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Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease in which selective destruction of motor neurons in the motor cortex, brainstem and spinal cord takes place. The annual incidence rate of ALS in the general European population was 2.16 per 100 000 person years. The incidence was higher among men than women increasing with age [1]. It has steady progressive course leading to muscle atrophy, weakness and immobility. Premature death caused by paralysis of respiratory muscles with subsequent respiratory failure is the outcome of the disease. Median survival time ranges from months to decades but on average is 19 months from diagnosis and 30 months from onset[2]. The cause of the disease is unknown. It is a sporadic disease mainly. However, in 5-10% of patients diagnosed with ALS there is an inherited, familial ALS form of the disease[3]. Unfortunately, ALS is incurable. Mainly, the treatment of ALS is essentially supportive and focused on symptom relief.

Stem cells in the treatment of amyotrophic lateral sclerosis

Currently the use of mesenchymal stem cells(MSCs) in the treatment of ALS represents a new perspective option and alternative for conventional treatment. The mechanism of MSCs action includes migration of stem cells at sites of nerve injury, production of neurotrophic factors which promote functional recovery and regeneration of host neurons. Also, MSCs can change the damaged tissue microenvironment enhancing endogenous neural regeneration and protection[4].

There are several clinical studies conducted between 2001 and 2010 by Mazzini L. et al.which have showed encouraging results of using autologous MSCs in the treatment of patients with ALS.
In the first clinical trial there were seven patients with ALS. All of them received autologous MSCs. No severe adverse events associated with stem cells therapy were recorded. In three months a slowing of the linear decline of muscular strength in the proximal muscle groups of the lower limbs was observed in patients. Moreover, it was noted that a mild increase in strength in the same muscle groups occurred[5].

In 2006 Mazzini L. et al. published the results of the second clinical trial in which seven patients affected by definite ALS were enrolled. They were treated by autologous MSCs. The stem cells therapy was well tolerated by all patients. It is worth noting that no significant side effects were observed. All patients were monitored for at least 3 years. A significant slowing of the linear decline of the forced vital capacity was noticed in patients after MSCs therapy [6].

Two years later Mazzini L. et al. reported the results of clinical trial in which 9 patients with ALS were included. All patients received autologous MSCs. The follow-up period was 4 years. It is important that no significant acute or late side effects were observed. Slowing of the linear decline of the forced vital capacity was observed in patients. Also, the ALS-Functional Rating Scale score was improved in these patients. Therefore, injection of MSCs in ALS patients is safe as evidenced by the results of the long term follow-up[7].

In 2010 Mazzini L. et al. once again demonstrated the safety and feasibility of autologous MSCs therapy for patients with ALS in clinical trial which included ten ALS patients. All of them were administered MSCs therapy. There were no immediate or delayed side effects related to stem cells treatment. The follow-up period was 24 months. It is noteworthy that in most patients no significant changes of the progression of the disease were detected after MSCs therapy. Moreover, significant slowing of the linear decline of forced vital capacity and the ALS-Functional Rating Scale score were observed in patients[8].

Another clinical study which has demonstrated safety and efficacy of autologous MSCs therapy for patients with ALS was published in 2010 by Karussis D. et al. Nineteen patients with ALS were enrolled. All of them received autologous MSCs. The patients were monitored for 25 months. During follow-up period no major adverse effects were reported in any of the patients. The mean ALS-Functional Rating Scale score remained stable during the first 6 months of observation. Therefore, results proved that autologous MSCs therapy is safe[9].

It is necessary to mention the results of clinical study conducted by Deda H. et al. in which autologous bone marrow-derived stem cells(BMSCs) were used for the treatment of patients with ALS. Thirteen patients with sporadic amyotrophic lateral sclerosis were recruited. All of them were treated by BMSCs. The follow-up period was 1 year. After stem cells treatment the patients had better functional status compared with their condition before therapy. It is necessary to notice that reinnervation was confirmed by electro neuromyography[10].

In 2012 Prabhakar S. et al. reported the results of an open-label pilot study in which autologous BMSCs were injected in patients with ALS. There were ten patients. The follow-up period was 12 months. It was noticed that patients receiving stem cells tended to maintain their functional status in 3 months after treatment. There was no significant deterioration in the ALS-Functional Rating Scale score from baseline at the end of follow-up period. Also, no significant adverse events were reported[11].

The results of long-term monitoring (up to 9 years) of nineteen ALS patients who received autologous MSCs were published recently by Mazzini L. et al. All patients were treated with autologous bone marrow derived MSCs. The stem cells therapy was tolerated well by all patients. The patients were monitored during long period until death. Every 3 months clinical, psychological and neuroradiologic assessments were conducted. A slowing of the disease progression over a long period was observed. Also, there was no deterioration in psychosocial status in all patients. The greatest value of this clinical trial is the neuroradiologic demonstration the lack of tumor formation or abnormal cell growth. During the entire follow-up period the MRI didn't show any evidence of new tissue formation. The obtained data has demonstrated the safety and feasibility of autologous MSC therapy in patients with ALS[12].

In conclusion, as established by various clinical trials using of autologous stem cells in ALS patients was safe. Also, available data show that stem cells therapy leads to a slowing of disease progression as well as gives meaningful survival benefits for ALS patients.

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