Successful antiarrhythmic therapy with combination of quinidine and mexiletine in Purkinje-related ventricular arrhythmia, persistent atrial tachyarrhythmia and DCM associated with R814W SCN5A mutation

Authors:
J Zakrzewska-Koperska¹, ZT Bilinska¹, GT Truszkowska¹, M Franszeczyk¹, K Kalin¹, K Guzek¹, A Hasiec¹, M Stepień-Wojno¹, M Orczykowski¹, R Bodalski¹, P Urbanek¹, R Baranowski¹, L Szumowski¹, R Płoski², M Bilinska¹, ¹Institute of Cardiology - Warsaw - Poland, ²Medical University of Warsaw, Department of Medical Genetics - Warsaw - Poland

Topic(s):
Ventricular Arrhythmias and SCD - Treatment

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Background:
SCN5A gene mutations are described in 2-4% of patients with dilated cardiomyopathy (DCM). In such cases DCM is associated with different arrhythmias like His-Purkinje-related ventricular contractions and atrial fibrillation/flutter (AF/AFL) as well as symptomatic sick sinus and conduction disturbances. Arrhythmia often occurs in young age and is the first symptom of heart disease.

Family case:
We present cases of 56 year old man and 36 year old woman, father and daughter, with symptoms of heart failure (HF) in the course of familial DCM and complex ventricular tachyarrhythmias (VEBs/VT) with atrial fibrillation. Father has 20-year history of HF and ventricular arrhythmias, which constituted 50-60% of whole rhythm, and longstanding AF/AFL for 10 years with coexistent diabetes mellitus type 2, hypertension, coronary artery disease. Daughter stays symptomatic at the age of 32, after significant increase of ventricular and supraventricular arrhythmias. Both have ICD-VR implanted since 2006. There were two cases of sudden cardiac death and one case of heart transplantation among their siblings.

We found a heterozygotic mutation R814W in SCN5A by whole exome sequencing in the proband and confirmed its presence in all affected subjects.

In a father after quinidine treatment we observed significant reduction of ventricular arrhythmia with reduction of HF symptoms and elevation of LVEF from 35% to 55%. This effect was constant during 2 year observation. Adding mexiletine to quinidine therapy reduced the arrhythmia (VEBs/including VT from 47 thousand/day to 6-8 thousand/day and reversion longstanding AF to sinus rhythm) and remains effective during 1,5 year follow-up. However, quinidine in monotherapy was unsuccessful and badly tolerated in daughter. In her case mexiletine and overdrive AAI/DDD stimulation were effective in ventricular arrhythmia treatment (VEBs decreased from 25 thousand/day to 50/day), reduced HF symptoms and improved of left ventricle function. Because of growing number of AF/AFL recurrences we used the combination of mexiletine with reduced dose of quinidine (then flecainide) with antiarrhythmic success in 6 month follow-up.

Questions:
When in DCM patients genetic testing should be offered?
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Institute: 1. Institute of Cardiology - Warsaw - Poland, 2. Medical University of Warsaw, Department of Medical Genetics - Warsaw - Poland

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Questions:

How to treat severe ventricular arrhythmia in SCN5A mutations? Is it possible to avoid/delay heart transplant in this subgroup of DCM patients?

Conclusions: Treatment with quinidine combined with mexiletine for patients with SCN5A R814W associated disease leads to significant reduction of severe ventricular arrhythmia, reversal of long-standing persistent AF and improvement in myocardial function. Genetic screening should be performed in patients with His-Purkinje related ventricular arrhythmia and DCM. Our report highlights the role of genetic testing for personalized treatment in cardiology.