

## Pharmacological Treatment of Ventricular Arrhythmias

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### Summary

*Several clinical studies were performed to demonstrate the effect of antiarrhythmic drugs on mortality in patients with or at risk of ventricular arrhythmias. As a primary prevention treatment, Class I and Class II drugs had a harmful and a beneficial effect on mortality, respectively. Among Class III drugs, d-sotalol had a negative effect on survival, and d-l-sotalol caused no change or an increase in the patient survival rate. In secondary prevention studies, electrophysiologically-guided sotalol and empirical amiodarone were found to be superior to the guided Class I drugs. Mortality in the guided conventional antiarrhythmic drug group and the empirical metoprolol group was unchanged. Randomized trials indicated that ICD therapy was more effective in increasing the survival rate.*

### Key Words

Antiarrhythmic drugs, cardiac mortality

### Pharmacological treatment of ventricular arrhythmias

Pharmacological treatment of ventricular arrhythmias will be discussed briefly in this paper. The first part of this review deals with treatment of ventricular extrasystoles and nonsustained ventricular tachycardia, and primary prevention of sustained ventricular tachycardia and -fibrillation; the second part summarizes the treatment of sustained ventricular tachycardia and ventricular fibrillation, and secondary prevention of malignant ventricular arrhythmias.

### Treatment of ventricular extrasystoles and nonsustained ventricular tachycardia, primary prevention of sustained ventricular tachycardia and ventricular fibrillation

For over a decade, several randomized clinical trials have been performed in order to determine a means of preventing sudden heart death [1-14]. The Cardiac Arrhythmia Suppression Trial (CAST) was designed to show that Vaughan-Williams Class Ic antiarrhythmic drug therapy would reduce the risk of death by suppressing ventricular arrhythmia. It was found, however, that the drugs used in this trial, encainide and flecainide, increased mortality. Subsequently, a meta-

analysis of previous trials using other drugs of the same class clearly indicated the likelihood that all Class I agents have a potential for harm and almost no potential for benefit.

From 1985-95, 13 randomized, controlled trials of amiodarone were performed. A meta-analysis of these trials has recently been reported. There were eight post-myocardial infarction (MI) trials and five heart-failure trials, with a total of 6,553 patients. With amiodarone, total mortality was reduced by 13% ( $p = 0.03$ ), and arrhythmic death was reduced by almost 30% ( $p = 0.003$ ); both of these figures are significant. There was no effect on deaths not due to arrhythmia. Amiodarone was generally well tolerated, although in some trials there was a high rate of drug discontinuation. A meta-analysis of the post-MI  $\beta$ -blocker trials showed a 20% reduction in total mortality. A very important aspect of the effect of  $\beta$ -blockers is the reduction of deaths due to arrhythmia. Recently, two large, randomized, controlled trials in high-risk patients demonstrated that dofetilide, a purely Class III agent, has no effect on mortality. Two prophylactic implantable cardiac defibrillator (ICD) trials have been performed. The Multicenter Automatic Defibrillator Trial (MADIT) studied patients with a low left-ventricular ejection fraction and nonsustained ventricular tachycardia.

Eligible patients had VT that was inducible with programmed electrical stimulation and non-suppressible with procainamide. The MADIT reported a marked reduction in overall mortality with ICD therapy as compared to conventional drug therapy (mainly amiodarone). The Coronary Artery Bypass Graft (CABG) Patch trial, however, found no difference in mortality among high-risk CABG patients receiving ICD therapy as compared to those undergoing conventional therapy.

Several ongoing studies are evaluating the benefits of prophylactic ICD therapy in both post-MI and congestive heart failure patients.

### **Treatment of sustained ventricular tachycardia and ventricular fibrillation; secondary prevention of malignant ventricular arrhythmias.**

Some studies have been conducted in the field of secondary prevention of malignant ventricular arrhythmias [15-19]. The most important drug studies are the following: CASCADE (Cardiac Arrest in Seattle: Conventional versus Amiodarone Drug Evaluation), ESVEM (Electrophysiological Study versus Electrocardiographic Monitoring), and the study conducted by Steinbeck et al. The objective of the CASCADE study was to compare empirical treatment with amiodarone and treatment with Class I antiarrhythmic drugs guided by electrophysiological testing or Holter monitoring for survivors of out-of-hospital ventricular fibrillation. Amiodarone appeared to be more effective than Class I drugs in the prevention of death (Survival rate at 6 years: 47% with amiodarone versus 60% with class I drugs,  $p = 0.007$ ).

Steinbeck et al. [16] compared the empirical treatment with metoprolol and treatment with conventional antiarrhythmic drugs (mainly class I drugs) guided by electrophysiological testing or Holter monitoring for patients with malignant ventricular arrhythmias. There were no significant differences in arrhythmia-recurrence or sudden cardiac death between the empirical metoprolol group and the conventional antiarrhythmic drug group guided by electrophysiological testing. However, the sudden cardiac death rate was lower for the patient group receiving conventional antiarrhythmic treatment.

The ESVEM study evaluated the effect of d-l sotalol and class I antiarrhythmic drugs for arrhythmia-recurrence, total mortality, cardiac mortality, and sudden

cardiac death. D-l sotalol was more effective than the Class I antiarrhythmic drugs in preventing arrhythmia recurrence ( $p = 0.001$ ) and in decreasing total mortality ( $p = 0.004$ ), cardiac mortality ( $p = 0.002$ ), and sudden cardiac death ( $p = 0.004$ ). Since 1985, the use of ICD therapy has become much more prevalent, and evidence has accumulated regarding the high efficacy of devices in controlling sudden cardiac death. Recent randomized trials (AVID, CASH, CIDS) compared the long-term effects of ICD- and drug therapy in the treatment of malignant ventricular arrhythmias. The results of these randomized trials indicated that ICD therapy was superior to drug therapy for patients suffering from ventricular tachycardia or ventricular fibrillation.

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