

Stem cell therapy for patients with spinal cord injury

Spinal cord injury (SCI) occurs with the incidence of 25.5 cases per million people annually. The mean age of spinal cord injury patients is 30 years. Also, the incidence is higher among men than women. Thus, it represents a high socio-economic problem considering the fact that SCI disables persons in the prime of their lives. Moreover, complete SCIs were found to be more common than incomplete injuries. SCI leads to sensory loss, motor paralysis and severe functional impairment. It was demonstrated that massive neuronal and glial cell loss, demyelination, cavitation and glial scarring occur as a result of mild contusion to the spinal cord[1,2].

To date no fully restorative therapies for SCI exist. The current treatment of SCI includes physical therapy. However, due to limited regenerative potential of neurons most patients fail to recover[3].

Stem cell therapy represents a promising alternative treatment for patients with SCI which promotes to the neurological functions recovery. 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]. In addition, they are involved in axon regeneration and remyelination as well as stem cells direct migration of endogenous neural stem cells[5,6]. Also, 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 central nervous system[7,8]. It was showed that stem cells encourage the formation of new neuronal pathways as well as propagation of the short regenerated neuronal fibers. Also, they facilitate the creation of connections between the distal and proximal ends of the spinal cord[9]. 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[10,11]. In addition brain-derived neurotrophic factor attenuates microvascular permeability disturbances, blood cerebrospinal fluid barrier breakdown, blood-brain barrier breakdown [12]. Anti-oedematous effect of neurotrophins contributes to reduction of lesion size in the spinal cord. 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[13]. 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 therefore reduction of tissue damage[14].

Encouraging results were obtained in controlled clinical trial in which the efficacy of autologous bone marrow derived mesenchymal stem cells (BMMSCs) therapy in patients with complete chronic cervical SCI was researched. Forty patients with complete chronic cervical SCI were recruited and allocated in two groups. The treatment group received BMMSCs. The second group was control. All patients were followed up to 6 months. A significant clinical improvement in motor function, American Spinal Injury Association (ASIA) Impairment Scale score and electromyogram were observed in the treatment group. It was noticed that patients in the treatment group showed the recovery of the completely lost muscle strength. Also, physical flexibility, coordination as well as sensory function were found to be improved. No amelioration in any of the neurological functions was detected in the control group. Importantly to note, that no transplantation-related adverse events were reported. Thus, BMMSCs therapy effectively improves neurological function in patients with complete chronic cervical SCI[15].

The long-term safety of autologous BMMSCs therapy of patients with SCI was evaluated in a pilot clinical trial which was conducted by Pal R. et al. There were thirty patients with complete SCI at cervical or thoracic level.

All of them received BMMSCs. The follow-up period was ranged from 12 month up to 3 years. No side effects linked to cell therapy had been observed in all patients during whole observational period[16].

In 2014 El-Kheir W.A. et al. reported encouraging results of a randomized controlled single-blind clinical trial in which treatment by autologous bone marrow-derived stem cells(BMSCs) was used in patients with chronic spinal cord injury. Seventy chronic traumatic cervical and thoracic SCI patients were enrolled in the study. All of them were allocated in two groups. The first one included patients who were treated with autologous BMSCs along with physical therapy. Patients in the second group had received only physical therapy. The follow-up period was 18 months. Significant functional motor and sensory improvements evaluated by using of the American Spinal Injury Association (ASIA) Impairment Scale were observed in the stem cells treated patients. It was noticed that several patients with a baseline AIS A (no preserved sensory or motor function) converted to AIS C(sensory and motor function are preserved). None of patients in the control group achieved AIS conversion. Moreover, in the stem cells treated group a considerable amelioration in functional independence was detected. No long-term side effects associated with stem cells therapy were reported[17].

It is important to mention the results of systematic review and meta-analysis of clinical trials in which autologous BMMSCs were used in the treatment of patients with traumatic SCI. Eight clinical trials with a total number of 337 participants were included in the review. Obtained data from published trials have demonstrated encouraging results of using the autologous BMMSCs in the treatment of SCI patients. It was showed that the mean change of motor, light touch and Pinprick scores in patients significantly increased after stem cells therapy. In addition, considerable improvement of Barthel Index was observed in the stem cell treated patients indicating amelioration of performance in activities of daily living. This review has confirmed that BMMSCs therapy is a safe intervention without serious adverse events[18].

In conclusion, according to available data of various clinical trials, using of autologous stem cells significantly improves neurological function of patients with SCI. It has a great potential to reverse the damage occurred in the spinal cord.



Reference

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