Advantageous antiarrhythmic and cellular electrophysiological effect of the metabolite of amiodarone (desethylamiodarone)

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Desethylamiodarone (DEA) is the major metabolite of amiodarone (AMIO), which is considered as one of the most effective drugs for the treatment of various types of cardiac arrhythmias including atrial fibrillation (AF). The therapeutic value of AMIO, however, is greatly limited by its non-cardiac adverse effects. Previous reports indicated that DEA had more binding affinity for the cardiac thyroid receptor than its parent compound AMIO. Therefore, the aim of our study was to compare the possible antiarrhythmic effect of DEA in comparison with AMIO in different experimental arrhythmia models. In a conscious rat model of coronary artery ligation-induced ventricular arrhythmias, per os 50 mg/kg/day (3 weeks) DEA administration exerted similar antiarrhythmic effects to 100 mg/kg/day (3 weeks) AMIO pre-treatment increasing survival from 23 % (n=39) to 80% and 75%, respectively. In the atrial tachypaced dog atrial fibrillation model, per os 50 mg/kg/day (4 weeks) AMIO treatment decreased the duration of AF episodes to a similar extent to per os 25 mg/kg/day (4 weeks) DEA treatment. Cellular cardiac electrophysiological effects of DEA treatment on action potential and transmembrane ionic current were also similar. After chronic treatment with AMIO and DEA the corresponding tissue (lung, liver and brain) drug level measurements yielded smaller drug levels with DEA compared to that of AMIO. Based on these results it can be expected that using DEA instead of AMIO would result in similar therapeutic effects with possibly reduced drug toxicity. Supported by GINOP-2.3.2-15-2016-00047