Transplantation of bone marrow regenerative cells after 5-Fu treatment in a rat model of focal cerebral ischemia

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Objective To evaluate the capacity of repair of bone marrow cells (BMCs) and bone marrow regenerative cells (BMRCs) after 5-FU treatment transplanted intravenously (IV) in focal cerebral ischemia induced by middle cerebral artery occlusion (MCAO) in rats, and in further to investigate the value and the mechanism of these two kinds of cells in MCAO treatment. **Methods** After purified, and marked with DAPI, the BMCs and BMSCs were injected intravenously into rats 24 h after focal cerebral ischemia. Functional outcome measurements using the modified Neurological Severity Scores (mNSS) were performed at 24 h post-MCAO, 1 week and 2 weeks post-transplantation respectively. Rats were euthanized at 14 days after MCAO, laser scanning microscopy was used to trace the transplanted cells. Brain sections were stained with TTC for surveying the volume of infarction, then PCR method was used to detect VEGF mRNA in boundary zone. Microvascular density in ischemic boundary zone was also detected with immunochemical staining of VIII factor. **Results** BMCs and BMRCs survived and were found to be localized especially in the ischemic region. In BMCs and BMRCs group, the infarct volumes of the brain were smaller than that of the first (control) group ($p < 0.05$), Neurological functions improved in rats treated with BMCs and BMRCs compared with the control group, as supported by the mNSS scores ($p < 0.05$). Statistically significant differences were also found between the second and third groups in terms of infarct volumes ($p < 0.05$). The VEGF mRNA and microvascular density was higher in the ischemic boundary zone of BMCs and BMRCs group than that in the control group ($p < 0.05$). In the above-mentioned results, the BMRCs group had better therapeutic outcome (vs BMCs group $p < 0.05$). **Conclusion** The intravenous administration of BMCs and BMRCs can promote the recovery of neurological functions of rats with focal cerebral ischemia. The therapeutic effect of BMCs and BMRCs on rats with focal cerebral ischemia may be derived from the promotion of VEGF secretion and the angiogenesis in the ischemic boundary zone. Compared with BMCs, BMRCs could be used to treat cerebral ischemia as a better candidate.

Keywords: brain infarction, bone marrow cells, bone marrow regenerative cells, transplantation

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