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The Effect of Intravenous Mesenchymal Cells Transplantation on the Functional Activity of K_{ATP} Channels of Pial Arteries after Brain Ischemia/Reperfusion

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The aim of the study was to examine the effect of intravenous transplantation of human mesenchymal stem cells (hMSC) on the function of the K_{ATP} channels of pial arteries at different time points during post-ischemic period. Using a device for intravital visualization of pial vessels, we checked the reaction of the pial arteries to the application of K_{ATP} channels blocker glibenclamide (GB), K_{ATP} channels activator pinacidil (PI), acetylcholine (ACh) and acetylcholine combined with GB (ACh/GB) on the 7, 14, and 21 day after cerebral ischemia/reperfusion and intravenous hMSC transplantation. Two to five time less arteries reacted by contraction to GB application and one-and-a-half times less arteries dilated after PI application on the 7th day after I/R than in sham group. hMSC transplantation

carried out on the day of I/R had no effect on the K_{ATP} channels functions 7 days after I/R: the contraction reaction to GB and dilation reaction to PI were the same as in I/R group. Fourteen days after I/R the number of arteries constricted in response to GB were 1.5–2 times less than in sham group, and number of arteries dilated in response to PI were 2–2.5 times less. At the same time after I/R in the cell therapy group the number of arteries constricted to GB and dilated to PI almost fully matched such in the sham group. The functional state of K_{ATP} channels following I/R was assessed by comparing the dilatory response of pial arteries to the application of ACh and ACh in combination with K_{ATP} channels blocker glibenclamide. GB blocked dilatory reaction to ACh in sham animals. Simultaneous application of ACh and GB induced an increase in dilated arteries 7–14 days after I/R, and twenty-one days after I/R we observed no difference in the number of dilated vessels in response to application of ACh/GB or ACh alone. After MSC application, GB blocked dilation of pial arteries following ACh application in the same way as in sham animals, except for the first 7 days. It may be concluded that cerebral cortex I/R alleviated K_{ATP} channels contribution to the maintenance of the normal tone of pial vessels. These changes retained during 14 days after ischemia. Simultaneously, between 7 and 14 days after I/R the role of K_{ATP} channels in dilation reaction of pial arteries to ACh decreased: by the 21st day the channels take almost no part in dilatory response. Intravenous MSC transplantation on the day of cerebral I/R induced earlier restoration of K_{ATP} channels participation in keeping the normal tone of pial vessels (14 days) and ACh-mediated dilation of pial arteries.

Keywords: ischemia-reperfusion, brain, pial arteries, intravenous transplantation, mesenchymal stem cells, K_{ATP} channels