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The role of ATP-dependent potassium channels and nitric oxide system in the neuroprotective effect of preconditioning

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Abstract

© 2016, Media Sphera. All rights reserved.Objective. To study a role of ATP-dependent potassium channels (K+ATP) in the neuroprotective effect of ischemic (IP) and pharmacological (PP) preconditioning and evaluate the dynamics of blood nitric oxide (NO) metabolites in cerebral ischemia. Material and methods. A model of ischemic stroke induced by the electrocoagulation of a middle cerebral artery (MCA) branch was used in male rats (n=86). Glibenclamide, a selective inhibitor of ATP-sensitive K+ channels, and diazoxide, a potassium channel activator, were used. IP and PP were performed 24 h before MCA occlusion. Blood concentrations of NO, NO3-and NO2-were measured 5, 24 and 72 h after occlusion. Results. IP decreased a lesion area by 37% (p<0/05) and the preliminary introduction ofglibenclamide levelled the effect of IP. A protective effect of PP was similar to that of IP. A decrease in oxygenated R-conformers of Hb-NO and a reverse increase in non-oxygenated T-conformers as well as NO3-и NO2-were noted 5h after MCA occlusion. In the first 24 h after MCA occlusion, contents of NO3-and NO2-returned to normal values. There were changes in the concentrations of Hb-NO complexes as well, with the predominance of R-conformers and minimal contents of T-conformers. Moreover, the correlations between K+ATP channel blockade and the decrease in serum NO3-and NO2 were found (p<0/03). Conclusion. The neuroprotective effect of preconditioning is caused by the activation of K+ATP channels. An analysis of NO metabolite concentrations in the blood of rats with IP suggests that Hb-NO complexes belonging to R-conformers deposit and carry NO in tissues releasing NO accumulated via R→T transfer in conditions of ischemia.

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Keywords

ATP-dependent potassium channels, Cerebral ischemia, Electron paramagnetic resonance, Hemoglobin, Ischemic tolerance, Neuroprotection, Nitric oxide, Phenomenon of preconditioning, Spectrophotometry