Fluvastatin reduces pulmonary vein spontaneous activity through nitric oxide pathway

陳亦仁

HU Y;Chen YC;Cheng CC;Higa S;Chen YJ;Chen SA

摘要

Abstract

Introduction: Pulmonary veins (PVs) are the most important focus for the generation of atrial fibrillation. The HMG-CoA reductase inhibitors (statins) can reduce the occurrence of atrial fibrillation. The purposes of this study were to evaluate whether statins may inhibit the PV arrhythmogenic activity to prevent atrial arrhythmias from PVs and to investigate the link between fluvastatin, nitric oxide synthase (NOS) activity, mechanical activity, and electrical activity.

Methods: Conventional microelectrodes and Western blot were used to record the electrical activity, diastolic tension, contractility and expression of Akt, endothelial nitric oxide synthase (eNOS), neuronal nitric oxide synthase (nNOS), and phosphorylated Akt and eNOS before and after the administration of fluvastatin in rabbit PVs or atria.

Results: Fluvastatin decreased the PV spontaneous activity, diastolic tension, and contractility, but did not change the action potential duration or resting membrane potential. The effects of fluvastatin on the PV firing rate and diastolic tension were attenuated in the presence of L-NAME (100 μM), wortmannin (100 nM), and ODQ (3 μM). Fluvastatin (1 μM) increased the phosphorylated Akt and eNOS, but did not change the total Akt or eNOS in the PVs and atria. In contrast, fluvastatin (1 μM) decreased the total nNOS in the PVs and atria.

Conclusions and implications: Fluvastatin produced nitric oxide through the PI3kinase/Akt pathway, thus reducing the PV vascular diastolic tension and PV spontaneous activity. These results may contribute to the beneficial effects

of statins.