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Stem cells therapy of patients with brain injury

Traumatic brain injury(TBI) represents damage of the brain parenchyma caused by an external physical force resulting in impairment of cognitive abilities and physical functions. It is one of the leading causes of morbidity and mortality in the world.

The mechanism of the brain injury was demonstrated to involve primary damage caused directly by trauma and a cascade of secondary events leading to excitotoxicity, increase in free radicals, cerebral ischemia, intracranial hypertension, hypo or hyperperfusion, impairment of cerebrovascular autoregulation as well as cerebral metabolic dysfunction. TBI is accompanied by release of neurochemical factors which are responsible for cellular death and generalized atrophy[1,2].

To date very few therapeutic options are available to treat TBI. The current treatment of TBI consists of surgery or conservative symptomatic treatment at the early stages then physical and occupational therapies during late stages. It is important to emphasize that two crucial elements play a core role in the neurological recovery of patients with TBI. First of all, uninjured neurons promote to restoration of the lost functions due to damage of the brain. Second, the migration and differentiation of neural stem cells. However, the quantity of own stem cells is limited. Also, their capability of enabling self-recovery is weak[3].

Hence, stem cell therapy represents a promising alternative treatment for patients with TBI which promotes the recovery of neurological function. The therapeutic effects are based on neuroprotective properties of stem cells such as production of growth and trophic factors, stimulation of endogenous neurogenesis, angiogenesis and synaptogenesis as well as modulation of neuroinflammation. In more details it is considered that the microenvironment of damaged tissues produces factors that attract stem cells to the site of injury and enhance their differentiation into desired cells. Thus, stem cells promote tissue regeneration by differentiating into the injured cells[4]. It is important to notice that stem cells secrete neurotrophins such as brain-derived neurotrophic factor and glial cell line-derived neurotrophic factor, which promote to anatomical and functional recovery of the brain[5,6]. Moreover, brain-derived neurotrophic factor reduces spasticity due to its ability to affect neuronal excitability and synaptic transmission as well as upregulate a potassium chloride co-transporter KCC2 which maintains activation of inhibitory receptors[7,8]. In addition brain-derived neurotrophic factor attenuates microvascular permeability disturbances, blood cerebrospinal fluid barrier breakdown, blood–brain barrier breakdown and therefore brain oedema[9].

Glial cell line-derived neurotrophic factor also ameliorates brain oedema[10]. Anti-oedematous effect of neurotrophins contributes to reduction of lesion size in the brain. Also, stem cells possess immunomodulatory properties. They limit the local inflammatory response due to inhibition of microglia and macrophages activation. In addition, they impair T-lymphocyte maturation[11]. Indeed, in the presence of stem cells immature or partially immature antigen presenting cells was showed to be produced. These cells turn off T cells leading to down-regulation of activated immune cell reactivity and thus reducing tissue damage[12].

Successful application of mesenchymal stem cells in the treatment of patients with TBI was demonstrated in clinical trial conducted by Wang S. et al. in 2013. There were forty patients with sequelae of TBI. All of them were randomly allocated into two groups. The first group included the patients who received mesenchymal stem cells. The second one was control. The follow-up period was 6 months. Significant ameleoration of neurological function in stem cells treated patients was observed. More specifically an improvement in upper extremity motor sub-score, lower extremity motor sub-score, sensation sub-score and balance sub-score were detected according to the results of The Fugl-Meyer Assessments. Moreover, the Functional Independence Measures results also showed dramatically improvement in the patient self-care sub-score, sphincter control sub-score, mobility sub-score, locomotion sub-score, communication sub-score and social cognition sub-score. It is important to mention that the control group exhibited no improvements. Thus, mesenchymal stem cells therapy represents a potential treatment for patients with sequelae of TBI safely and effectively improving neurological function in these patients [13].
In 2015 Sharma A. et al. reported encouraging results of a pilot study in which treatment by autologous bone marrow derived stem cells(BMSCs) were used in patients with traumatic brain injury. Fourteen patients were enrolled in the trial. All of them were administered BMSCs. Patients were followed up 6 months. Significant symptomatic improvements were observed after intervention. Along with amelioration of major symptoms of chronic TBI such as affected upper limb and lower limb activity, impaired speech, muscle tone, coordination etc. improvement in fine motor skills, attention and concentration, socialization skills as well as sensation and contractures/deformities were detected. The Functional Independence Measure scale, the SF-8 Health Survey Scoring and the disability rating scale demonstrated a positive shift in scores. Amelioration of various symptoms as well as improvement in activities of daily living was observed. It is important to mention that improvement in physical components and in mental component of the SF-8 Health Survey Scoring were noticed indicating improved quality of life. Also, PET CT scan showed significant positive changes which corresponded to the symptomatic improvement. The obtained data have indicated that stem cell therapy promotes to functional recovery of patients with traumatic brain injury improving their quality of life[14].

In conclusion, according to available data stem cell therapy significantly improves neurological function of patients with TBI. It has a great potential to reverse the damage occurred in the brain after TBI.

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