Electrophysiologic Evaluation of Antiarrhythmic Drugs

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Summary. Electrophysiologic techniques are used to assess the properties of antiarrhythmic drugs and also to provide support for the selection of antiarrhythmic therapy for individual patients. Assessment of the antiarrhythmic efficacy of drugs requires that the arrhythmia can be induced by programmed electrical stimulation and is critically dependent on the stimulation protocol. Continued inducibility on drug therapy appears to be a strong predictor of recurrences and sudden death, although the predictive value of electrophysiologic testing remains controversial for some drugs. These techniques may also be useful for determining the proarrhythmic potential of antiarrhythmic agents, but the aggravation of tachycardia that occurs in 10–30% of patients during electrophysiologic testing is unpredictable and its significance is unknown. The electrophysiologic approach to drug therapy has limitations, but, nevertheless, it is useful and should maintain a prominent place in the evaluation of antiarrhythmic therapy.

Key Words. electrophysiologic studies, supraventricular arrhythmia, ventricular tachycardia, sudden death, proarrhythmia, antiarrhythmic drugs

Electrophysiologic techniques have been used for many years to evaluate the efficacy of single drugs. However, these techniques are being used increasingly to select appropriate drug regimens for patients with recurrent or life-threatening arrhythmias. Both the efficacy and the side-effect potential in individual patients may be assessed using electrophysiologic methods. Electrophysiologic stimulation (EPS) techniques are used to demonstrate the acute antiarrhythmic effects of drugs and may be useful for predicting long-term efficacy [1].

Methods and Evaluation Criteria

The EPS procedure is now well known. The technique involves catheterization of the right heart and programmed cardiac stimulation (PCS) with pacing at increasing rates to induce an arrhythmia similar to that occurring naturally in the patient. The procedure allows for the assessment of the functional properties of the heart, including the sinoatrial and atrioventricular function as well as the refractory periods of the heart, before and after drug administration, by repeat testing. The drugs can be administered either intravenously and/or as short-term oral treatment.

A drug is considered to be effective if the arrhythmia that was induced by EPS before drug therapy cannot be induced after administration of the drug. In this model, inducibility of the arrhythmia with a high degree of consistency before drug administration is essential for a meaningful assessment of the drug’s efficacy. A drug is also considered to have been efficacious if the arrhythmia is modified after drug administration. Such modifications include conversion of sustained tachycardia to unsustained tachycardia, a simple slowing of the rate of tachycardia, the persistence of only short bursts of tachycardia, or an increase in the number of stimuli required to induce the arrhythmia.

Supraventricular Tachycardias

EPS evaluation of supraventricular tachycardias is usually restricted to AV nodal reentry tachycardias and tachyarrhythmias associated with accessory pathways. It is not ordinarily used in patients with atrial fibrillation or atrial flutter. The results of these acute studies can be used in some cases to select the therapeutic regimen in patients with recurrent or dangerous arrhythmias, mainly, for example, in patients with Wolff-Parkinson-White syndrome.

The most commonly used drugs for AV nodal tachycardia are digitalis, beta blockers, and calcium inhibitors such as verapamil and diltiazem. They depress AV nodal conduction and prolong AH conduction time. In some cases Class I agents are also able to interrupt this tachycardia by blocking conduction on the retrograde AV nodal pathway. Amiodarone, sotalol, and bepridil seem able to act on both the antegrade and retrograde AV nodal pathways. All the Class I drugs, as well as amiodarone, sotalol, and be-
pridil, can depress conduction within accessory pathways. Amiodarone, sotalol, and bepridil are also able to slow conduction within the AV node and are particularly useful in patients with circus movement tachycardia and Wolff-Parkinson-White syndrome [2-4].

Figure 1 shows the action of sotalol in a patient with reciprocating tachycardia and an accessory pathway [3]. This tachycardia is initiated by ventricular stimulation. There are narrow QRS complexes. Antegrade conduction during tachycardia is occurring along the AV nodal pathway, and retrograde conduction utilizes accessory AV connections. The first atrial depolarization appears in the coronary sinus lead. After sotalol, the same procedure is only able to induce a short burst of tachycardia, and the last QRS complex is not followed by an atrial activity. It is a retrograde block along the accessory pathway that is responsible for the interruption of the tachycardia. But sotalol is also able to prolong the AH conduction time and to depress AV nodal conduction, as seen in this example.

Ventricular Tachycardias

The evaluation of ventricular tachycardia (VT) using EPS requires that the tachycardia be inducible using a well-defined stimulation protocol. The protocol employed in our laboratory uses one to three ventricular pacing cycle lengths, up to three extrastimuli, and one to two right ventricular stimulation sites. Very rarely left ventricular stimulation sites must be used if the procedure is unsuccessful in the right ventricle. Drug evaluation by EPS is mainly used with Class I and III agents. The drugs in the other classes have a low degree of efficacy against inducible VT.

The success rate measured in terms of suppressing the induction of VT is 20–30% for most Class I agents. The Class IB agents have a lower efficacy. The success rate with amiodarone is about 20%, with sotalol about 45%, and with bepridil about 30% [5,6]. Thus, in more than half the cases it is not possible to suppress the induction of VT with these drugs. Propranolol and verapamil have practically no efficacy in the prevention of VT induction.

Figure 2 shows an example of induced VT in the control state and the suppression of inducibility after sotalol. Before sotalol, the tachycardia is induced by two ventricular extrastimuli applied during a paced ventricular rate. After sotalol, three extra stimuli are necessary to initiate even a short burst of VT. In this case it is only possible to say that the drug is effective...