Electrical storm: still a cryptogenic phenomenon?

Wilhelm Haverkamp

Department of Cardiology, Charité – Campus Virchow Clinic, Augustenburger Platz 1, 13353 Berlin, Germany

Online publish-ahead-of-print 22 November 2006

The implantable cardioverter/defibrillator (ICD) has become the dominant therapeutic modality for the treatment of life-threatening ventricular tachyarrhythmias. However, the ICD does not prevent the occurrence of ventricular tachycardia (VT) or ventricular fibrillation (VF). Repeated tachyarrhythmias occurring in a short period of time may therefore result in the delivery of multiple shocks. This phenomenon has been termed 'electrical storm' (ES). ES constitutes a medical emergency, which usually results in hospitalization. Occasionally, individual patients may experience more than 50 consecutive shocks. Most patients become anxious and agitated, and psychosocial consequences often outlast the acute event. ES may also cause premature ICD battery depletion necessitating generator replacement.

Fortunately, patients experiencing extremely frequent ICD discharges are rare. In order to make it possible to study the mechanisms, predictors, and the prognostic significance of ES, its definition has been broadened. Some studies defined ES as two or more arrhythmia episodes resulting in ICD activation (either antitachycardia pacing or shock delivery) within 24 h, whereas others used three or more arrhythmia episodes. Most investigators have considered multiple consecutive shocks occurring within several minutes as one arrhythmia episode. However, all of these definitions are arbitrary. It cannot be determined whether patients who have a few arrhythmia episodes within 24 h significantly differ from those who have multiple episodes during the same time window in terms of the underlying mechanism.

Most published studies are single-centre retrospective evaluations that have assessed the frequency of ES in consecutive ICD patients. The results of these studies suggest an incidence of ES ranging from 10 to 28% during follow-up durations. The results of these studies suggest that low left ventricular ejection fraction (LVEF) and sustained VT as the initial arrhythmia leading to ICD implantation are independent risk factors for the occurrence of ES.

So far, only one study has prospectively studied the clinical characteristics and prognostic relevance of ES. In the Antiarrhythmic Versus Implantable Defibrillators (AVID) trial, ES was a significant risk factor for subsequent death, independent of LVEF and other prognostic variables. The development of single episodes of VT/VF was not associated with an increased risk of subsequent death.

Hohnloser et al. present the results of another prospectively designed study. As a prespecified secondary efficacy endpoint of the Shock Inhibition Evaluation with Azimilide (SHIELD) trial, all episodes of ES were documented and subsequently analysed. The primary aim of SHIELD was to assess the safety and efficacy of azimilide in reducing symptomatic tachyarrhythmia recurrences and subsequent ICD therapies in patients with ICDs. In fact, compared with placebo, a significant reduction of all ICD therapies was observed in patients taking 75–125 mg of azimilide. Of note, five patients in the azimilide groups and one patient in the placebo group developed torsade de points.

In the ES substudy presented here, 148 (23%) out of 633 patients experienced at least one episode of ES (three or more arrhythmia episodes within 24 h) within a 12-month period. This incidence is higher than that described by the AVID analysis (20% of patients developed ES, mean follow-up 31 ± 13 months). More than one half of the patients suffered from more than one ES episode. Most patients had VT storms, the first ES episode occurred within a mean of 3 months after study enrolment. Frequently, ES resulted in emergency hospitalization. Patients with ES had a significantly higher risk for hospitalization compared with patients with isolated VT/VF events. A detailed analysis of the clinical features of ES did not reveal independent predictors of the event. In contrast to previous retrospective studies, the LVEF was not lower, but significantly higher in patients with ES. In congruence with earlier studies, identifiable precipitating causes for ES were rare (new or worsening of heart failure, 9%; electrolyte disturbances, 4%). Azimilide did not significantly reduce the number of patients with ES; only a trend towards a dose-dependent reduction of patients with ES was observed: of the 148 patients who experienced at least one episode of ES, 58 (27%) were on placebo, 51 (23%) on 75 mg and 39 (20%) on 125 mg azimilide. Furthermore, a statistical analysis of the time-to-first ES event did not reveal significant differences between the treatment groups. Compared with placebo, only the risk of recurrent ES was significantly reduced by

The opinions expressed in this article are not necessarily those of the Editors of the European Heart Journal or of the European Society of Cardiology.

Corresponding author. Tel: +49 30 450 553 961; fax: +49 30 450 553 961. E-mail address: wilhelm.haverkamp@charite.de

doi:10.1093/eurheartj/ehl276

© The European Society of Cardiology 2006. All rights reserved. For Permissions, please e-mail: journals.permissions@oxfordjournals.org
azimilide (by 37% in the 75 mg group and by 55% in the 125 mg group, respectively).

These, at first glance, contradictory results are difficult to explain. Do they just reflect antiarrhythmic effects of azimilide, which are smaller than those that can be detected based on the number of patients included in the study and/or the methods of statistical analysis applied? Anyway, the results show that the efficacy of azimilide in reducing ES is at least very limited. In the original SHIELD trial, compared with placebo, a significant reduction of all ICD therapies was observed in patient receiving azimilide. However, a clinically useful drug should first and foremost prevent the most severe and compromising arrhythmia, e.g. episodes of ES (not only ES recurrences but above all the clinical manifestation of this problem, i.e. the first ES episode).

One factor that may have potentially affected the results of the present study may be pro-arrhythmia associated with azimilide. Torsade de pointes associated with azimilide treatment was documented in five patients (1.2%). All episodes occurred early during treatment. The real incidence of torsade de pointes may have been even higher and torsade de pointes may have also contributed to some episodes of ES. It is noteworthy that in 40% of all arrhythmia episodes only ICD log data and no electrograms, which would have allowed a more accurate arrhythmia analysis, were available. The occurrence of torsade de pointes is not limited to the early phase of therapy. It is well known that it may occur even years after the start of treatment. Recently, Mazur et al. studied the effect of dofetilide on the incidence of torsade de pointes and ICD electrograms from arrhythmia episodes compatible with torsade de pointes in a multicentre study that randomized ICD patients to placebo (n = 87) or dofetilide (n = 87). In contrast to azimilide, which blocks both the slow (IKs) and the fast (IKr) activating components of the delayed rectifier potassium current, dofetilide is a pure IKr blocker. Five episodes of torsade de pointes were identified early during dofetilide therapy (<3 days), 10 episodes developed later during therapy (median time to the event was 22 days (range 6–107 days). These late events were identified by ICD electrogram analysis. The authors concluded that either long-term treatment with dofetilide was associated with an increased incidence of torsade de pointes or that the drug had changed the characteristics of VT. Although speculative, it cannot be excluded that in the present study the pro-arrhythmic effects associated with azimilide may have outweighed antiarrhythmic effects of the drug.

The study by Hohnloser et al. is the first study that has prospectively studied the role of antiarrhythmic drug therapy in preventing ES. Previous studies have shown that sotalol and amiodarone in combination with a beta-blocker may be effective in preventing shocks from implantable ICDs, but the problem of ES was not specifically addressed by these studies. Since sotalol may also cause pro-arrhythmia in a significant proportion of treated patients and amiodarone has relatively frequent clinically relevant side effects necessitating drug withdrawal, particularly during long-term treatment, a safe and effective prophylactic antiarrhythmic treatment for ICD recipients is currently not available. Beta-blockade alone is insufficient to prevent ES. In the study by Hohnloser et al., more than 80% of patients received concomitant beta-blocker treatment. The decision to prescribe an antiarrhythmic drug to an ICD recipient should be individualized, taking into account not only the possible improvement in quality of life but also the increased risks of drug-related pro-arrhythmia and side effects.

The paper by Hohnloser et al. is a welcomed initiative. The major message is that ES needs further evaluation with regard to its mechanisms, potential predictors, and clinical features. It is hoped that with this information, effective and safe preventive measures will become available in the near future.

Conflict of interest: none declared.

References