

## CASE REPORT

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### Fatal Disopyramide Intoxication from Suicidal/Accidental Overdose

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**ABSTRACT:** Disopyramide is an oral antiarrhythmic drug which reduces conduction velocity, prolongs duration of action potential and the effective refractory period, and exerts vagolytic properties. The drug is usually well absorbed orally. The principal use of the drug is to suppress ventricular extrasystoles with usual oral dosage of 100 to 200 mg every 6 h, until blood levels of 2 to 4  $\mu\text{g}/\text{mL}$  are attained. The use of the drug for suicide is uncommon as it is a prescription drug.

Two cases of fatal disopyramide intoxication seen at the Los Angeles County Medical Examiner's Office will be discussed followed by a review of the literature of fatal suicidal disopyramide overdose. Case 1 was a 31-year-old male pharmacist with known history of depression and no history of heart disease. His decomposed remains were found with a suicide note and with several disopyramide tablets. At autopsy the blood level for disopyramide was 146  $\mu\text{g}/\text{mL}$ . Case 2 is a 40-year-old male with history of alcoholism and prior suicidal attempts who regularly took disopyramide to control ventricular arrhythmias. He apparently ingested 36 100-mg tablets of disopyramide before his final collapse. At autopsy his blood level of disopyramide was 63  $\mu\text{g}/\text{mL}$ .

**KEYWORDS:** pathology and biology, disopyramide, suicide

Disopyramide is used in the treatment of cardiac arrhythmias of both atrial and ventricular origin. It is similar to quinidine in that it reduces conduction velocity, prolongs the duration of action potential, and prolongs the effective refractory period. It also has vagolytic properties. The usual oral dose of 100 to 200 mg every 6 h results in plasma concentration of 2 to 4  $\mu\text{g}/\text{mL}$ . Adverse side effects to the drug include aggravation of cardiac decompensation and atrioventricular block, vomiting, diarrhea, and anticholinergic effects like urinary retention, dry mouth, blurred vision, constipation, and exacerbation of glaucoma. Toxic levels usually result in abnormal QRS complex and worsening of congestive heart failure as a result of varying degrees of conduction disturbances [1].

#### Case 1

Case 1 consists of a 31-year-old male who lived alone, an unemployed pharmacist with no known history of heart disease, who was suffering severe depression. He had previously

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worked for a pharmaceutical company. His body was found highly decomposed in bed in a secured apartment on 4 April 1984. A suicide note was recovered along with eight disopyramide 100-mg capsules at the scene. He had no known cardiac problems. Autopsy findings revealed incised wounds on the left wrist. The heart was slightly enlarged (weight 440 g). There was a left testicular silicone implant. No evidence of any organ trauma was found. A toxicological screen of the autopsy tissues and fluids removed at autopsy revealed the following disopyramide levels: blood, 146.0  $\mu\text{g}/\text{mL}$ ; bile, 6.2  $\mu\text{g}/\text{mL}$ ; spleen, 10  $\mu\text{g}/\text{mL}$ ; and liver, 17  $\mu\text{g}/\text{g}$ .

## Case 2

A 40-year-old male with history of prior suicidal attempts and alcoholism was taking disopyramide to control ventricular arrhythmias. On 15 Nov. 1979, he cut his right wrist with a butter knife, then ingested alcohol and 36 100-mg disopyramide tablets, collapsing in front of his wife. He was taken to a local hospital where he was pronounced dead after resuscitative efforts failed. Autopsy findings included superficial incised wounds on the right wrist, the right little finger, abrasions in both forearms, and congestion of internal organs. The coronary arteries showed mild arteriosclerosis. A toxicological screen revealed a blood disopyramide level of 63.0  $\mu\text{g}/\text{mL}$ , ethanol of 0.09%, chlordiazepoxide of 9.2  $\mu\text{g}/\text{mL}$ , and lidocaine of 0.7  $\mu\text{g}/\text{mL}$ .

## Analytical Procedure

### *Brief Statement of Procedure*

Disopyramide is extracted from alkalized postmortem specimens with diethylether containing an internal standard. The diethylether is washed twice, extracted into acid, then back into chloroform. The extract is then analyzed by gas chromatography.

### *Reagents and Materials*

The stock solution was 1 mg/mL of disopyramide in ethanol.

The standards were 1, 2, 3, and 5  $\mu\text{g}/\text{mL}$  in water.

The internal standards were SKF (525-A) 100  $\mu\text{g}/\text{mL}$  in water; diethylether, anhydrous; 2*N* sulfuric acid; 0.5*N* sodium hydroxide; 10*N* sodium hydroxide; chloroform; and sodium bicarbonate.

All reagents are analytical grade and obtained from Baker Chemical Company.

### *Instrumentation*

Quantitations were performed with a Model 5890 gas chromatograph (Hewlett Packard) equipped with a nitrogen phosphorous detector (NPD). The column is a 10-m 50% phenylmethyl silicone fused silica capillary column, 0.54-mm inside diameter (ID). Helium is the carrier gas and was measured to be 30 mL/min, the hydrogen was measured to be 5 mL/min, and the air measured to be 300 mL/min. A temperature program was used with the following conditions: initial temperature—200°C held for 0.5 min, then the oven temperature increased 10°C/min until 280°C. This final temperature was held for 5 min.

### *Method*

Of the sample (blood, bile, stomach, or tissue homogenate), 15 mL together with 5 g of sodium bicarbonate are added to an 8-oz (237-mL) glass bottle. Then 120 mL of diethylether

TABLE 1—Review of literature of fatal suicidal disopyramide overdose.

Age and Sex of Person	Amount Ingested	Death Occurred (Time After Ingestion in Hours)	Symptoms	Levels of Disopyramide		
				Blood	Liver Spleen Contents	Gastric Contents
Hutchison et al. [3] 2-year-old male	6 of 100 mg	28 h.	Presented unconscious with cardiac arrhythmia.	No blood level done. Qualitative testing was positive.		
Hayler et al. [2]						
1. 16-year-old female	unknown amount	25 $\frac{1}{2}$ h.	Admitted unconscious.	Plasma level 4.3 mg/L 9 h after ingestion.		
2. 26-year-old female	40 of 150 mg	Within 12 h.	Found to be breathing oddly during the night by her husband. Was unconscious in the morning when taken to the hospital.	Postmortem blood level 114 mg/L.		
3. 24-year-old female	unknown amount	Within a few hours.	She was found to be drowsy and cyanosed while she was a patient in the hospital, then became unconscious.	Blood level 35 mg/L 3 h after ingestion.		
4. 17-year-old male	unknown amount	Within 14 h after ingestion of medication in the hospital.	He apparently had been admitted to the hospital after ingesting an unknown amount of temazepam from which he recovered. On the date of death, he was found unresponsive in lavatory in cardiac arrest. He was resuscitated but then subsequently became hypotensive arresting a few more times and expired 14 h after initially being found.	Blood level 35 mg/L 3 h after ingestion.		
5. 35-year-old male	68 of 100 mg	15 h after ingestion.	He was admitted unconscious.	Plasma level of disopyramide was 25.5 mg/L 4 h after ingestion. 14 h post-ingestion, his blood level was 34 mg/L. His stomach content was 2.3 g/L.		
Michaielek et al. [5] 19-year-old male	15 g	Unknown hours later.	Admitted unconscious.	More than 13 h after ingestion, his blood level was 8.3 mg/L. At autopsy, his blood level was 8.5 mg/L.		
				Blood level 57 mg/L. Liver level 115 mg/kg.		

TABLE 1—(Continued).

Age and Sex of Person	Amount Ingested	Death Occurred (Time After Ingestion in Hours)	Symptoms	Levels of Disopyramide				
				Blood	Liver	Spleen	Gastric Contents	Bile
Anderson et al. [4] 45-year-old female	Unknown amount of medication	Death occurred unknown time after ingestion.	Was unconscious.		Blood level was 26.6 mg/L. Liver level was 35 mg/kg.			
Powell et al. [6] 19-year-old female	3.75 g	Death occurred after 1 h.			29 mg/L in blood.			
Case 1, L.A. County Coroner		See narrative.						
Case 2, L.A. County Coroner		See narrative.						
					Blood level 146.2 mg/L. Stomach level 6.59 mg. Spleen level 10 mg/kg. Liver level 17 mg/kg. Bile level 6.2 mg/L.			
					Blood level 63 mg/L.			

containing 15  $\mu\text{g}$  of internal standard are added to the sample. The bottle is capped and placed on a platform shaker for 30 min. After shaking, the ether is decanted into a 250-mL separatory funnel and washed twice; once with 9 mL of 0.5*N* sodium hydroxide and then with 9 mL of distilled water. The ether is then extracted with 3.3 mL of 2*N* sulfuric acid for 3 min. The sulfuric acid layer is then drained into a 12-mL conical centrifuge tube. Then 1 mL of 10*N* sodium hydroxide is added. After the tube has cooled, 100  $\mu\text{L}$  of chloroform are added and the tube vortexed for 1 min. One microlitre of the chloroform layer is injected into the gas chromatograph.

### Calculations

A blank, standard, and quality control sample are run with each analysis. The standard and quality control are both in the therapeutic range for disopyramide (2 to 6  $\mu\text{g}/\text{mL}$ ). Sample calculations are based on the area for disopyramide with relation to the internal standard of a standard of known concentration. Any sample with a concentration greater than 5  $\mu\text{g}/\text{mL}$  must be diluted to bring its concentration within the linear range.

The sensitivity is 0.3  $\mu\text{g}/\text{mL}$  and the linearity is 0.5 to 5.0  $\mu\text{g}/\text{mL}$ .

### Discussion

Disopyramide is an unusual drug to be used for suicide. Hayler et al. [2] discussed five fatal overdose cases of disopyramide in the *The Lancet* (see Ref 1 and Table 1 below). The most common clinical finding in the five patients was an early loss of consciousness after an apneic episode. Most patients deteriorated rapidly with cardiac arrhythmias and loss of spontaneous respiration. The necropsy findings in four of their cases were mainly pulmonary congestion secondary to cardiac failure. Fatal levels in the blood and plasma in their cases ranged between 4.3 to 114 mg/L.

Hutchison et al. [3] discussed a two-year-old male who ingested 600-mg tablets of disopyramide who became unconscious following this (see Table 1).

Anderson et al. [4] discussed a case of a 44-year-old female who ingested an unknown amount of disopyramide medication. Her postmortem blood level was 26.6 mg/L.

Michealek et al. [5] discussed a case of a 19-year-old male who ingested 15 g of disopyramide with his blood level being measured as 57 parts per million (57/L).

Powell et al. [6] discussed a case of a 19-year-old female who ingested 3.75 g of disopyramide and had a level of 29 mg/L an hour later. She apparently died 5 h after ingestion in ventricular fibrillation after having regained consciousness for a short time in between.

### Conclusion

Disopyramide is regarded as a safe and effective antiarrhythmic drug when administered in correct dosage. When taken with suicidal intention, it causes early loss of consciousness after apneic episode. Necropsy findings are mostly that of pulmonary edema secondary to left ventricular failure which is compatible to negative inotropic effect of the drug. Concentrations of the drug in the fatal cases range anywhere between 4.3 to 146 mg/L.

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