Efficacy of Oral Sotalol in Reentrant Ventricular Tachycardia

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Summary. Oral sotalol was given to 64 patients (78% postinfarction) with recurrent, reentrant ventricular tachycardia (VT) during an average follow-up period of 19.7 months. Fifty-nine (92%) patients had previously experienced recurrent ventricular tachycardia, in spite of having received an average of three conventional antiarrhythmic drugs (13 had previously failed on other Class III drugs). The nature and mechanism of the VT was proved with electrophysiologic testing (EPS), and the chronic sotalol dosage was determined by repeated EPS at 3- to 4-day intervals until the VT was no longer inducible.

Sotalol failed in five patients and was discontinued in six patients because of severe side effects (three proarrhythmic effects, including two with torsades de pointes)—a total of 18%. Sotalol was successful alone in 42 patients (65%) and in combination with another antiarrhythmic drug in 11 patients (18%). The average dose of sotalol required for success was 589 mg; 658 mg was the mean daily dose when given alone and 486 mg when given in combination.

Side effects were common and were due mainly to the beta-blocking effects of sotalol. Dual chamber pacing was required by 11 patients because of poorly tolerated bradycardia, and 14 patients remained symptomatic from worsening of the cardiac failure in spite of pacing, increased diuretics, or vasodilator therapy. The average drug dosage was the same for symptomatic (680 mg) and asymptomatic (627 mg) patients.

Sotalol is a valuable antiarrhythmic drug for reentrant ventricular tachycardia. High doses are needed, and at these doses the beta-blocking activity is responsible for most of the side effects.

Key Words. sotalol, reentrant ventricular tachycardia, reentrant supraventricular tachycardia, long-term follow-up, electrophysiologic testing, proarrhythmia, torsades de pointes

Patients and Methods

Sixty-four successive patients, 55 males and 9 females, 19–78 years of age, with a mean age of 57.5 years, with documented monomorphic ventricular tachycardia, proved to be reentrant, were entered into the trial. All patients presented with symptoms of hemodynamic compromise during the tachycardia. These included syncope or near syncope in the majority of cases. Others presented with episodes of hemodynamic collapse, often with obtunded consciousness. In no case were the only symptoms those of recurrent palpitations. The only exclusion parameter was airway obstruction aggravated by beta blockade. Clinical heart failure (NYHA grade III and IV) was present in 37% of the patients on entry. All but five patients had failed treatment with at least two antiarrhythmic drugs (average, 3.03) including 13 patients who had previously received amiodarone. Of the 64 patients, 50 had ischemic heart disease, 10 had congestive cardiomyopathy, and 4 had other etiologies (Table 1).

The nature and mechanism of the ventricular tachycardia was proved by an electrophysiologic study (EPS) done in the nonsedated drug-free state. Up to three programmed stimuli were delivered at basic cycle lengths of 600, 500, and 400 ms at the right ventricular apex. This programmed stimulation was repeated...
Table 1. Etiology of cardiac disease in 64 patients included in study

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease (postinfarct)</td>
<td>50</td>
</tr>
<tr>
<td>Congestive cardiomyopathy</td>
<td>10</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>1</td>
</tr>
<tr>
<td>Arrhythmogenic RV dysplasia</td>
<td>1</td>
</tr>
<tr>
<td>Previous electric abnormality</td>
<td>1</td>
</tr>
<tr>
<td>Post right ventriculotomy congenital heart disease</td>
<td>1</td>
</tr>
</tbody>
</table>

at the right ventricular outflow tract if stimulation at the apex was unsuccessful. Inducibility restricted to the RV outflow tract occurred in only one patient in this series. The final dosage for chronic oral therapy was determined by repeated programmed electrical stimulation (PES) every 3–4 days until the VT was no longer inducible. The dosage scheme is given in detail below. For the repeated PES challenge, a temporary pacing lead passed via the subclavian vein was left in the RV apex. At second and repeated studies, up to two timed stimuli at the above cycle lengths were given. It was felt that up to three stimuli could be given as a diagnostic procedure and that, since the VT was shown electrocardiographically to be identical to that of spontaneous arrhythmia, sufficient specificity had been achieved. For control, however, only two stimuli were given, since it was felt that a third stimulus would decrease the specificity of the response, in view of the fact that the milieu had been altered by the exhibition of the drug. The corrected QT interval (QTc) was calculated according to the formula of Bazzet [1].

Dosage schedules

Initially patients were started on 160 mg of sotalol daily divided into two oral doses, but the initial daily dose was soon increased to 320 mg daily when it became clear that success was most unlikely with 160 mg daily. Following the initial dose, successive increments were given at 3-day intervals to 640, 720, 960, 1280, 1440, and 1600 mg per day. Occasionally, an intermediate dose was given. If the ventricular tachycardia was still inducible and not partially controlled at a dose of 960 mg, the drug was abandoned. If there was some indication at PES that the drug was partially effective at a dose range of 960 mg, the higher doses were tried. If sotalol was unsuccessful alone, but some amelioration of tachycardia was seen at PES, such as increased difficulty in induction or slowing of the tachycardia, an additional antiarrhythmic drug was added at a dosage level of sotalol slightly below that associated with the amelioration and testing was repeated.

The follow-up period was 6–62 months, with an average of 19 months, and the number of EP studies was one initial EPS to qualify the patient for the trial and a mean of 3.26 repeats, giving a total mean of 4.26 EP studies to establish the effective dose. All patients received Holter monitoring at least once in the follow-up period, and there was an average of 2.83 Holter monitorings per patient.

Criteria for success of failure

The criteria for success were inability to reinitiate sustained monomorphic ventricular tachycardia and an absence of spontaneous episodes detected at follow-up. The failure level was defined as 30 or more successive beats of ventricular tachycardia. A final criterion for failure was a patient's inability to tolerate drug-induced side effects.

Results

Average effective daily dose

Average daily dose for patients successfully controlled with sotalol alone was 658 mg (range, 360–1600 mg). For patients who required a second antiarrhythmic drug for successful therapy, the average daily sotalol dose was 486 mg (range, 320–960 mg), and the average dose for those patients in whom the drug failed was 930 mg (range, 640–1400 mg). The median dose of sotalol was in the range of 640 mg daily (Table 2).

Efficacy

Sotalol was successful in preventing reinduction and/or recurrence of arrhythmia in 53 patients (82%). It was successful alone in 42 patients (65%) and in combination with other drugs in 11 (17%). Primary failure of sotalol to prevent reinduction of the tachycardia occurred in five patients, and the drug was discontinued because of side effects in a further six patients. Of the latter, three had serious proarrhythmic effects including one with facilitation of induction of the tachycardia, which developed into a rapid polymorphous ventricular tachycardia, and two cases of torsades de pointes. In neither of the cases of torsades de pointes was there a detectable biochemical abnormality, such