Nebivolol regulates eNOS and iNOS expressions and alleviates oxidative stress in cerebral ischemia/reperfusion injury in rats

Aims: Oxidative stress-induced cell damage is reported to contribute to the pathogenesis of cerebral ischemia/reperfusion injury. This study investigated the neuroprotective effect of nebivolol against cerebral ischemia/reperfusion insult in rats. Main methods: The model adopted was that of surgically-induced forebrain ischemia, performed by means of bilateral common carotid artery occlusion for 1 h, followed by reperfusion for 24 h. The effects of 5 and 10 mg/kg nebivolol, treated for 7 days prior to ischemia/reperfusion insult, were investigated by estimating endothelial and inducible nitric oxide synthases (eNOS and iNOS) protein expressions and assessing oxidative stress-related biochemical parameters in the rat forebrain. Also, infarct volume measurement and histopathological study of the forebrain were examined. Key findings: Administration of nebivolol increased eNOS expression with simultaneous decrease in iNOS expression in a dose dependent manner. Moreover, nebivolol inhibited ischemia/reperfusion-induced depletion of reduced glutathione level and decreased the elevated total nitric oxide end production and malondialdehyde levels, superoxide dismutase and lactate dehydrogenase activities. A notable finding is that catalase activity was not changed in response to either ischemia/reperfusion insult or nebivolol treatment. However, the results confirmed that nebivolol significantly reduced infarct volume and alleviated ischemia/reperfusion-induced histopathological changes. Significance: The present study demonstrates the neuroprotective effect of nebivolol against cerebral ischemia/reperfusion insult. Neuroprotection observed with nebivolol may possibly be explained by regulating eNOS and iNOS expressions and by inhibition of oxidative stress-induced injury. Thus, nebivolol may be considered as a potential candidate for treatment in patients who are prone to stroke. (C) 2011 Elsevier Inc. All rights reserved.