

Chronic and acute antiarrhythmic effects of atorvastatin and omega-3 fatty acids documented in rats suffering from hypertriglyceridemia (HTG).

Bacova, B¹; Knezl, V²; Radosinska, J³; Barancik, M¹; Karas, S⁴; Tribulova, N¹

¹Institute for Heart Research, Bratislava, Slovakia; ²Institute of Pharmacology, Bratislava, Slovakia; ³Comenius University Faculty of Medicine, Bratislava, Slovakia; ⁴Institute of Measurement, Bratislava, Slovakia

Atorvastatin (Ato) and omega-3 FA exhibit antiarrhythmic effects in clinic but underlying mechanisms are not elucidated yet. This study was aimed to examine whether these compounds exert antiarrhythmic effects upon chronic and acute administration and whether intercellular connexin (Cx) channels, which ensure electrical coupling and myocardial synchronisation, are implicated. Experiments were conducted on VF prone HTG rats that were treated with Ato (0.5mg/kg/day) and omega-3 FA (400mg/kg/day) for 2mth. VF inducibility was tested on isolated working heart preparation using electrical stimulation. In acute experiments the hearts were perfused with 1.5, 7, 15 μ mol atorvastatin and omega-3 FA, i.e. EPA and DHA during 10 min prior el. stimulation. Prolonged application of Ato and omega-3 FA was accompanied by reduction of plasma triglycerides and resulted in significant increase of stimulation threshold for VF to 40+0.2 mA and 45+0.2 mA vs 15+0.1 mA. HTG rats were characterized by abnormal elevation of phosphorylated forms of Cx43 compared to healthy rat hearts, while omega-3 FA and atorvastatin significantly decreased it. Acute application of Ato, EPA and DHA reduced VF incidence to 33%, 71.4% and 80% in male and to 60%, 75% and 60% in female rats. Bolus of either EPA or DHA (150 μ mol) administered directly to fibrillating heart defibrillated it. It is concluded that chronic administration of atorvastatin and omega-3 FA resulted in antiarrhythmic effects that were associated with beneficial Cx43 alterations. It is very likely that modulation of connexin-43 channels function is implicated in acute effects. Findings point out the role of intercellular communication in pleiotropic effects of statins and non-pharmacological approaches in prevention of malignant arrhythmias.