

## **Chronic obstructive pulmonary disease (COPD)**

Chronic Obstructive Pulmonary Disease (COPD) represents a progressive chronic inflammatory disease in which persistent airflow restriction caused by chronic inflammation occur. There are two nosological forms of COPD: chronic bronchitis and emphysema. Chronic bronchitis is characterized by chronic airways inflammation leading to secretory cell hyperplasia, increased bronchial secretions and bronchoconstriction. Pulmonary emphysema is accompanied by the destruction of the alveolar walls which results in the enlargement of air spaces distal to terminal bronchioles. COPD has progressive course leading to lung function loss[1]. Recent data demonstrate that mortality due to COPD is increasing. As expected COPD will be the third-leading cause of death worldwide by the year 2020. Moreover, to date COPD represents a worldwide high socio-economic problem[2].

It is believed that COPD is caused by the interaction of genetic and environmental factors. Oxidative stress, air pollution and cigarette smoke represent the main etiological factors which can lead to development of COPD[3]. About 1-3% of cases of emphysema develop due to deficiency of the enzyme  $\alpha$ 1-antitrypsin caused by a defective gene at 14q32.1, known as the Serpin A1 gene[4].

It is important to emphasize that current pharmacologic treatment of COPD doesn't modify the progressive course of the disease. So it doesn't influence on the progressive decline of lung function. Therefore, it is only palliative therapeutic option which is directed to reduction of symptoms, frequency and severity of exacerbations, also to improvement of health status and exercise tolerance of the patients[5].

## **Using stem cells in the treatment of chronic obstructive pulmonary disease**

To date stem cell therapy represents a promising alternative for COPD patients. More than 10 years stem cells have been used in the treatment of different diseases, most importantly in refractory chronic inflammatory diseases. Stem cells have unique properties such as immunomodulatory, proangiogenetic and antifibrotic, therefore, stem cells inhibit inflammation, fibrosis and promote regeneration of tissue damage. It is important to emphasize that stem cells are non-immunogenic and can be transplanted without conditioning and without immunosuppressive prophylaxis. It is considered that the microenvironment of damaged tissues produces factors that attract stem cells to the site of injury and enhances their differentiation into desired cells. Thus, stem cells promote tissue regeneration by differentiating into the injured cells[6]. Moreover, in the presence of stem cells, immature or

partially immature antigen presenting cells are produced which turn off T cells leading to down-regulation of activated immune cell reactivity. Due to their immunomodulatory potential, MSCs reduce tissue damage[7].

In recent clinical trial which was published by Weiss D.J. et al. in 2013 it was showed that using of mesenchymal stem cells(MSCs) in patients with moderate or severe chronic obstructive pulmonary disease was save. There was a prospective, placebo-controlled, double-blinded, randomized clinical trial which included sixty-two patients with moderate to severe COPD who were recruited from six different institutions. All of them were randomly divided into two groups. First one included the patients who received four monthly intravenous infusions of MSCs. The second group was control. The follow-up period was two years. It is important to notice that infusion of MSCs wasn't accompanied by any side effects in patients. Systemic MSC administration led to decrease of inflammation as evidenced by lowering of C-reactive protein levels in MSCs-treated patients with elevated circulating C-reactive protein at baseline. Also, it was noticed that the mean pulmonary arterial pressure was decreased more significant in MSCs treated group compared with control group at 6 months. The obtained data showed the feasibility and safety of using MSCs as a treatment for patients with moderate to severe COPD [8].

Encouraging results were obtained in clinical trial in which patients with advanced COPD who failed to respond to conventional treatment were treated by infusion of autologous bone marrow derived stem cells. Four patients with advanced pulmonary emphysema were enrolled. All of them received intravenous infusion of autologous bone marrow derived stem cells. The follow-up period was 3 years. It is important to notice that there were no adverse reactions after stem cell therapy in any of the patients. It was observed that parameters of the spirometry were improved after stem cells treatment. Moreover, all patients demonstrated a slowdown in the pathological degeneration. Also, improvements in the clinical condition and quality of life were reported in all patients. The changes observed in the clinical trial confirmed that autologous bone marrow derived stem cells transplantation is safe and effective in the treatment of patients with COPD[9].

The results which have been observed in the clinical trials have demonstrated the feasibility, safety and efficacy of using stem cells as a treatment for patients with COPD. Moreover, available data have showed that stem cell therapy leads to a slowing of disease progression.

## References

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