



K15 Fatal Intoxication With Amiodarone: Report of Two Cases

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The goal of this presentation is to describe and discuss a case of fatal intoxication with amiodarone.

This presentation will impact the forensic science community by increasing awareness of toxicity of this widely used drug and its potential hazardous effect.

Amiodarone has become a widely used class III antiarrhythmic drug and is effective in treating both supraventricular and ventricular arrhythmias. It has been found to be more effective than other antiarrhythmic drugs in maintaining sinus rhythm, but because of its serious and potentially life threatening side effects, it is not the drug of first choice. Common side effects of amiodarone treatment are bradycardia, pneumonitis, liver function disturbances, hyperthyroidism, hypothyroidism, photosensitivity, cornea deposits, etc. Torsades de pointes and AV conduction disturbances are seldomly seen.

When amiodarone has been absorbed, it is metabolized in the liver to produce the active metabolite desethylamiodarone. Due to its lipophilic nature, it has strong tissue affinity and a large volume of distribution. In chronic users, high concentrations are found in fatty tissue, liver and lung and lower concentrations in kidneys, heart, skeletal muscle, thyroid gland and brain. The distribution to these tissues is relatively slow, and therefore a steady state of tissue concentration is reached only after two months. The relation between serum concentration and clinical effect is not very clear. The therapeutic concentrations of amiodarone in serum are 1-2.5 mg/l and serum concentrations > 2.5 mg/l have been associated with an increased risk of toxicity. The most commonly used oral dose is 200 mg per day. In Denmark due to potential risk of toxicity, only cardiologists are allowed to prescribe amiodarone.

Case 1: A 69-year-old woman was found dead at home in her bed. She had been prescribed amiodarone for atrial fibrillation. Three days earlier she was discharged from the hospital, where she was subjected to a catheter ablation in the left atrium. Previously, she complained of chest pain and a shortness of breath, and twice she was seen by the doctor from the emergency unit, who thought she was all right. At autopsy there were two small holes in the foramen ovale and discoloration in the septum and back wall as follows from the operation. Histology examination showed that the SA-node, the AV-node, and the bundle of His was normal. Routine drug testing was performed on the peripheral blood, and it revealed the concentration of amiodarone was 2.8 mg/kg. The medical examiner concluded that the cause of death was heart rate disturbances likely related to amiodarone intoxication.

Case 2: A 48-year-old woman was found dead at home. She was taking amiodarone for atrial fibrillation, and had gone through a catheter ablation in the left atrium two weeks earlier. Two days before her death, she was administered an electrical cardioversion at the hospital, and was discharged the next day. In the evening she called the hospital, because she had a feeling, her heart was not beating correctly. She was told to contact her general practitioner in the morning. The autopsy revealed a slight enlargement of the left atrium with discoloration of the wall, and arteriosclerosis of the left coronary artery and stenosis of the LAD. Histology examination revealed a normal SA-node, AV-node, and the bundle of His. Drug testing was performed on the peripheral blood, and the concentration of amiodarone of 4.0 mg/kg was found. The cause of death was established to be heart rate disturbances probably in relation to amiodarone intoxication.

Discussion: These two cases illustrated deaths due to unintended intoxication with amiodarone. The cases show how doctors need to keep the possibility of intoxication with amiodarone in mind when prescribing amiodarone to patients with persistent atrial fibrillation. Despite amiodarone's long history and current widespread use, there are no broadly accepted evidence-based monitoring recommendations. Since the serum concentration has little relation to the clinical effect, measuring it usually is of limited use. However, in such cases the measurement of concentration of amiodarone in serum can be considered in order to prevent the intoxication and death.

Amiodarone, Intoxication, Death