Torsades de Pointes Therapy With Phenytoin

We present the case of a woman with myocardial infarction complicated by malignant ventricular arrhythmia and torsades de pointes. The torsades de pointes was refractory to conventional therapy but responsive to phenytoin. This case supports the clinical usefulness of phenytoin for adjunct therapy of life-threatening ventricular arrhythmias when standard treatment modalities fail. [Vukmir RB, Stein RS. Torsades de pointes therapy with phenytoin. Ann Emerg Med February 1991;20:198-200.]

INTRODUCTION
Ventricular tachycardia and fibrillation account for 75% to 85% of sudden cardiac death victims.1 Torsades de pointes, described originally by Duerrenstein, is a transitional arrhythmia between ventricular tachycardia and fibrillation.1,2 The incidence of torsades de pointes has been suggested to be as high as 32% in sudden cardiac death.3

We present the case of a 37-year-old woman who suffered a myocardial infarction complicated by dysrhythmias involving torsades de pointes. Although she died later that day, the torsades de pointes responded promptly to treatment with phenytoin.

CASE REPORT
A 37-year-old woman presented in cardiac arrest after complaints of chest pain. She was found unresponsive by the family and was without resuscitative effort for ten minutes. Emergency medical services personnel found the patient pulseless and apneic. ECG monitoring revealed ventricular fibrillation, asystole, and idioventricular rhythms. Standard advanced cardiac life support intervention included intubation, CPR, defibrillation, and administration of atropine, epinephrine, naloxone, fluids, bicarbonate, calcium, lidocaine, magnesium, and dopamine.

Emergency department assessment found that her medical history included hypertension treated with warfarin, an unknown kidney disorder, and an abortion two weeks before presentation. There was neither history of drug or alcohol abuse nor significant family medical history. Physical examination found the patient to be unresponsive with a systolic blood pressure of 70 mm Hg and heart rate of 130, undergoing assisted ventilation. Neurologic examination revealed dilated pupils with decerebrate posturing. Cardiopulmonary examination found scattered rhonchi, no rales, venous distention, and normal heart tones without murmur or gallop. A temp cerebrospinal fluid showed no evidence of trauma.

Laboratory evaluations revealed a hematocrit of 16.0, hematoctis, 44.3, platelets, 229,000 mm$^3$, and WBC, 30,100 mm$^3$. Electrolytes were remarkable for hypokalemia with potassium of 3.9 mEq/L and hyperglycemia with glucose of 447 mg/dL, sodium, 135 mEq/L, chloride, 100 mEq/L, HCO$_3$, 15 mEq/L, blood urea nitrogen, 15 mg/dL, creatinine, 1.2 mg/dL, calcium, 11.1 mg/dL, P$_{O_2}$, 2.9 mg/dL, and magnesium, 1.9 mg/dL. Liver function tests showed mild elevation of parenchymal enzymes with SGPT of 178 and SGOT of 346 U/L. Urinalysis showed microscopic hematuria and pyuria. Arterial blood gas analysis was remarkable for pH 7.53, P$_{CO_2}$ 27 mm Hg, HCO$_3$ 11 mEq/L, base excess, −15, and P$_{O_2}$ 161 mm Hg on an F$_{O_2}$ of 100%. ECG was significant for acute changes consistent with anteroseptal myocardial infarction with an intraventricular conduction...
Phenylpyrimidine is considered standard therapy for digitalis toxicity, which results in ectopy, conduction defects, and suppression of sinus pacemaking function and is associated with high mortality rates. Phenylpyrimidine is found to be the most effective agent for digitalis toxic arrhythmias in both animals and human beings, with a decrease in mortality rates in the range of 30% to 50%. Similarly, phenytoin is the drug of choice for tricyclic antidepressant overdose. In one study of patients with atrioventricular block or intraventricular conduction defect, normalization of the QRS complex was achieved in 50% of cases within 44 minutes and in the remainder by 14 hours at a mean total dose of 5.7 mg/kg.

The antitachyarrhythmic activity of phenytoin has been demonstrated in experimental ventricular tachycardia induced by coronary artery ligature, hypothermia, or toxin exposure, as well as in atrial tachyarrhythmias. The efficacy of phenytoin for ventricular tachycardia has been demonstrated in patients with congenital heart disease by reduction of postoperative arrhythmias occurring within 12 hours. A larger study of similar patients revealed that conventional therapy found control complete in 78.5% or reduction of ectopy in 91% of patients. Phenytoin was given in a bolus dose resulting in serum levels of 16.8 mg/dL or more after intravenous administration. A study suggesting a 10 to 18 mg/mL therapeutic range of phenytoin for control of ventricular arrhythmias. Phenytoin has also been valuable in the management of atrial fibrillation with repeatable atrioventricular tachycardia with response rates of 34% to 92.3% in prospective, placebo-controlled trials. In addition, phenytoin has been described as effective therapy for torsades de pointes in two case studies. The suggested dose of phenytoin for atrial fibrillation is 3.5 to 5.0 mg/kg administered at 50 mg/min to a maximum of 500 to 1000 mg/hr. Metabolites proceed by hepatic microsomal enzymes to produce 5-phenyl-5-para-aminosalicylic acid phenylhydantoin, which conjugates with glucuronic acid and is excreted by the kidneys. A duration of action is five to six hours. Side effects include skin rash at injection site [25%], dizziness [18%], and hypotension [5.2%]. Sinusartrial arrest in conjunction with lidocaine use has been described and attributed to depressant effect manifested as prolonged QRS complex width and length and recovery time. A single-agent therapy has resulted in one reported fatality after administration of 750 mg phenytoin over three minutes for atrial tachyrhythmias. Contraindications to the use of phenytoin include bradyarrhythmia and high-grade atrioventricular block.

Standard therapy for torsades de pointes typically includes magnesium, lidocaine, and atropine or other antiarrhythmic medications. Alternative therapeutic modalities include atrioventricular blockade, lidocaine, and amiodarone, either alone or with propranolol, calcium gluconate, and atropine.

**SUMMARY**

Torsades de pointes occur as a complication of lidocaine occurrence increases in malignant arrhythmias resistant to routine therapy, as in our patient. This case illustrates the use of routine pharmacological intervention for atrial fibrillation, including torsades de pointes, without effect. The case emphasizes the additional support for inclusion of phenytoin into the armamentarium of pharmacologic agents used for refractory ventricular arrhythmias.

**REFERENCES**


TORSADES DE POINTES
Vakhr & Stein

FIGURE 1. Prolonged QT interval.

TORSADES DE POINTES
Vakhr & Stein

FIGURE 2. Torsades de pointes in Parkin genes, particularly those depressed by digitals.7 Phenylpropionate is considered standard therapy for digitals toxicity, which results in ectopy, conduction defects, and suppression of sinus pacemaking function and is associated with high mortality rates.8 Phenylpropionate was found to be the most effective agent for digitals toxic arrhythmias in both animals and human beings, with a decrease in mortality rates in the range of 80% to 95%.9 Similarly, phenylpropionate is the drug of choice for tricyclic antidepressant overdose.10,11 In one study of patients with atrioventricular block or intraventricular conduction defects, normal QRS duration was 50% after 46 minutes and in the remainder 14 hours at a mean total dose of 5.7 mg/kg.4

The antiarrhythmic activity of phenylpropionate has been demonstrated in experimental ventricular tachycardia induced by coronary artery ligation, hypoxia, or toxin exposure, as well as in atrial tachycardias.9

The efficacy of phenylpropionate for ventricular tachycardia has been described in an animal model of patients with congenital heart disease by reduction of postoperative arrhythmias occurring within 12 hours.12 A larger study of similar patients with ventricular tachycardia responsive to conventional therapy found complete control in 78.5% or reduction of ectopy in 100% of patients after a mean dose resulting in serum levels of 16.8 mg/L.12

Standard therapy for torsades de pointes includes magnesium sulfate, isoproterenol, and atrial or ventricular pacing.13 Altern-ative therapeutic modifications include: ICD cadence, lidocaine, mecamylamine, phenytoin, procainamide, propafenone, calcium gluconate, and atropine.1415

SUMMARY

Although torsades de pointes occurs in a high-risk setting, the occurrence increases in malignant arrhythmias resistant to routine therapy, as in our patient. This case illustrates the use of routine pharmacologic interventions. The antiarrhythmic value of phenylpropionate has been proved in malignant ventricular rhythms, including torsades de pointes, without effective therapy. The case demonstrates additional support for inclusion of phenylpropionate into the armamentarium of pharmacologic agents used for refractory ventricular rhythms.

REFERENCES