Insights in Stem cells

Extended Abstract
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MSC Transplantation in Eight Severe COVID-19 Patients: Can Cytokine Storm Be Reversed?

Nesrin O. Ercelen[1*], Beliz Bilgili[2] , Berrin Monteleone[3] , Fethi Gul[4] , Gokay Rasit Gulay[1] , Nagihan Alpaydin1 , Ozan T. Demir[5] , Murat Simsek[5] , Davut Turan[1] , Omer Karadeniz[1] , Elif Karadeniz[1] , Nagihan Batıgun[5] , Ismail Cinel[6]

[1]Atigen - Cell Technology Center, Turkey; [2]Marmara University, Turkey [3]New York University, Langone Heath Winthrop Pediatric Associates, [4]Marmara University School of Medicine, [5]Geneis, Genetic System Solutions, Istanbul, Turkey; [6]Marmara University, Turkey

The COVID-19 disease is a global pandemic, with the first case diagnosed in December 2019, as reported by World Health Organization (WHO). In 17% of patients, COVID-19 causes severe Acute Respiratory Distress Syndrome (ARDS) due to release of large amounts of pro-inflammatory cytokines and chemokines in the lungs. In a retrospective observational study from Milan, 9% of the people, who tested positive for COVID-19, needed ICU care with respiratory support. The demand for ICU beds and health care personnel brought significant overload to sustain the care of these patients. Search for effective therapies is underway. However, the result of severe infection of COVID-19 still leads to the inevitable fatalities with the current available therapies. Mesenchymal Stem Cells (MSCs) have been isolated about 30 years ago (Supplementary Data 1). There are over 5,000 articles published on MSCs. Moreover, anti-inflammatory and immunemodulatory properties of MSCs have been well studied. Exogenously administered MSCs are medicinal. They generate positive therapeutic outcomes by secreting bioactive factors that exhibit immunomodulatory, and regenerative effects by fabricating, and secreting antibiotic proteins, where they hone in on sites of injury or disease. Hence, Arnold Caplan has proposed recently to change the name of MSCs to Medicinal Signaling Cells. As MSCs arise from pericytes, they can be isolated from a variety of vascularized tissues. Each separate tissue-specific stem cell interacts with its underlying vascular endothelial cells, and adjacent specific pericyte/MSC "Universal Stem Cell Niche" (pMSCs). Each specific pMSCs have both pMSCs common, and unique chemical, and functional features. Meanwhile, the major therapeutic role of pMSCs in vivo at various sites of disease or injury are very similar when comparing these different pMSCs. Over the past decade, the emphasis has shifted toward harnessing the pMSCs' ability to produce factors and cytokines that stimulate innate tissue repair, modulate inflammation, and immune responses. MSCs express function on Toll-Like Receptors (TLRs). Triggering different TLRs, depending on exposure times promote either pro- or anti-inflammatory function in MSCs. Pre-clinical studies demonstrated that the majority of infused MSCs initially distributed in the lungs. Subsequent studies showed improved pulmonary functions beginning shortly after administration with no evidence of pulmonary safety risk. These studies indicated the local beneficial MSCs-mediated effect on pulmonary airways . A recent pilot study from China explored the therapeutic outcomes of MSC transplantation in seven poor prognoses COVID-19 patients with pneumonia. The results revealed that MSC transplantation was safe and effective treatment option. The peripheral lymphocytes increased after the treatment, and the overactivated cytokine-secreting immune cells disappeared in 3-6 days. A group of regulatory DC cell population dramatically increased. Meanwhile, the level of TNF-α is significantly decreased, while IL-10 increased in the MSC transplantation group compared to the placebo control group. Furthermore, the gene expression profile showed MSCs were ACE2- and TMPRSS2-, which indicated MSCs were free from COVID-19 infection . Here we report our clinical observations of eight cases, before and after MSC transplantation, to assess the clinical therapeutic effects of MSC transplantation on COVID-19 severe/critically severe patients. Though broader studies are needed, we advised a clinical application protocol and algorithm by evaluating the poor prognostic markers significantly related by MSC transplantation to prevent the overload in ICU clinics, as well as, to shorten hospitalization time.

nesrinercelen@gmail.com

Bottom Note: This work is partly presented at Journal of Stem Cell Research & Therapy