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Propranolol Versus Metoprolol for Treatment of Electrical Storm in Patients With Implantable Cardioverter-Defibrillator

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ABSTRACT

BACKGROUND Electrical storm (ES), characterized by unrelenting recurrences of ventricular arrhythmias, is observed in approximately 30% of patients with implantable cardioverter-defibrillators (ICDs) and is associated with high mortality rates.

OBJECTIVES Sympathetic blockade with β-blockers, usually in combination with intravenous (IV) amiodarone, have proved highly effective in the suppression of ES. In this study, we compared the efficacy of a nonselective β-blocker (propranolol) versus a β_1-selective blocker (metoprolol) in the management of ES.

METHODS Between 2011 and 2016, 60 ICD patients (45 men, mean age 65.0 ± 8.5 years) with ES developed within 24 h from admission were randomly assigned to therapy with either propranolol (160 mg/24 h, Group A) or metoprolol (200 mg/24 h, Group B), combined with IV amiodarone for 48 h.

RESULTS Patients under propranolol therapy in comparison with metoprolol-treated individuals presented a 2.67 times decreased incidence rate (incidence rate ratio: 0.375; 95% confidence interval: 0.207 to 0.678; $p = 0.001$) of ventricular arrhythmic events (tachycardia or fibrillation) and a 2.34 times decreased rate of ICD discharges (incidence rate ratio: 0.428; 95% CI: 0.227 to 0.892; $p = 0.004$) during the intensive care unit (ICU) stay, after adjusting for age, sex, ejection fraction, New York Heart Association functional class, heart failure type, arrhythmia type, and arrhythmic events before ICU admission. At the end of the first 24-h treatment period, 27 of 30 (90.0%) patients in group A, while only 16 of 30 (53.3%) patients in group B were free of arrhythmic events ($p = 0.03$). The termination of arrhythmic events was 77.5% less likely in Group B compared with Group A (hazard ratio: 0.225; 95% CI: 0.112 to 0.453; $p < 0.001$). Time to arrhythmia termination and length of hospital stay were significantly shorter in the propranolol group ($p < 0.05$ for both).

CONCLUSIONS The combination of IV amiodarone and oral propranolol is safe, effective, and superior to the combination of IV amiodarone and oral metoprolol in the management of ES in ICD patients. (J Am Coll Cardiol 2018;71:1897–906)

Patients with an implantable cardioverter-defibrillator (ICD) carry a significant baseline risk for the development of recurrent ventricular arrhythmias (1). Furthermore, approximately 30% of ICD recipients ultimately develop an electrical storm (ES), which is a life-threatening syndrome presenting with recurrent episodes of ventricular arrhythmias in a short period of time that subsequently results in appropriate device interventions (2,3). The incidence of ES varies depending on

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ABBREVIATIONS AND ACRONYMS

ACE = angiotensin-converting enzyme

ATP = antitachycardia pacing

CI = confidence interval

ES = electrical storm

HF = heart failure

HR = hazard ratio

ICD = implantable cardioverter-defibrillator

ICU = intensive care unit

IRR = incidence rate ratio

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

VF = ventricular fibrillation

VT = ventricular tachycardia

the under-investigation populations; interestingly, 10% to 58% of ICD recipients for secondary prevention while 4% to 7% for primary prevention experience an ES during their lives (2).

Given its poor short- and long-term prognosis, developing effective strategies for the ES episodes is of paramount importance (4,5). Sympathetic blockade with β-blockers, usually in combination with intravenous (IV) amiodarone, has proved highly effective in the suppression of ES in patients with recent myocardial infarction (6). Our initial experience indicates that a nonselective β-blocker is more effective in the suppression of ES compared with a selective one (7). However, large cohort studies comparing the efficacy of selective and nonselective β-adrenergic blockade on ES in ICD patients are missing. The aim of the present study was to investigate the short-term effects of oral metoprolol (β_1-selective blocker), in comparison with propranolol (nonselective β-blocker), on the termination of ES in ICD patients.

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METHODS

STUDY SETTING AND POPULATION. In this prospectively designed study, we analyzed data from patients with an ES initiated within 24 h before their admission. Patients were recruited between January 2011 and December 2016 from the "Alexandra" Hospital, Athens, Greece. The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board and all participants provided written consent forms. The diagnosis of ES was defined as 3 or more episodes of ventricular tachycardia (VT) or ventricular fibrillation (VF) separated by a period of at least 5 min that developed within a 24-h period and resulted in device intervention. Exclusion criteria were defined as coexistence of at least 1 of the following comorbidities: 1) drug-induced arrhythmias, or arrhythmias secondary to acute myocardial ischemia or acute congestive heart failure (HF); 2) patients with prolonged QT interval defined as >0.50 s; 3) patients with hypokalemia, impaired renal or hepatic function; and 4) baseline systolic blood pressure <90 mm Hg. Acute coronary syndrome was ruled out by detailed patient history, physical examination, electrocardiographic criteria for myocardial ischemia, and serum kinetics of creatine kinase-myocardial band and troponin I and T, which—although slightly increased due to ICD discharges—were not indicative of ischemia. High suspicion for myocardial ischemia in 2 patients necessitated the performance of coronary angiography that eventually revealed no significant coronary artery lesions in both cases.

STUDY PROTOCOL AND RANDOMIZATION. Patients were randomly assigned to an antiarrhythmic drug therapy with either a nonselective β-blocker (short-acting propranolol, peak plasma time 1 to 4 h) or a β_1-selective blocker (short-acting metoprolol tartrate, peak plasma time 1.5 to 2 h) in a 1:1 ratio. The study was blinded to all except for a designed third party who did not participate in the evaluation or the care of patients. Each β-blocker was administered per os for 48 h in every patient. Group A patients initiated on 40-mg propranolol followed by 40 mg every 6 h (cumulative dose 160 mg/24 h). Group B patients initiated on 50-mg metoprolol followed by 50 mg every 6 h (cumulative dose 200 mg/24 h). At the same time, amiodarone was administered intravenously in both groups with an initial rapid infusion rate of 30 mg/min over 10 min, followed by continuous infusion with a maintenance dose of 1,000 mg/24 h for 48 h.

All patients were admitted to the intensive care unit and were closely monitored by continuous electrocardiography telemetry and blood pressure monitoring. VT or VF events as well as changes in blood pressure or heart rate, or adverse reactions, were recorded every 60 min for a total period of 48 h. Following 48 h, patients continued the treatment with propranolol (Group A) or metoprolol (Group B) at the same dose, in combination with per os amiodarone 200 mg once daily until hospital discharge. In case of serious adverse events, namely severe hypotension, congestive HF, bronchospasm, or arrhythmia exacerbation, the study had to be discontinued and patients were treated accordingly.

In all patients, previous antiarrhythmic medications, including β-blockers (carvedilol, metoprolol, or bisoprolol), calcium-channel antagonists, and amiodarone were discontinued upon entering into our study. Other necessary therapies including angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, aldosterone antagonists, and diuretics were continued in accordance to the respective clinical guidelines (8). After hospital discharge, all patients were advised to continue on the maximum tolerated dose of the β-blocker they were receiving before the study enrollment, in combination with 200-mg oral amiodarone per day for the following 2 months.