

# Mesenchymal stem cells for the treatment of severe COVID-19

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Current regenerative medicine is based on the use of mesenchymal stem cells through which regenerative and immunomodulatory properties have been seen. In this last respect, it has been hypothesized that the use of mesenchymal stem cells in severe acute inflammatory conditions such as those seen in cases of Sars Cov2 infection may benefit from the use of this therapy due to the anti-inflammatory, immunomodulatory, regenerative properties coupled with These cells do not express the ACE2 receptor, which gives them resistance to the virus.

Mesenchymal stem cells are obtained from embryonic origin, umbilical cord, human dental pulp, and Wharton's jelly. Its main function is to regulate the inflammatory response and promote tissue repair and regeneration. It also has immunomodulatory effects mainly by paracrine secretion of cytokines, acting as a messenger between immune cells through cellular crosstalk that culminates with immunomodulatory effects and finally generating extracellular vesicles in the form of exosomes (which stimulate cell proliferation and protection against apoptosis) [1-3].

The main mechanism of its therapeutic effect is through the secretion of soluble factors, such as cytokines, chemokines, angiogenic factors, growth factors, and extracellular exosomes and vesicles [4].

Intravenously infused mesenchymal stem cells have been found to migrate directly to the lungs, where they can secrete numerous factors that play an important role in immunomodulation, protecting alveolar epithelial cells, resisting pulmonary fibrosis, and improving lung function, which it is a great benefit for the treatment of severe lung disease in COVID-19 [5].

Historically, mesenchymal stem cells have been used in the treatment of H7N9 influenza in China with good results, highlighting lower mortality and no adverse events.

In the COVID-19 era, the FDA does not recommend the use of mesenchymal stem cell therapy unless it is a controlled clinical trial.

Currently small investigations have been carried out in series of cases:

- A pilot study of intravenous stem cell transplantation included 10 patients with severe inflammatory pneumonia, 7 of whom presented significant clinical improvement.
- A small clinical trial evaluated the infusion of human umbilical cord mesenchymal stem cells (hUC-MSC) in patients with severe COVID-19, including 12 patients who received such therapy who did not require mechanical ventilation and recovered without sequelae [6,7].

Potential risks with mesenchymal stem cell therapy are: failure of cells to function as expected, possibility of mesenchymal stem cells multiplying or turning into inappropriate cell types, product contamination, tumor growth, infections, thrombus formation and reactions at the administration site [8].

66 studies with mesenchymal stem cells are registered in the clinicaltrials.gov database, of which encouraging results are expected that may favor the full indication of therapy in severe COVID-19, since physiologically and pathologically the indications of this therapy seem very promising over other non-cellular therapies [9].

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