Pharmacological Reports
2011, 63, 967–974
ISSN 1734-1140

Protective effect of novel pyridoindole derivatives on ischemia/reperfusion injury of the isolated rat heart

Zuzana Broskova, Vladimir Knezl

Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, Dubravska cesta 9, 841 04 Bratislava, Slovak Republic

Correspondence: Zuzana Broskova, e-mail: zuzana.broskova@savba.sk

Abstract:
Generation of reactive oxygen species is a major, well-known cause of heart injury induced by ischemia-reperfusion. This injury is manifested through myocardial stunning, reperfusion and lethal reperfusion injury of cardiocytes. The pyridoindole stobadine has been shown to exhibit significant antioxidant, free-radical scavenging and hypoxic-tissue-protecting properties. The present study examined the effects of stobadine and two novel derivatives, SMe1 and SMe1EC2, which exhibit improved pharmacodynamic and toxicity profiles, on the functional properties and reperfusion dysrhythmias of the isolated rat heart in ischemia-reperfusion conditions. All experiments were performed on isolated Langendorff-perfused hearts isolated from 3-month-old male Wistar rats. After 15 min of stabilization, the hearts were subjected to a 30-minute period of global no-flow ischemia, followed by a 30-minute reperfusion period. Stobadine, SMe1 and SMe1EC2 were applied at a concentration of 1×10^{-5} M 10 min before the onset of ischemia, and during reperfusion through the perfusion medium. As compared to the untreated group, addition of SMe1EC2 during reperfusion significantly increased left ventricular developed pressure, decreased pathologically elevated left ventricular end-diastolic pressure and enhanced recovery of the stunned myocardium after ischemia. Both SMe1 and stobadine failed to influence these parameters; however, all derivatives tested inhibited serious life-threatening reperfusion dysrhythmias such as ventricular tachycardia and ventricular fibrillation. Our findings suggest that SMe1EC2 promotes an improved recovery of the left ventricular function following ischemia compared to either stobadine or SMe1. However, both SMe1EC2 and SMe1 manifested a significant anti-dysrhythmic effect comparable with that of stobadine and partially reduced myocardial ischemia-reperfusion-induced injury.

Key words:
pyridoindole, stobadine, isolated heart, ischemia-reperfusion, dysrhythmias