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Modified Bone Marrow Stromal Cells Therapy for Central Nervous System Disorders

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Abstract

This article concluded our serial studies on the therapeutic protective effects of modified bone marrow stromal cells on central nervous injury. Hope this will provide a prelusion of transition of central nervous disease treatment from experimental treatment to the idea of clinical application.

Keywords: Stromal cell; Ischemia; Spinal injury

Abbreviations

BMSC: Bone Marrow Stromal Cells; CNS: Central Nervous System; OEC: Olfactory Ensheathing Cell; Sal B: Salvianolic acid B; EPO: Erythropoietin; SCI: Spinal cord Ischemia; VEGF: Vascular Endothelial Growth Factor; Gd-DTPA: Gadolinium-diethylenetriaminepenta-acetic acid; SCD-1: Stromal Cell-Derived factor 1; CXCR4: Chemokine Receptor type 4

Editorial

Stem cells are a kind of cells characterized of species diversity, self-replication and renewal ability, high proliferation potential and multiple differentiation potential [1-4]. Compared with other types of stem cell transplantation, treatment using Bone Marrow Stromal Cells (BMSCs) has more advantage, which has rich resources, easy to access, multiple potential, ethical limits, subculture amplification etc. It is popular attended as appropriate seed cells [5,6]. There were increasing evidences that transplanted BMSCs significantly promote nervous functional recovery after Central Nervous System (CNS) injured in the animal models [7-9]. The BMSCs treatment for neural disease would be of great benefit, but the mechanism is still unclear [6,10,11]. Focusing on cerebral ischemia and spinal cord injury, we concluded our studies of how the modified BMSCs protect the target organs and potential strategies, which may contribute to successful clinical transplantation and outcomes improvement of central nervous system disease.

Stem cell therapies provide unique opportunities for diseases of the Central Nervous System [12-14]. By co-transplantation of BMSCs and embryo Olfactory Ensheathing Cell (OECs) in vivo, we confirmed that spinal nervous cells conduction performance improved and the histological analysis suggested that the BMSCs differentiating into neurons cell proportion increased significantly. In addition, axons dyeing were densely distributed in the damage area. BMSCs and OECs transplantation together to treat spinal cord injury may be a potential method to improve the treatment of SCI [15]. To explore the cellular protective mechanisms of BMSCs, we transplanted BMSCs into ischemia rats and found that they could promote the functional recovery through secrete neurotrophic factors. BMSCs protect hypoxia-induced PC12 cells against apoptosis at least in part through the VEGF/PI3K/Akt/FoxO1 pathway [16]. Another study revealed that the protective effects of BMSCs against PC12 cell apoptosis induced by CoCl2 might be dependent on erythropoietin (EPO) expression, at least in part, via the regulation of Bcl-2 family members and caspases [17].

Treatment of ischemic stroke with BMSCs transplantation combining with Salvianolic acid B may improve the removal of thrombus and stimulation of neogenesis [18,19]. In order to improve the survival rate of stem cells after transplantation, Salvianolic acid B (Sal B) was found effectively inhibit the release of TNF-a then protecting BMSCs from the inflammation stimulation and promoting the leg's function recovery in SCI rats [20]. Study in rat also found that Sal B could directly reduce the generation of reactive oxygen levels in the cell oxidative stress situation, inhibiting apoptosis genes before the activation of p-ERK1/2. All these findings demonstrated that Sal B could enhance BMSCs oxidative stress resistance, reducing the H_2O_2 stimulation caused by cell apoptosis [21]. In other studies, the results indicated that Curcumin could promote the spinal cord repair via inhibition of glialscar formation and inflammation [22,23]. It could block cell injury by virtue of its antioxidant properties [24]. Curcumin is a double-edgeds word for both JAK2/STAT3 and NF-γB inhibition in injured spinal cord [23].

Combination stem cells with biomaterials is another direction in the research of the central nervous system injury [25,26]. Some research had constructed biological composite materials to control the releasing of neurotrophic factors and stem cells transplantation. It confirmed that the combined transplantation could provide functional benefits [27,28]. However, how to choose the effective way of the combination of growth factors and materials need further exploration [29].

For further facilitate the therapeutic effects using BMSCs, cell imaging plays a pivotal role in this regenerative therapy study [31]. When BMSCs were labled by Gadolinium-diethylene triamine penta-acetic acid (Gd-DTPA), the migration and proliferation of BMSCs could be traced by MRI in animal models. We confirmed that BMSCs spread through the damage areas to promote the functional recovery 14 day after transplanted in vivo [32]. Our previous observations indicated that systemically administered BMSCs could migrate to the ischemic lesion of brain along with the olfactory-thalamus and hippocampus-cortex route. We revealed that the interaction of locally produced SDF-1a and CXCR4 expressed on the BMSCs surface played an important role in the migration of transplanted cells [33].

Gratifying progress has been made in the therapeutic study with BMSCs transplantation to some certain disease, but outcome of neurol disease therapy remained limited improvement in clinic. This may be because of the neural disorder is more complex, involving more cell types, more complicated cerebral blood circulation and micro environment [2]. We have to face more clinical hurdles including (1) limited engraftment, survival, and proliferation; (2) immunogenicity with allogenic transplantation; (3) poor differentiation, maturation, and integration [34]. And yet, the successful experimental nervous regeneration therapy with modified BMSCs will provide a prelusion of central nervous disease treatment in clinic.

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