of carbamazepine require the administration of exceptionally high doses, which the majority of patients in this study did not consume. Furthermore, Isbister et al.[35] explained that most of their valproic acid patients were less severe due to the low ingested overall dose. Moreover, lithium poisoning in patients who have not previously received lithium causes minimal poisoning due to rapid drug dissolution, whereas overdose in those receiving prior treatment causes greater poisoning due to tissue saturation.[42] In addition, Wills et al.[43] found that among 67 lamotrigine-poisoned patients, 26 cases had a minor outcome severity score, 20 cases were moderate, and 4 cases were severe. A systematic review conducted on 22 cases of lamotrigine poisoning reported that most cases were mild or had no toxicity and only 2 deaths.[40] Thus, the use of second-generation mood stabilizing drugs such as lamotrigine as they are more tolerable and have fewer side effects.[3]

Concerning the outcomes, no reported deaths from carbamazepine, lithium, and lamotrigine poisoning. However, three deaths were reported from valproic acid poisoning. The incidence of the need for ICU admission, endotracheal intubation, mechanical ventilation, development of complications, and duration of hospital stays showed favorable outcomes that coincide with different previous literature[12,27,40,43] The report from Ain Shams Poison Center demonstrated 3 deaths from carbamazepine poisoning and no deaths from valproic acid, lithium, or lamotrigine poisoning.[27] The American Poison Centers reported that only one death from carbamazepine poisoning, 2 deaths from valproic acid, 7 deaths from lithium poisoning, and 2 deaths from lamotrigine poisoning (2 cases out of 10,912 cases).[12] Perez and Wiley[44] conducted a cohort study of 427 children with carbamazepine poisoning and found an overall mortality rate of 13%. Generally, most cases of carbamazepine poisoning have favorable outcomes if they are treated soon after the overdose.[45] However, severe valproic acid poisoning can result in life-threatening neurological and metabolic abnormalities.[46] Rapid hospitalization after drug ingestion could be another factor that results in favorable outcomes. Where, the geographic location of TUPCC in the Delta region of Egypt, as well as the readily available transportation options could explain the rapid transfer. Moreover, the majority of patients in this study were intentionally poisoned, indicating that the patients involved did not typically ingest large amounts of harmful substances. Additionally, a significant proportion of individuals who engaged in self-poisoning did so to attract attention, rather than with the sole objective of causing their demise.

In the present study, the assessments of acute carbamazepine-poisoned patients and valproic acid-poisoned patients with PSS were significantly related to the need for ICU admission, the development of complications, and the hospital stay. The poison severity score was initially designed to define the severity of poisoning at a given point in time.[25] However, several studies[14–17] support the prospective use of the PSS in poisoning cases. These studies reported a notable relation between the initial PSS and the outcomes of antipsychotic poisoning, antidepressant, and anticholinesterase poisoning[15–17] Furthermore, among antiepileptic drugs, Basyoni et al.[26] found a significant association between PSS and duration of hospital stays of carbamazepine, valproic acid, and lamotrigine poisoning. Therefore, it is a relevant scoring system that can be used as a predictor of outcomes, particularly in the absence of serum drug levels.

Strength and limitations

This study highlighted the necessity for meticulous administration of these medications to patients, particularly those identified as being at an elevated risk of suicidal behavior. In addition, it was the first study to evaluate pattern, severity, and outcomes using the PSS in acutely poisoned patients with mood-stabilizing drugs. Poison severity score provides a reliable score to predict the need for ICU admission, the development of complications, and the length of hospital stays in carbamazepine and valproic acid poisoning. The early identification of severity, followed by prompt treatment, can prevent the onset of neurological and cardiovascular complications and consequently reduce the incidence of unfavorable outcomes. A sequential single-center case series offers a more comprehensive understanding of the clinical implications of mood stabilizer overdose than multiple case reports.

Our main limitation was that diagnoses were mainly based on history and clinical assessment; serum drug levels were not available. The number of lithium and lamotrigine patients was not enough to show differences in outcomes. Further large multicentered studies, including all Poison control centers are needed.

Conclusion

Among mood-stabilizing drugs, carbamazepine and valproic acid are commonly encountered as opposed to lithium and lamotrigine poisoning. Furthermore, this study highlights the importance of rigorous monitoring and management when administering this medication to patients, particularly those who are at an increased risk of suicidal behaviors. Mild to moderate poisoning with favorable outcomes represents most acutely poisoned patients with mood stabilizer medications. The PSS is a readily accessible and straightforward measure that can predict the likelihood of requiring ICU admission, the occurrence of complications, and the length of hospitalization among patients with acute carbamazepine poisoning or valproic acid poisoning.

Author contributions

All authors contributed equally to the study. The corresponding author is responsible for communication during and after the manuscript submission.

Funding

This research did not receive any funding support.

Conflict of interest statement: There are no conflicts of interest to declare.

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Toxicology Research, 2024, **13**, 1–8
https://doi.org/10.1093/toxres/tfae193
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