Investigating the Immunomodulatory Effects of Manipulated Mesenchymal Stem Cells with IDO1 Gene and Their Small Extracellular Vesicles in the Repair of Heart Damage in MI Rat Model

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Background: The treatment method based on the use of stem cells to improve the symptoms of patients with heart attacks was first reported in 2001. Since then, the use of stem cells from different sources in patients with cardiovascular diseases is being considered from time to time. In addition to their ability to differentiate, MSCs also have the capacity to modulate the function of the immune system, which has made them an attractive therapeutic tool. In recent decades, the importance of innate and acquired immune responses in the control of myocardial function has been seriously discussed during health and diseases. It has been shown that dysregulation of the immune system can lead to the induction of local devastating immune responses and trigger inflammatory events causing serious side effects associated with acute MI. IDO1 is a key enzyme in the tryptophan catabolism pathway. The immunomodulatory role of this enzyme has been reported in several studies and conditions, including pregnancy, chronic infection, autoimmune diseases, organ transplantation, and drug resistance in a variety of cancers.

Methods: A rat model of heart attack was created based on the Cryo method and hTRET-IDO1 cells and their Exosomes were injected into the desired heart area. Histological examinations and immune cells examination were performed by CBC test and differential white blood cell count. Repair of heart damage was also evaluated by echocardiography on the day before surgery plus the days 1, 28, and 55 post surgery followed by a TTC test.

Results: In this study, it was shown that by modulating the immune system and reducing inflammation by cells and Exosomes, carrying a higher level of IDO1, in the damaged heart the repair rate is significantly increased.

Conclusion: Inflammation has been considered a key factor for the development of complicated diseases such as atherosclerosis, the creation of arterial platelets and delay in tissue repair during heart attack. It has been shown that targeting inflammatory pathways can effectively reduce atherosclerosis in animal models of cardiovascular diseases. In the conditions of inflammation, the presence of pro-inflammatory cytokines is essential for the activation and calling of functional cells of the immune system and the regeneration of damaged tissue. The problem appears when the level of pro-inflammatory cytokines continuously increases and rises above the appropriate level. In this case, instead of calling progenitor cells to the damaged tissues, autoimmune responses are created, and inflammatory mechanisms destroy the tissue structure. So by modulating the immune system, it is possible to increase cardiac function.

Keywords: Mesenchymal Stem Cells, Heart Damage, IDO1, MI Rat Model, Modulation of the Immune System