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Optimized Protocol is the Key for Clinical Use of Stem Cell Therapy in Stroke

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Perspective

Stroke is the second cause of mortality in industrial countries after ischemic heart disease [1]. Ischemic stroke results from an artery occlusion and leads to oxygen and glucose shortage in brain [2]. Cerebral ischemia results in inflammation and oxidative stress leading to neuronal loss and brain damage [3,4]. To these days, rt-PA is the only approved drug for stroke; however, increasing the risk of bleeding and golden time limitation are the problems associated with rt-PA [5].

Stem cell therapy is believed to be useful for treating neurodegenerative diseases including stroke. Mesenchymal stem cells (MSCs) have beneficial effects including anti-inflammatory effects, anti-apoptotic effects and their role in protection against oxidative stress [6,7]. Several characteristics of neural stem cells (NSCs) have made them suitable for stem cell therapy including promotion of angiogenesis and neurogenesis after cerebral ischemia [8], anti-apoptotic and immunomodulatory effects [9-17]. Most importantly, NSCs could promote regeneration due to their ability to differentiate into three neural lineage cells that are neurons, oligodendrocytes and astrocytes [18,19]. By using combination stem cell therapy we take advantage of both MSCs and NSCs and we would get better results for treating cerebral ischemia. To promote the outcome after combination stem cell therapy, we should optimize its protocol. For this purpose, we found the optimum time for using MSCs and NSCs. The optimum time for injecting MSCs is 12 hours after cerebral ischemia and the optimum for NSCs is 3 days. Administration of MSCs in acute phase (12 hours) makes the microenvironment suitable for NSCs transplantation in sub-acute phase (3 days) after cerebral ischemia [20,21].

Stroke leads to astrocytosis and formation of glial scares by increasing the expression of GFAP that can inhibit regeneration [22-26]. Although NSCs have numerous positive effects for stem cell therapy, they increase astrocytosis [27]. Astrocytes secrete inflammatory cytokines [28]; therefore, they might be an obstacle for achieving the optimum effect of NSCs transplantation. By omitting the astrocytes, the efficacy of NSCs transplantation would be increased [29].

Conclusion

In spite of several improvements in combination stem cell therapy protocol, several challenges still remain towards improving the efficacy and the success rate. More researches needed to turn this enthusiasm into a grand clinical use.

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