Editor's Note

Atrial Fibrillation/Flutter: Rapid Conversion to Sinus Rhythm with Ibutilide

Introduction

When I began my career as a physician, the treatment of atrial fibrillation consisted mainly of quinidine administration until the patient developed wide QRS complex or prolongation of the QT interval or intolerant symptoms of the quinidine. Electrical cardioversion (using AC defibrillators) was coming into

vogue. Occasionally, ventricular fibrillation would occur immediately after cardioversion.

In the past, atrial fibrillation did not seem to be terribly important. However, as our patients age and heart failure has become the number one diagnosis-related group in patients over 65 years of age, atrial fibrillation now constitutes the commonest clinically important arrhythmia in my clinical practice. Setting aside the issue of anticoagulation in patients with chronic atrial fibrillation, I would like to focus on a new (for me) addition to the treatment of new onset atrial fibrillation. In the past year or so, I have gained some clinical experience with the drug ibutilide. Ibutilide was approved for use on December 28, 1995. Since this is a relatively new FDA-approved drug, I thought it might be useful to the readers of *Clinical Cardiology* to summarize what I have learned about this treatment of atrial fibrillation.

Indication for Use and Mechanism of Action

Ibutilide is a substituted methane sulfonamide derivative indicated for rapid conversion of atrial fibrillation or atrial flutter to normal sinus rhythm. Ibutilide is a Class III antiarrhythmic agent that exerts its action by promoting the influx of sodium through slow inward sodium channels, thus prolonging the action potential duration and causing a mild slowing of the sinus rate and AV conduction. When the drug converts atrial fibrillation or flutter to normal sinus rhythm it does so without lowering blood pressure or heart rate.

Metabolism

Ibutilide is administered by intravenous infusion. It is rapidly cleared from plasma. Ibutilide is metabolized in the liver and there is one active metabolite, but it makes up less than

10% of the ibutilide in the plasma. Elimination half-life of ibutilide is about 6 hours with a range of 2–12 hours.

Administration

The drug should be infused intravenously over 10 minutes and the infusion should be stopped as soon as the arrhythmia is terminated, or if sustained or nonsustained ventricular tachycardia occurs, or if there is marked prolongation of the QT or QTC interval. If the arrhythmia is not terminated within 10 minutes after the end of the initial infusion, a second 1 mg intravenous infusion may be given.

Contraindications

Some of the contraindications include significant bradycardia, breast feeding, severe heart failure, hypokalemia, pregnancy, patients whose QT interval is initially prolonged, patients with a history of torsade de pointes, patients with known ventricular arrhythmias, and patients with known ventricular tachycardia.

Clinical Experience

I am impressed by the ease with which this drug can be administered and by its high degree of success. In my personal experience using the drug in an academic in-patient cardiac unit, my success rate is about 60% in patients with atrial fibrillation of new onset. I don't have enough experience in the patients with atrial flutter to comment, but have not been impressed that atrial flutter is any easier to convert to sinus rhythm than atrial fibrillation. However, the literature indicates otherwise. At any rate, the problem of atrial fibrillation is not going to go away. As our population ages, the number of patients with atrial fibrillation will increase and we will be dealing with this arrhythmia more often than in the past.

Caution

Ventricular arrhythmias can occur in patients without documented QT prolongation. Thus, I don't think the drug should be used in the office setting. My preference is to treat patients in a place where the patient is observed and monitored by telemetry for a significant period of time. Since the half-life of the drug is approximately 6 hours, 6 hours is the time frame I use to monitor the patient. I have used the drug only in hospitalized patients. Others have used it in the emergency department setting. I do not recommend this unless the patient can be observed for the same period of time as an in-patient would be.

Time to Termination of Atrial Fibrillation/Flutter

The time to termination of the arrhythmia varies from minutes to hours. I have seen one patient who converted to sinus rhythm 2 1/2 hours after administration of a second dose of the drug. Of course, this may have been a spontaneous conversion unrelated to the drug. However, others have noted delayed conversion to sinus rhythm after administering this drug.

Which Patients Respond to the Drug?

Ibutilide seems to work in patients with new onset atrial fibrillation/flutter who have ischemic heart disease, large left atrium, small left atrium, no structural heart disease, dilated cardiomyopathy, and mitral stenosis. It seems to work less well in patients after cardiac surgery, but that may be related to other drugs administered postoperatively—for example, epinephrine, dobutamine, and so forth.

When Can Ventricular Arrhythmias Occur?

Polymorphic ventricular tachycardia can occur as early as 10 minutes after an ibutilide infusion. However, the majority occur within less than an hour after the start of the infusions. Most polymorphic ventricular tachycardia occurs while the patient is still in atrial fibrillation, but it can also occur after the patient has been converted to sinus rhythm.

Concomitant Drug Use

Digoxin, beta blockers, and calcium antagonists can safely be given prior to ibutilide infusion. Patients should not be treated with other antiarrhythmics prior to administration of ibutilide.

Conclusion

The beauty of ibutilide is that it works quickly, seems to be well tolerated, and does provide an alternative to cardioversion for rapid conversion of atrial fibrillation or atrial flutter to sinus rhythm. Others have reported that if the drug does not work after two doses, the patient can be cardioverted electrically with direct current, usually at a lower electrical energy. Another factor that makes ibutilide an attractive drug is the fact that it is short-acting and thus patients do not require long-term monitoring.

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Selected Reading

1. Ellenbogen KA, Stambler BS, Wood MA, Sager PT, Wesley RC Jr, Meissner MD, Zoble RG, Wakefield LK, Perry KT, Vanderlugt JT for the Ibutilide Investigators: Efficacy of intravenous ibutilide for rapid termination of atrial fibrillation and atrial flutter: A dose-response study. *J Am Coll Cardiol* 1996;28:130–136