Abstract

Mesenchymal stem cells (MSC) possess a multilineage differentiation potential and have the ability to regulate reactivity of the immune system. They are usually isolated and expanded from the bone marrow, adipose tissue or umbilical cord. MSC represent promising cell population for the treatment of some severe diseases, such as amyotrofic lateral sclerosis (ALS), due to the combination of regenerative and immunomodulatory properties. The aim of this study is to compare MSC from ALS patients and healthy donors in their phenotype, proliferative activity and mainly their immunomodulatory properties. The assessment of impact of the disease on the properties of MSC is important for their autologous use in clinical trials. In this study we used MSC isolated from bone marrow of 14 ALS patients and 15 patients undergoing mostly orthopedic surgery as control group. We also used MSC stimulated for 24 hours by poinflammatory cytokines. Cells were compared in terms of immunophenotype, differentiation in adipocytes and osteoblasts, metabolic activity, expression of selected genes for immunomodulatory molecules and for inhibition of lymphocyte proliferation. Further experiments were focused on evaluation of immunomodulatory properties of MSC. The effect of MSC on peripheral blood mononuclear cells stimulated with either phytohemagglutinin or lipopolysaccharide was assessed by flow cytometry, real-time PCR and ELISA. MSC from ALS and control group showed standard phenotype, methabolic activity and differentiation potential. MSC from ALS and control group also comparably inhibited lymphocyte proliferation and activation in a dose-dependent manner. MSC in ALS group responded differently to stimulation by proinflammatory cytokines and produced less hepatocyte growth factor, had lower ability to inhibit cytotoxic T lymphocyte activation and increase percentage of regulatory T lymphoctyes. On the other hand they exerted higher ability to inhibit production of tumor necrosis factor-α and expressed higher levels of gene for interleukin 6 in comprarison with MSC in control group.

Key words: mesenchymal stem cells, immunomodulation, neurodegenerative diseases, amyotrophic lateral sclerosis, autologous cell therapy, neuroinflammation