Curr Pediatr Res, Volume 23
DOI: 10.4066/0971-9032-C1-012

Umbilical cord mesenchymal stem cells and umbilical cord blood mononuclear cells improve neonatal rat memory after hypoxia-ischemia

1Juan Chen, 1Jie Zhang, 1Yi Qu, 1Dezhi Mu, 2Chao Yang and 2Qiang Chen
1West China Second University Hospital Sichuan University Chengdu, China
2Sichuan Neo-life Stem Cell Biotech Inc., China

Background: Neonatal hypoxic-ischemic encephalopathy (HIE) is a severe disease, and there's no effective treatment for severe HIE. In recent years, a large number of animal experiments have confirmed that stem cell transplantation has shown great potential in regenerative medicine, such as in the treatment of hypoxic-ischemic brain damage (HIBD)[1]. The most widely used are human umbilical cord-derived mesenchymal stem cells (UC-MSCs) and mononuclear cells from cord blood (CB-MNCs) because of their ample availability[2, 3]. However, there are still many problems on their applications, for instance, it is unclear which types of cells is more effective for HIE? Methods: HIBD was produced using Rice-Vannucci method postnatal day 7 (P7) rats[4]. Briefly, after a 30min rest, the rats were exposed to a hypoxic environment of 8% at 37□ for 2 hours. 24 hours later, UC-MSCs and UCB-MNCs labeled with PKH26 and Hu-Nu respectively were transplanted into the lateral ventricle of rats. A control group underwent ligation of the left carotid artery and hypoxia in the same manner,but received an equivalent volume of PBS alone. The sham group underwent neither left carotid artery ligation nor hypoxia. At 24 h after transplantation, the number of apoptotic cells was detected by TUNEL. We monitor the migration of transplanted cells, and the expression of myelin basic protein (MBP) and glial fibrillary acidic protein (GFAP) at 2 weeks post-transplantation respectively. The Morris water maze was used to assess animal learning abilities at 3 weeks post-transplantation. Results: On the three day after transplantation, UC-MSCs and CB-MNCs were mainly located in cerebral cortex and corpus callosum around the hypoxic-ischemic region of the ipsilateral hemisphere. However hardly any labeled cells were found after 2 weeks post-transplantation. Treatment with UC-MSCs and CB-MNCs did not affect cortical neuronal apoptosis, but was associated with reduced neuronal apoptosis in the striatum on the second day after HIBD ($P<0.05$). After 2 weeks post-transplantation, compared to the sham group, levels of GFAP labeling in control group were upregulated significantly in the cerebral cortex and striatum ($P<0.05$). CB-MNCs inhibited up-regulation of GFAP in the striatum ($P<0.05$), while UC-MSCs inhibited this in both the striatum ($P<0.01$) and the cortex ($P<0.05$). When compared to the control group, MBP expression levels in the CB-MNCs group were upregulated in the cerebral cortex and corpus callosum ($P<0.05$). However, there were no significant differences between the UC-MSCs group and the control group ($P>0.05$). The rats in the transplanted groups showed significant improvement in escape latency to find the submerged platform than those of rats in the control group ($P<0.01$), repeated measures ANOVA). In the probe trial, control rats exhibited significant spatial memory deficits. A one-way ANOVA revealed that the number of times animals crossed the platform location decreased in the control and transplanted groups below sham group levels, though the transplanted group animals crossed more than the control group animals ($P<0.05$). Furthermore, there were no statistically significant differences between the transplanted groups across either stage of testing (training trials or probe trial) ($P>0.05$). Conclusions: Both UC-MSCs and CB-MNCs could have a beneficial effect on recovery of neurological function in HIBD rats, although the possible mechanisms may be different between the two groups. Our data suggest that UC-MSCs and CB-MNCs could serve as a potential approach for the treatment of neonatal HIE and develop a guidance in clinical cellular therapeutics.

e: chenjuan2000@163.com