Antiarrhythmic Drug Treatment for Atrial Fibrillation: Effectiveness of Drug Depends on Electrophysiological Profile

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Introduction: Antiarrhythmic drug efficiency is not well described in Atrial Fibrillation (AF) as the final effect on the patient depends on specific characteristics such as the genetic expression.

Aims: To study the effect of 5 antiarrhythmic drugs on a population of mathematical models with chronic AF.

Methods: 127 mathematical models were tested for a fixed tissue size (40000 nodes i.e. 2cmx2cm) and under the effect of five antiarrhythmic drugs: flecainide, verapamil, amiodarone, dofetilide and sotalol at three different increasing concentrations each. Electrophysiological biomarkers (e.g. action potential duration, APD90, and Conduction Velocity) were measured at 1Hz.

Results: Antiarrhythmic drugs, except of sotalol, produced an expected homogeneous reduction on conduction velocity in all preparations, following the same behavior observed during in-vivo experiments. Interesting, different effects were observed in the population at the highest concentration of each drug: elongation of APD90 for all drugs was observed for 18 profiles (14.17%) (Figure 1A), shortening of APD90 was observed for 12 profiles (9.45%) (Figure 1B) and divergent effects depending on the drug was observed for 97 profiles (76.38%) (Figure 1C). Effect of each drug on APD90 was mainly dependent on the balance between I_{Na}, I_{CaL} and I_{K1} conductances.

Conclusions: Our analysis demonstrated that same antiarrhythmic drug can have completely opposite effects on action potential duration depending on the specific electrophysiological properties. Those results could help to improve AF patients stratification and an increase antiarrhythmic drug efficacy.