Cardiovascular complications of desipramine overdose

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The cardiovascular manifestations in a 36-year-old woman with desipramine intoxication are presented. Bradycardia, hypotension, electrocardiographic conduction abnormalities, and severe arrhythmias seen in our patient demonstrate the wide spectrum of cardiovascular complications associated with an overdose of this tricyclic agent. The definite need for prolonged ECG monitoring is indicated by the late mortality in our patient despite significant clinical improvement, and by the high incidence of life-threatening arrhythmias reported in patients with tricyclic overdose.

Desipramine hydrochloride is an antidepressant compound of the tricyclic class. It is used in treatment of both acute and chronic depression and is said to be less sedating than other tricyclics. The widespread use of tricyclic antidepressants in clinical practice has been associated with a marked increase in overdoses.

Reports from a number of studies provide data on electrocardiographic changes and deterioration in hemodynamic performance after toxic and therapeutic doses of tricyclic antidepressants. The cardiotoxicity of imipramine and amitriptyline the two most frequently prescribed tricyclic derivatives, has been well described. However, little is known about the cardiovascular effects of desipramine. In this report we describe the cardiovascular complications seen in a case of fatal desipramine intoxication.

Case report

A 36-year-old woman was admitted to the emergency room with coma and hypotension. She had no known history of cardiac disease but she did have a long history of psychiatric illness. She had been treated for depression as an outpatient by the psychiatric clinic, and her history was remarkable for multiple suicide attempts. On the day of admission the patient had taken an undisclosed amount of desipramine 50 mg.

In the emergency room she was immediately treated with 50% dextrose in water and 2 mg pethidine IV, without response. Permanent ventricular contractions were observed, 100 mg IV lidocaine was administered, and a generalized seizure occurred. After endotracheal intubation the heart rate slowed to 50 beats/min, after Ambu bag ventilation the heart rate increased to 70 beats/min. The blood pressure was noted by palpation to be 70 mm Hg, and one unit of plasma protein fraction (human) was given.

In the intensive care unit, the patient was unresponsive to deep pain. Her pulse was 90 and regular, respirations were 15/min assisted by a respirator, blood pressure was 70 to 80 mm Hg by palpation, and rectal temperature was 96° F. There were conjugate eye movements, absent corneal and oculocephalic reflexes, and normal fundi. The neck was supple and the lungs were clear. No heart murmurs, rales, or gallops were noted, but the patient had wide splitting of the second heart sound. The abdomen was unremarkable and no other neurologic deficits were observed.

On admission the white blood cell count was 5100/mm³ and the hematocrit 29. The blood urea nitrogen was 9 mg/dl, glucose 505 mg/dl, sodium 133 mEq/l, potassium 3.4 mEq/l, chloride 99 mEq/l and bicarbonate 20 mEq/l. Serum transaminases, ketones, and salicylates were all negative; osmolality was 330 mosm. Arterial blood gas obtained in the emergency room were pH 7.28, PO₂ 71 mm Hg, PCO₂ 31.4 mm Hg. and SaO₂ 92%. Urinalysis was normal. The chest roentgenogram revealed a normal-size heart, no infiltrates, and an endotracheal tube above the carina. The electrocardiogram showed trifascicular block (first-degree atrioventricular block, left anterior hemiblock, and a right bundle branch block pattern), prolongation of the Q-T interval, and ST-segment and T-wave abnormalities (Fig. 1).

In the ICU the patient received 8 mg IV phenytoin over a half hour and awakened, becoming responsive to verbal commands. She was then placed on a pethidine drip, and infusions of

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normal saline, plasma protein fraction (human), and diphenhydramine were required to maintain her blood pressure. On the second hospital day the blood pressure was stabilized at 100/70 mm Hg and supportive therapy was discontinued. The ECG showed a dramatic resolution of the previously seen triventricular block with shifting of the Q-T interval toward the normal range. Diffuse ST-segment and T-wave abnormalities were the only remaining abnormal findings (Fig. 2).

On the third hospital day the patient was weaned from the respirator and extubated. All blood cultures were negative. On the fourth hospital day she suddenly developed agonal respirations followed by a cardiopulmonary arrest. Ventricular fibrillation was noted on the ECG at the time of cardiac arrest and all resuscitative efforts were unsuccessful.

**Discussion**

This case of desipramine overdose with associated bradycardia, hypotension, electrocardiographic conduction abnormalities, arrhythmia, and late fatality demonstrates the wide spectrum of cardiovascular complications seen with tricyclic agents.

In evaluating the electrophysiologic properties of tricyclic compounds (imipramine and desipramine), experimental studies have shown a dose-dependent decrease in cardiac impulse generation and conduction. The prolongation of the P-R and Q-T ECG intervals, widening of the QRS complex, and ST-segment abnormalities seen on the surface ECG of our patient reflect these electrophysiologic changes and resemble those produced by quinidine and phenothiazine derivatives.32-35

His bundle electrocardiographic recordings have been done in humans to evaluate the therapeutic and toxic dose levels of tricyclic drugs on the intracardiac conduction system. The studies demonstrate a marked prolongation of atrioventricular conduction manifested by prolongation of the His-Purkinje conduction interval. On the surface electrocardiogram this
prolongation in conduction is reflected by various forms of AV node, bundle branch, and fascicular block. In contrast with the effects of the tricyclic compounds, methyline, trimipramine, and amitriptyline are the His-Purkinje conduction time, overdrive of dopamine (another tricyclic) in six patients did not cause intracardiac conduction defects. This study by Vohra et al supports the concept that different tricyclic compounds may differ in their effects on intracardiac conduction. The significant widening of the QRS complex in our patient with infarct-related block suggests a marked impairment of intracardiac conduction caused by desipramine. Tricyclic compounds have been shown to block the uptake of catecholamines by the heart, expelling them to enzymatic degradation. Administration of tricyclic compounds produces both negative inotropic and negative chronotropic effects. Decreased conduction velocity and the effects on catecholamine uptake in the myocardium and adrenergic receptors may explain the reasons behind the profound hypotension and bradycardia in this patient. The occurrence of bradycardia during endotracheal intubation seen in our patient was first reported by Williams and Sherter and demonstrates the hazards associated with increased vagal tone in patients with tricyclic intoxication. Since endotracheal intubation is usually indicated in most of these patients, pretreatment with atropine seems to be advisable.

There have been other reports of cardiac arrest and sudden death in patients taking large overdoses of tricyclic antidepressants. The clinical course of our patient is particularly noteworthy, since she died after significant improvement in level of consciousness and circulatory status.

**Conclusion**

Although ECG monitoring was not available just before the patient died, her death was probably related to ventricular fibrillation. The high incidence of life-threatening ECG disturbances reported in patients with tricyclic overdose supports this assumption. In addition, tricyclic agents have a half-life in the body of 60 to 90 hours—a factor that may explain the death of our patient four days after toxic ingestion. Considering this late mortality, there is a definite need for prolonged ECG monitoring, even after patients regain consciousness, in cases of toxic ingestion of tricyclic antidepressants.

**Nonproprietary names and trademarks of drugs**

methyline—Envi

desipramine—Norpramin, Pamelor

**References**


