

## CLINICAL VIGNETTE

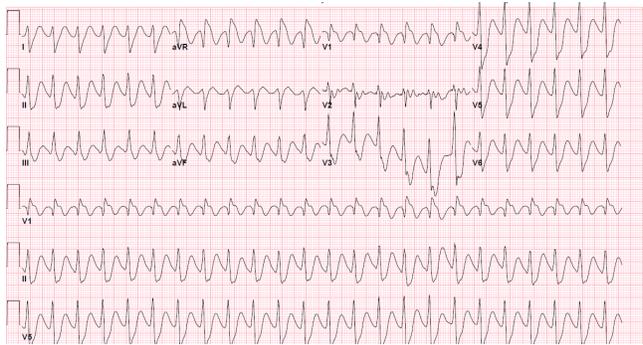
# A Fatal Case of Tricyclic Poisoning – Cardiotoxicity

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### Case Report

A 33-year-old female with history of depression was brought in by the paramedics after an apparent suicide attempt by ingesting medications. The patient was unresponsive and pulseless. She was in cardiopulmonary arrest and hemodynamic collapse. She was intubated and placed on mechanical ventilation. She was initially in a wide complex rhythm. During resuscitation efforts, the patient exhibited various cardiac arrhythmias. Ventricular tachycardia was observed, and the patient was cardioverted. PEA arrest and agonal rhythm were documented as well. Seizure activity was also noted.

Her electrocardiogram (EKG) below shows wide complex tachycardia with no clear evidence for ventricular origin, and more compatible with supraventricular origin with conduction abnormality.



Resuscitation efforts were carried out per ACLS protocol. She received intravenous fluids, sodium bicarbonate, and magnesium. Inotropic medications were infused. Benzodiazepines were given for seizures. Her work-up in the ER did not reveal any immediate reversible causes. Despite continued efforts, the patient expired in the ER. Her urine toxicology eventually returned positive for tricyclic antidepressants.

### Discussion

The adverse effects of tricyclic antidepressants (TCA) overdose were first reported 1959<sup>1</sup>. TCA are

frequently involved in cases of drug overdose as TCA are often prescribed to individuals whom are at risk of overdosing<sup>2</sup>. TCA remain a common cause of fatal drug poisoning, and in cases of fatal drug overdose, they are second only to analgesics as the causative agent<sup>3,4</sup>. Significant morbidity and mortality are associated with TCA overdose, and these complications are often related to cardiovascular and neurologic toxicity. Life-threatening arrhythmias and death due to TCA poisoning usually occur within 24 hours of ingestion.

The toxic effects of TCA are caused by four main pharmacological mechanisms<sup>5</sup>. These include: 1) inhibition of norepinephrine (NE) reuptake at nerve terminals, 2) direct alpha adrenergic blockage, 3) quinidine-like effect on the myocardium, and 4) anticholinergic effect<sup>5,6</sup>.

Cardiovascular toxicity of TCA overdose is manifested by EKG abnormalities, arrhythmias and hypotension. Tachyarrhythmias and bradyarrhythmias both can be seen with TCA toxicity. Tachyarrhythmias may occur from supraventricular or ventricular origin. Sinus tachycardia is the most common arrhythmia due to anticholinergic activity and inhibition of NE uptake by tricyclic antidepressants<sup>5</sup>. Ventricular tachycardia (VT) and ventricular fibrillation (VF) occur in approximately 4 percent of TCA overdose cases<sup>7</sup>. VT and VF are more common in severe poisonings, particularly those involving extreme QRS prolongation<sup>6,7</sup>. Torsade de pointes may occur infrequently<sup>8</sup>. Bradyarrhythmias have also been observed, and these arrhythmias can be caused by atrioventricular block.

Significant cardiac arrhythmia may contribute to hypotension and hemodynamic instability. Hypotension may ensue following significant TCA poisoning, resulting from reduced myocardial contractility and reduced systemic vascular resistance due to alpha-adrenergic blockade<sup>5,6</sup>. Patients with TCA overdose may develop mixed acidosis with metabolic acidosis and respiratory acidosis due to

respiratory depression.<sup>5</sup> Metabolic acidosis can occur secondary to myocardial dysfunction and hypotension, which results in tissue hypoperfusion and lactic acidosis<sup>5</sup>. Refractory hypotension may lead to an eventual death.

The ingested dose of TCA is relatively a poor predictor of clinical outcome<sup>5</sup>. There are variation in absorption, protein binding, metabolism, and elimination amongst individuals. On the other hand, EKG abnormalities carry predictive value in TCA overdose. EKG findings have become preferable to serum drug level in predicting complications following TCA overdose<sup>5,9</sup>. EKG can be used in risk stratification and management of such patients. Studies have demonstrates that EKG abnormalities are fairly good predictors of serious complications including death, seizures, and ventricular arrhythmias.

Cardiac conduction abnormalities are common in patients with TCA poisoning. Obtaining an EKG immediately upon presentation is essential in patients with known or suspected TCA poisoning. Arrhythmias from TCA overdose can develop quickly, and EKGs should be obtained frequently until the patient has been free of any symptoms or signs of cardiac toxicity for several hours<sup>10</sup>. The cardiotoxic effects of TCA are mediated by inhibition of the sodium channels which slows depolarization in the myocardium and conducting tissues. As a result, there is prolongation of QRS complex, PR and QT intervals<sup>5,6</sup>.

The following EKG findings suggest cardiotoxicity:<sup>10,11</sup>

- QRS prolongation over 100 msec
- Abnormal QRS morphology (eg, deep, slurred S wave in leads I and AVL)
- Abnormal amplitude and ration of R and S waves in lead AVR: R wave in AVR >3 mm; R to S ratio in AVR >0.7

Various EKG abnormalities may predict complications in cases of TCA overdose. QRS width greater than 100 msec is predictive of complications, and the risk of arrhythmia increases as the QRS complex widens<sup>6</sup>. QRS duration over 160 msec is associated with 50% incidence of arrhythmias, and such QRS prolongation has been shown to be a better predictor of seizures and ventricular arrhythmias when compared to plasma drug concentration<sup>9</sup>. Other EKG findings are also associated with adverse clinical outcome. QTc prolongation over 430 msec is

associated with ventricular arrhythmias, and EKG findings in lead aVR carry prognostic value. Terminal R wave greater than 3 mm in lead aVR is a useful predictor, and R/S ratio > 0.7 in lead aVR has a high positive predictive value for predicting ventricular arrhythmias.<sup>9</sup> While these EKG changes are predictive of clinical outcome, it is prudent to recognize that the timing of EKG recording is important and serial recordings should be considered.

Other potential EKG findings with TCA poisoning include prolongation of the PR and QT intervals, block within the His-Purkinje system, and intraventricular conduction delay (eg, bundle branch block)<sup>12</sup>. Because of its relatively longer refractory period, the right bundle branch is especially sensitive to block from TCA overdose. Brugada type pattern following TCA overdose has also been described<sup>12</sup>.

The EKG can neither unequivocally rule in nor rule out impending toxicity. Recognizing these limitations, the emergency physician can use the EKG findings in combination with other clinical data during the assessment of patients with TCA poisoning. EKG abnormalities can be used in the diagnosis, risk stratification, and management of affected patients. However, it is important to emphasize that none of the EKG findings is completely reliable in the individual patient, and significant toxicity can occur despite falsely reassuring indices.

The initial treatment of an acute overdose includes gastric decontamination by administering activated charcoal either orally or via a nasogastric tube<sup>9</sup>. Activated charcoal is most useful when administered within 1-2 hours of ingestion<sup>9</sup>. The immediate treatment for cardiac arrhythmias involves correcting hypoxia, electrolyte abnormalities, hypotension and acidosis. Intravenous sodium bicarbonate is the mainstay of treatment, and it may resolve arrhythmias even in the absence of acidosis<sup>9</sup>. Only if this therapy fails, should conventional antiarrhythmic drugs be used. The class 1b agent phenytoin has been studied in TCA poisoning, but its usage is controversial, and it is not generally recommended. There is also limited evidence for benefit from magnesium infusion<sup>5</sup>. Class 1a (quinidine, procainamide, disopyramide) and class 1c (flecainide) antiarrhythmic drugs should be avoided since they worsen sodium channel blockade, further slowing conduction velocity and depressing contractility<sup>5</sup>. Class II agents (beta-blockers) may also precipitate hypotension and cardiac arrest<sup>5</sup>. Class III drugs (bretylum and amiodarone) may

prolong QT interval, and therefore, increase the risk of arrhythmia<sup>5</sup>. Even though Lidocaine is a sodium channel blocker, it has been reported to effectively treat ventricular ectopy during TCA cardiotoxicity. Lidocaine has not been consistently effective in terminating ventricular arrhythmia, and as a result, it is not routinely used as a first line therapy. Hypotension is often treated with fluids and intravenous sodium bicarbonate<sup>9</sup>. If hypotension persists, pressor support with dopamine, epinephrine, or norepinephrine may be considered. Recent studies have suggested that lipid emulsions may reverse cardiotoxicity seen in TCA overdose; however, clear indications have not yet been established.

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