Electrocardiogram Abnormality in Poisoned Patients with Tricyclic Antidepressant

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Abstract

Background: A wide variety of electrocardiogram (ECG) changes can manifest with antidepressant drugs, occurring at both therapeutic doses and toxic levels. Notably, ECG abnormalities like wide QRS and QT prolongation may be observed in poisoned patients with tricyclic antidepressants (TCAs), indicating severe conditions that necessitate the implementation of cardiac monitoring systems. This study aimed to investigate ECG Abnormality in poisoned patients with tricyclic antidepressants.

Methods: This retrospective patient record study was conducted at Razi Hospital in Ahvaz, Iran, from 2006 to 2009. Patient information was extracted from hospital medical records after the established protocol. The chi-square test was employed for initial analysis; subsequently, logistic regression was applied to identify risk factors associated with abnormal ECG findings. We analyzed the data using SPSS (Version 19; IBM) statistical software. $P < 0.05$ was defined as statistically significant.

Results: Among the 210 poisoned patients, comprising 88 men (41.9%) and 122 women (58.1%), the majority fell within the age range of 15 to 25 years. In our study, the most commonly ingested drugs by poisoned patients were amitriptyline in 134 patients (63.8%) and nortriptyline in 42 patients (20%). A significant portion of 137 patients (65.2%) exhibited poisoning symptoms within < 6 hours, while 73 patients (34.8%) showed symptoms between 6 and 24 hours. Our findings indicated that the initial symptoms in poisoned patients included a decreased level of consciousness in 168 patients (80%), nausea and vomiting in 20 patients (9.5%), and various other symptoms. Notably, our results revealed ECG changes in 70 patients, with 32 patients (15.2%) showing a QRS widening (> 0.1sec), 5 patients (2.4%) displaying a tall R wave in aVR, 5 patients (2.4%) exhibiting right axis deviation, and other observed changes.

Conclusion: QRS widening in poisoned patients with tricyclic antidepressants is more frequently observed in symptomatic patients, highlighting the importance of ECG screening in these patients.

Keywords: ECG changes, TCA poisoning, Overdose, Suicide

Introduction

Drug overdose represents a highly prevalent and potentially hazardous form of poisoning, particularly within home environments. Emergency department statistics indicate that tricyclic antidepressants (TCAs) drugs are frequently misused for suicidal purposes (1). TCAs stand out as one of the leading causes of drug poisoning (2), despite the availability of safer alternatives with a less toxic profile,

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↑What is "already known" in this topic:
Tricyclic antidepressants (TCAs) are one of the most common causes of drug poisoning. Teenagers and young adults are more likely to experience acute poisoning, particularly intentional poisoning, according to the study's findings. TCA toxicity is assessed by electrocardiogram (ECG), a fast diagnostic clinical sign.

→What this article adds:
Investigating the poisoning pattern in patients with TCAs overdose in a period in Ahvaz according to cultural differences. In our study, the wide QRS complex (15%) was more than other ECG symptoms, and it seems to have a higher value in diagnosis and treatment than the others.

such as selective serotonin reuptake inhibitors (SSRIs). Surprisingly, TCAs continue to be prescribed extensively for various indications in both children and adults, (3) ranging from major depressive disorders to chronic pain syndromes, panic attacks, severe anxiety, phobic disorders, obsessive-compulsive disorders, migraine, eating disorders, and attention deficit hyperactivity disorders (4). Their mechanism involves primarily blocking norepinephrine and postsynaptic α-adrenergic receptors while also influencing the cholinergic and histaminergic systems and α-adrenergic activity, along with quinidine-like effects on cardiac condition (2, 3, 5). Tricyclic antidepressants possess a narrow therapeutic index, primarily responsible for inducing adverse effects and accounting for a significant proportion of severe poisoning cases after TCAs overdose. The continued use of TCA necessitates careful consideration of their potential toxicity and the need for effective prevention strategies (2, 5). In the early stages of poisoning, symptoms such as dry mouth, blurred vision, sinus tachycardia, and drowsiness arise due to anticholinergic activity, while drowsiness results from antihistaminergic activity (6). Acute TCA poisoning, considered a life-threatening condition, is generally associated with central nervous system and cardiovascular toxicity; this manifests as altered consciousness levels, seizure frequency, electrocardiogram (ECG) abnormalities, arrhythmias, and hypotension (6).

The ECG serves as a diagnostic and rapidly available clinical marker, aiding in assessing TCA toxicity (7, 8). Atrioventricular (AV) block, ventricular ectopy, sinus tachycardia, PR interval prolongation, QRS complex duration (> 0.1 sec), widened QT interval, right axis deviation, and Brugada pattern changes, including Right Bundle Branch Block and downward ST segment elevation in V1-V6 leads, are common ECG findings. The recognition of these ECG markers is crucial for timely intervention and effective management of TCA overdose cases (8).

ECG changes arising from TCA poisoning are intricately linked to Na+ channel blockade and the compound's various impacts on cardiovascular function. Common ECG manifestations include sinus tachycardia, QRS complex widening, QT interval prolongation, and a prominent R wave in lead aVR. Notably, delayed conduction on the right side of the heart can result in a right bundle branch block, a pattern more frequently observed in cases of TCA poisoning; these distinctive ECG alterations provide valuable insights into the underlying mechanisms and help guide clinicians in the accurate diagnosis and management of TCA-induced cardiovascular toxicity (9). Given the significance of ECG changes as a screening tool for diagnosing the type of drug poisoning and assessing the severity of danger in poisoned patients, this study aimed to characterize ECG abnormalities in patients intoxicated with tricyclic antidepressants. Moreover, the study sought to explore the potential relationship between ECG changes, the quantity of administered sodium bicarbonate, and the mortality rate during the hospitalization period By investigating these associations, the research aimed to contribute valuable insights into the correlation between ECG findings, treatment interventions, and patient outcomes in TCA poisoning cases.

Methods
This retrospective patient record study enrolled a total of 210 cases of suicide attempts by overdose in Razi Hospital, Ahvaz, Iran, from 2006 to 2009. Their records were reviewed and extracted information from databases of the poisoning department and recorded in predetermined checklist that includes sex, age, ECG change, bicarbonate vials, intensive care unit (ICU) admission, number of TCAs, type of TCAs, first symptoms, underlying medical conditions, time of hospital admission, first symptom, concomitant use of other drugs, and mortality variables. Extracted information was coded regardless of the patient's name. The Ethics Committee of Ahvaz University of Medical Sciences approved this study.

Statistical Methods
Data were analyzed using SPSS (Version 19; IBM) statistical software. The chi-square test was used for the frequency and percentage of qualitative variables. Patients with abnormal ECG changes (15.2%) were separated into 2 groups based on the ECG changes: those with an abnormal change (abnormal change = wide QRS complex >0.1sec, tall R wave in aVR, right axis deviation, coincident QRS widening and tall R wave, coincident QRS widening and right axis deviation). We used simple and multiple logistic regression to determine the relationship between ECG abnormality change and the involved factors study. $P < 0.05$ was regarded as statistically significant.

Results
This study examined 210 poisoned patients in total Razi Hospital in Ahvaz, Iran (88 men, 41.9%, and 122 women, 58.1%). The patients' ages were divided into 3 groups: 15–25, 25–45, and > 45 years old (Table 1). Most of these patients were in the age range of 15 to 25 years. Our findings showed amitriptyline (63.8%) and nortriptyline (20%) most frequently ingested between poisoning patients. A total of 137 patients (65.2%) developed poisoning symptoms < 6 hours, and 73 patients (34.8%) developed symptoms between 6 and 24 hours. Our results indicated that the first symptom occurred in poisoned patients, including decreased level of consciousness in 168 patients (80%), nausea and vomiting in 20 patients (9.5%), and other symptoms. In this study, 75 patients (35.7%) were with underlying medical conditions, and 58 patients (27.6%) only used TCA, but 152 patients (72.4%) used TCA with other medication (Table 1).

Effect of TCA on ECG Change and Abnormality
Our results have shown that about two-thirds of the 140 patients (66.7%) had normal ECG. The majority of abnormal ECG changes included 32 patients (15.2%) with QRS widening > 0.1sec, 5 patients (2.4%) with tall R wave in aVR, and 5 patients (2.4%) with right axis deviation. A small number of TCA poisoning patients exhibited multiple ECG changes: 3 patients (1.4%) exhibited the 3 changes listed above, 4 patients (1.9%) the right axis deviation and tall R wave, 2 patients (1%) the QRS widening and right axis deviation, 1 patient (0.5%) the right axis deviation and QRS widening, and 18 patients (8.6%) the other change

Table 1. Tricyclic Antidepressant use and ECG change in patients with suicide

Variable		N (%)	ECG Normal	ECG Abnormal	P- value
Total		210	188 (84.8)	32 (15.2)	
Sex	Female	122 (58.1)	86 (70.5)	36 (29.5)	0.099
	Male	88 (41.9)	54 (61.4)	34 (38.6)	
Age	<25	106 (50.5)	72 (67.9)	34 (32.1)	0.286
	25-45	94 (44.8)	65 (69.1)	29 (30.9)	
	>45	10 (4.8)	3 (30)	7 (70)	
Type of drug	Amitriptyline	134 (63.8)	85 (63.4)	49 (36.6)	0. 853
	Nortriptyline	42 (20)	26 (61.9)	16 (38.1)	
	Imipramine	23 (11)	19 (82.6)	4 (17.4)	
	Doxepin	3 (1.41)	3 (100)	0	
First symptoms	Decreased level of consciousness	168 (80)	108 (64.3)	60 (35.7)	0.591
	Nausea and vomiting	20 (9.5)	14 (70)	6 (3)	
	convulsion	5 (2.4)	4 (80)	1 (20)	
Underlying medical	Yes	75 (35.7)	43 (57.3)	32 (42.7)	0.147
	No	135 (64.3)	97 (71.8)	38 (28.2)	
Icu admission	Yes	95 (45.2)	50 (52.6)	45 (47.4)	0.0001
	No	115 (54.8)	90 (78.3)	25 (82.7)	
Time from ingestion (h)	<6	137 (65.2)	92 (67.1)	45 (32.9)	0.990
	6-24	73 (34.8)	48 (65.7)	25 (24.3)	
Bicarbonate vial	1 vial	117 (55.7)	88 (75.2)	29 (24.8)	0. 001
	2 vial	82 (39.1)	50 (61)	32 (39)	
	3 vial	11 (5.2)	2 (18.2)	9 (81.8)	

Table 2. Predictor variable for ECG change based on the result of simple and multiple logistic regression

variable		Simple logistic regression		Multiple logistic regression	
		OR (95%CI)	P. value	OR$_{adj}$ (95%CI)	P- value
Age	<25	1			
	25-45	0.94 (0.51-1.71)	0.852	-	- -
	>45	4.94 (1.2-20.3)	0.027	-	- -
ICU Admission	No	1		1	
	Yes	3.24 (1.78-5.89)	0.0001	2.61 (1.37-5.005)	0.004
	1 vial	1		1	
Bicarbonate vial	2 vial	0.073 (0.015-0.36)	0.001	1.71 (0.902-3.25)	0.124
	3 vial	0.142 (0.029-0.70)	0.017	10.2 (2.01-51.64)	0.005

(Figure 1). This research evaluated the relation between ECG changes and age, sex, bicarbonate vials, ICU admission, type of TCAs, underlying diseases et cetera were evaluated with statistical analysis. The chi-square test results showed that there was a statistically significant difference between ECG alterations and ICU admission ($P < 0.05$)

Only 10 patients (8.7%) with QRS widening and 90 patients (78%) with normal ECG were among the patients who did not require ICU admission; in contrast, the majority of patients who displayed ECG changes required ICU admission. Of the patients who required ICU admission, there were 32 patients (15.23%) with QRS widening and 50 patients (52%) with normal ECG.

In addition, the results of this study revealed a strong significant difference between ECG change and bicarbonate usage ($P < 0.05$). Simultaneously, the ECG abnormalities of poisoned patients gradually improved as they received additional bicarbonate. Results revealed no significant differences in other variables such as age, sex, number of TCAs, type of TCAs, first symptom, and concomitant use of other drugs; nonetheless, there was a clinically significant relationship. Simple regression results also showed a significant association between age, ICU admission, and bicarbonate with ECG changes (Table 2). Multiple logistic regression showed that ECG abnormality in patients who received 3 vials of bicarbonate was 10.2 times more than in those who received 1 vial of bicarbonate (odds ratio, 10.2 (95% CI, 2.01-51.64); $P = 0.005$). Also, ICU admission in patients with ECG abnormality was 2.6 times more than in those who did not need ICU admission (OR, 2.6 (95% CI, 1.37-5.05); $P = 0.004$) (Table 2).

Discussion

The global increase in the use and prescription of tricyclic antidepressants, particularly in developing countries for depression treatment, underscores the urgent need for
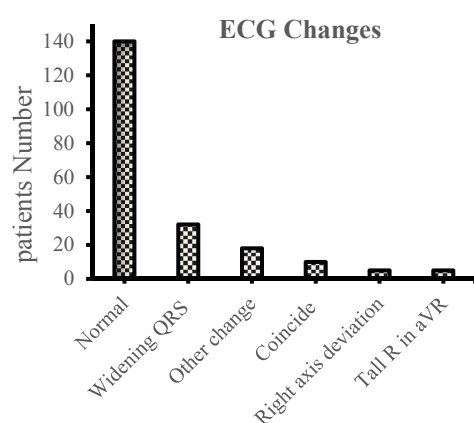
Figure 1. Effect of TCAs on ECG changes and abnormality

effective strategies in timely diagnosis and treatment. Tricyclic antidepressants, a prevalent choice, have become one of the leading causes of suicide attempts involving medication overdose. In recent years, there has been a growing imperative to establish efficient protocols for prompt identification and intervention in cases of antidepressant overdose. It is essential to recognize that overdose with antidepressants, notably TCAs, imposes significant hospital costs, is often overlooked, and warrants consideration in the formulation of future policies governing antidepressant prescriptions (10). This acknowledgment is vital for shaping comprehensive and informed approaches to antidepressant use, considering both therapeutic benefits and potential risks. Our data reveal that 58.1% of the patients in the study were women, potentially attributed to the higher likelihood of women experiencing depression and anxiety disorders, prompting them to seek treatment. Conversely, factors such as family disputes, oppressive marriage, psychological disorders, early-age marriages, poverty, rape, and sexual abuse contribute to the elevated suicide risk among women compared with men (10-12). These results were consistent with the results of Emamhadi's study, reinforcing that TCA poisoning is more prevalent in women (13). The study further underscores that poisoning incidents predominantly occurred in young adults, with the highest frequency observed in the 15-25 age group, followed by the 25-45 age group, aligning with findings in other studies. Rahman AU et al, in a survey at Dhaka Medical College Hospital, reported that 86.3% of poisoned patients were <30 years of age (14). The heightened incidence of TCA self-poisoning in the young age group may be attributed to various factors, including academic pressures, a pursuit of independence, medication misuse, social challenges, feelings of isolation, coping with problems without support, high unemployment rates, and financial dependency issues (11). Our demographic findings highlight that amitriptyline and nortriptyline stand out as the most frequently ingested antidepressant and sedative drugs, often misused for suicidal purposes.

This prevalence may be attributed to the accessibility of antidepressant drugs for treating depression and the perceived simplicity, convenience, and painlessness of this method for individuals contemplating suicide (13). A prospective study revealed that patients with amitriptyline overdose constituted the highest percentage (41%) compared with other antidepressants (2). This observation aligns with similar findings in other studies, such as the study by Farzad Gheshlaghi et al, where nortriptyline (63.9%) and amitriptyline (35.7%) were reported as the most commonly used drugs (8). In our study, a majority of patients (72.4%) had concomitant use of more than one type of drug; this contrasts with Albertson's study, where concomitant use of more than one type of drug was observed in 29 patients (28%). The disparity may be attributed to variations in sample size across studies and the ease of drug accessibility (15). Clinical manifestations observed in TCAs overdose encompass antimuscarinic symptoms, including blurred vision, sinus tachycardia, drowsiness, dryness of the mouth and skin, and pupillary dilatation, as well

as cardiotoxicity leading to hypotension, respiratory insufficiency, decreased level of consciousness, convulsions, and rarely, death (10). In our study, the predominant and initial symptom of TCA poisoning was a decrease in the level of consciousness, observed in 168 patients (80%). Coincident use of other drugs was higher (72%) than in other studies, possibly accounting for the variance in the primary symptom (decreased consciousness) observed in our study compared with other research (hypotension). Nastaran Eizadi-Mood et al also demonstrated that among anticholinergic manifestations, the most prevalent cause was the loss of consciousness (73.3%) (1). Conversely, another study conducted in a Turkish Hospital identified drowsiness, dizziness, and urinary retention as the most common clinical presentations (10). It appears that the coincidental use of TCAs with other drugs in our study may be associated with the observed decrease in consciousness. However, a study conducted at Noor Hospital in Isfahan, Iran, identified hypotension (72.7%) as the most prevalent symptom among patients, contrasting with our study results (1). In our investigation, most patients (137 patients = 65.2%) experienced symptoms within 6 hours of ingestion, aligning with findings from a study at the California Medical Center in 1987, reporting an average time of 4.9 hours. Among patients exhibiting ECG changes in our study (70 patients = 33.3%), the most common alteration was related to QRS widening (32 patients = 15.2%) (15). This prevalence of QRS widening in our study was higher than other ECG symptoms, suggesting its potential significance in diagnosis and treatment. In a survey by Lavoei FW et al, 62% of patients showed a QRS widening (16), while a similar study by Foulke et al found that 44.1% of poisoned patients with TCA exhibited QRS widening (15). Our findings are consistent with the Rahman et al study, which noted QRS widening (27.8%) in patients with TCA poisoning (14).

In our study, although there was no statistically significant correlation between the type of drug and ECG changes, the clinical significance was evident, emphasizing its importance in the treatment stage. Notably, in our investigation, the most prevalent ECG abnormality changes were observed among patients with amitriptyline poisoning. Specifically, QRS widening > 0.01sec. A previous study highlighted that amitriptyline is frequently used in drug overdoses because of its affordability and widespread prescription by clinicians (17).

Most patients who exhibited ECG changes were admitted to the ICU, with right-axis deviation and concomitant ECG changes observed exclusively in patients admitted to the ICU. Our findings indicate a statistically significant relationship between ECG changes and admission to the ICU. In our study, ICU admission was required for 45% of patients, whereas in Foulke's study, this rate was higher (76%) (18), and in Amira's study, the ICU admission rate was lower (22.9 %) (17).

Our data have demonstrated a statistical significance between the ECG change and the required bicarbonate dose. Clear evidence indicates that sodium bicarbonate effectively treats QRS widening from TCA poisoning and improves ECG abnormalities. The QRS complex affects the

depolarization of the ventricles through voltage-gated sodium channels. Therefore, the use of sodium bicarbonate for the treatment of ECG abnormalities is convincing (19).

No studies determine the adjusted dosing of sodium bicarbonate (20). In general, the findings of the present study indicate a higher prevalence of acute poisoning, especially intentional poisoning, in teenagers and young adults, considering the higher prevalence of intentional poisoning in women. Early and accurate diagnosis of poisoning and its appropriate treatment can be vital, and knowledge of the general pattern of poisoning in each geographical region and according to the culture of that region helps in this field.

Limitations

Our study had some limitations. The study was retrospective, and it could not show accurate causal relationships because the time sequence was not clear. Also, the sample size was small.

Conclusion

In our study, common drugs taken by patients were amitriptyline and nortriptyline. According to the results of the present study, patients admitted to the ICU have more ECG abnormality changes. Therefore, ECG monitoring is recommended for outcome prediction in poisoned TCA patients. This study was conducted to determine the pattern of acute poisoning in poisoned patients who were referred to the emergency department of Razi Hospital in Ahvaz.

Acknowledgment

Ethics Approval

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Conflict of Interests

The authors declare that they have no competing interests.

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