

Electrocardiographic changes in acute tricyclic antidepressant overdose

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RESUMEN

La sobredosis de antidepresivos tricíclicos (ADT) es una causa frecuente de envenenamiento, asociada a una elevada mortalidad secundaria y a involucro cardiovascular que se manifiesta con alteraciones electrocardiográficas, arritmias e hipotensión. La toxicidad cardíaca secundaria a ADT es consecuencia del bloqueo de los canales de sodio y del enlentecimiento de la fase 0 del potencial de acción, lo que ocasiona un retardo en la conducción a través del sistema His-Purkinje y miocardio. Las alteraciones electrocardiográficas son una manifestación frecuente de esta intoxicación, se presenta taquicardia sinusal, prolongación de los intervalos PR, QRS, QTc, cambios no específicos de la onda T y del segmento ST, bloqueo auriculoventricular, desviación del eje a la derecha, patrón de Brugada y alteraciones en la onda R en la derivación aVR y una relación R/S en aVR > 0.7. El objetivo de este trabajo es describir las alteraciones electrocardiográficas que desarrolló un paciente intoxicado con ADT

Palabras clave. QTc. Onda R. Relación R/S.

ABSTRACT

Tricyclic antidepressants (TCAs) overdose remain a common cause of fatal drug poisoning as a result of their cardiovascular toxicity manifested by electrocardiographic (ECG) abnormalities, arrhythmias and hypotension. Cardiac toxicity secondary to TCAs is due mainly to sodium-channel blockade and slowing of phase 0 depolarization of the action potential results in slowing of conduction through the His-Purkinje system and myocardium. ECG changes are a frequent manifestation of TCAs overdose and include sinus tachycardia, prolongation of the PR, QRS and QTc intervals, nonspecific ST and T wave changes, atrioventricular block, right axis deviation, Brugada pattern and R wave changes in aVR, R/S ratio in aVR > 0.7 and ventricular arrhythmias. The aim of this paper is to describe the ECG alterations in a patient intoxicated with TCAs.

Key words. QTc. R wave. R/S ratio.

INTRODUCTION

Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are antidepressant drugs used in the treatment of major depression, neurosis, panic disorder or chronic pain. Both may cause expansions in the QTc interval and TCAs, which may cause defect in the cardiac conduction due to the slowdown in the cardiac depolarization and lethal arrhythmias. TCAs are absorbed quickly in the gastrointestinal tract, therefore most of the electrocardiographic (ECG) changes are seen early after the ingestion of these agents and much before the clinical manifestations or drug screening results that are available.¹ The aim of this paper is to describe the ECG abnormalities in a patient intoxicated with TCAs.

CASE REPORT

A 35 year old patient with history of major depressive disorder treated with TCAs. His family reported that the patient ingested at home 25 tablets of amitriptyline of 50 mg each one, with a total dose of 625 mg. The patient was admitted to the Intensive Care Unit (ICU) with altered mental status and metabolic acidosis. During the physical examination, the patient appeared in distress with confusional state, tachycardia, mydriasis and abdominal distention. Blood pressure 90/60 mmHg, pulse 130/min. The 12-lead ECG reveal sinus tachycardia (130/min), normal QRS complex duration (86 ms), prolonged QTc interval (503 ms), axis in 34 degrees, R wave in the lead aVR was prominent with amplitude of 2 mm and R/S ratio of 0.25,

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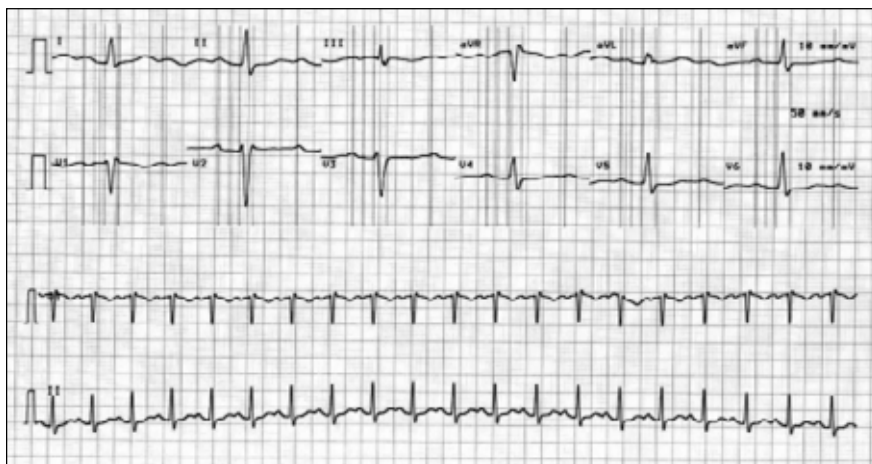


Figure 1. Electrocardiogram taken at time of presentation demonstrates sinus tachycardia (130/min), normal QRS complex (86 ms), prolonged QTc interval (503 ms), prominent R wave in lead aVR (2 mm) and R/S ratio of 0.25.

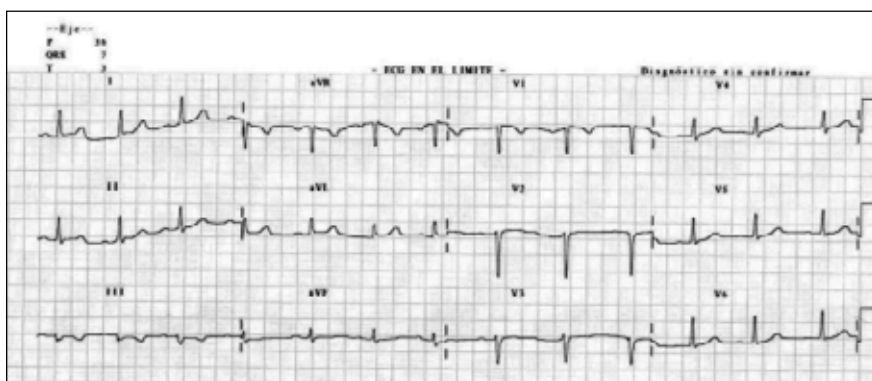


Figure 2. Electrocardiogram after treatment demonstrates normal heart rate (76/min), normal QTc (427 ms), normal R wave in aVR and R/S ratio of 0.14.

and diffuse alterations in repolarization (Figure 1). With diagnosis of tricyclic antidepressant overdose, the patient was treated with intravenous saline, sodium bicarbonate drip, low dose of noradrenaline, lipid-emulsion infusion and charcoal through a nasogastric tube. With this treatment, the pupils regained their normal size, abdominal distension disappeared and normalized blood pressure and heart rate. Control 12-lead ECG showed sinus rhythm, normal heart rate (76/min), normal QTc (427ms), axis in 81 degrees, no prominent R wave in lead aVR and R/S ratio of 0.14 and repolarization normalized (Figure 2).

DISCUSSION

The manifestations of TCAs overdose presented by this patient, were characterized by anticholinergic features (tachycardia, midriasis and abdominal distension), hypotension, neurological alterations (confusional state) and ECG changes characterized by sinus tachycardia, nonspecific T wave changes, prolonged QTc, and prominent R in lead aVR.

Several studies have shown that TCAs poisoning is common and is associated with a high morbidity and mortality. In 2004, the American Association of Poison Control Centers recorded 7,430 exposures to amitriptyline, 185 to desipramine, 1,288 to doxepin and 819 to imipramine.² Henry, *et al.*³ showed in a large study, that TCAs had the highest mortality rates specially with desipramine, amitriptyline and imipramine. In adults, the toxic dose of TCAs varies according to the pharmacological characteristics of each one. In relation to amitriptyline, low dose of 50 mg may be associated with moderate toxicity and severe toxicity at dose above 300 mg, ranging from 150 mg to 10 g.⁴ The minimum acute toxic dose of amitriptyline and imipramine in children less than 6 years is 15 mg/kg to 30 mg/kg. Goel, *et al.*⁵ recommended that children who ingest tricyclics, in any dosage, should always be admitted in the hospital.

TCAs may cause serious cardiovascular and neurologic toxicity. Even among the patients who take therapeutic doses of the tricyclic antidepressants, 20% will display mild ECG changes including prolongation of QTc

interval, displacement of ST segment, and T-wave abnormalities.⁶

TCA's have "quinidine like" activity. This class I antiarrhythmic effect causes a slowdown at the 0 phase depolarization of ventricular action potential, slowdown in the His-Purkinje system and myocardial conduction are proarrhythmic. TCAs act by blocking the reuptake of biological amines at presynaptic terminals and producing a hyperadrenergic state, which produces initial hypertension and tachycardia. Subsequently, peripheral alpha adrenergic blockade and depletion of norepinephrine result in supine and postural hypotension. Anticholinergic effects produce tachycardia and central nervous system stimulation. The class I antiarrhythmic effect by blocking the fast sodium channels may cause a negative inotropic effect. TCAs prolong conduction through the His-Purkinje system and myocardium. Tachycardia and hypertension are the early physical signs of the tricyclic antidepressant's cardiovascular toxicity, whereas cardiac conduction abnormalities and decreased cardiac output are seen in advanced cases.⁷⁻⁹

TCAs are commonly associated with prolongation of the QTc interval by delaying the inward sodium current into cardiomyocytes and have also demonstrated disruption in the delayed rectifier potassium and the inward slow calcium currents, both leading to delayed repolarization. Prolongation of the QT interval increases the risk for ventricular fibrillation and torsades de pointes leading to sudden cardiac death (SCD).¹⁰ Vieweg, *et al.*¹¹ highlighted several case reports of QTc interval prolongation with the use of TCAs. Ray, *et al.*¹² conducted a study to establish the risk of SCD in patients receiving TCA or an SSRIs. The use of SSRIs did not increase the risk of SCD. Patients receiving a tricyclic antidepressant had a slightly higher but dose-dependent risk of SCD. The risk was 2.5 times greater in patients taking at least 300 mg of amitriptyline equivalents (RR, 2.53; CI, 1.04-6.12).

Other ECG changes associated to TCAs overdose are tachycardia, prolonged PR and QRS, ventricular arrhythmias, Brugada sign and ST segment elevation resembling ischemic heart disease.¹³⁻¹⁶

The ECG abnormalities that usually precede the development of significant and clinically evident cardiovascular and neurologic toxicity are widening of QRS complexes greater than 100 ms, axis from 120 to 270 degrees, prolonged QTc interval, and R-wave amplitude of 3 mm or more in the lead aVR.⁹ R wave changes are the better predictor of TCAs, the sensitivity and specificity of R-wave changes are 81% and 73% respectively.¹⁷ Buckley, *et al.*¹⁸ demonstrated that the R/S ratio in aVR > 0.7 is a better

predictor of complications in TCAs overdose (PPV 41.2%, NPV 94.7%, likelihood ratio 9.33), and concludes that a QRS > 120 ms, QTc > 500 and an increased R/S ratio in aVR on the first ECG have the strongest association with the occurrence of arrhythmia in TCA overdose.

TCAs overdose is a frequent cause of admission to the ICU. Electrocardiographic changes are common and precede the development of lethal arrhythmias, refractory hypotension and neurological deterioration, therefore close ECG monitoring is recommended in these patients.

ABBREVIATIONS

- TCAs: tricyclic antidepressants.
- ECG: electrocardiographic.
- ICU: Intensive Care Unit.

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