

# MSCs transplantation may be a potential therapeutic strategy for COVID-19 treatment

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**Abstract.** – At present, SARS-Cov-2 is spread all over the world, becoming a serious threat to people's health. SARS-Cov-2 has a strong infection, and the mortality rate of severe patients after infection is high, but there is no effective treatment. Mesenchymal stem cells (MSCs) have anti-inflammatory and immunomodulatory functions, which can reduce the occurrence of cytokine storm syndrome and acute respiratory distress syndrome. At the same time, MSCs can reduce the level of pulmonary fibrosis and enhance tissue injury repair. In this short report, combined with the progress of preclinical and clinical research, we comment the efficacy of MSCs in the treatment of COVID-19.

*Key Words:*

SARS-Cov-2, COVID-19, Mesenchymal stem cells, Anti-inflammatory, Injury repair.

## Introduction

Coronavirus Disease 2019 (COVID-19) refers to pneumonia caused by SARS-Cov-2 infection, which has broken out for the first time in Wuhan of China<sup>1</sup> and has spread to all over the world from December 2019 to March 2020. As of March 31, 2020, people suffering of SARS-Cov-2 infection have been confirmed in more than 150 countries of the world, with more than 780 thousand laboratory-confirmed cases and 37,605 deaths.

According to recent research, most patients with COVID-19 experienced fever, fatigue, dry cough as the main manifestations, while some also had headache, stuffy nose, runny nose, diarrhea, and other symptoms<sup>2</sup>. After the analysis of the first batch of 99 cases with COVID-19, it was found that severe patients developed cytokine storm syndrome (CSS) and 17 patients (17%) developed acute respiratory distress syndrome (ARDS). Among them, 11 patients (11%) worsened

and died of multiple organ dysfunction (MOD) syndromes in a short period of time<sup>2</sup>. CSS, a variety of inflammatory factors of rapid production after infection with virus or bacteria, is an important cause of ARDS and multiple organ failure. However, current treatment for COVID-19 is limited. Therefore, there is an urgent need to explore effective treatments.

Mesenchymal stem cells (MSCs) are non-hematopoietic stem cells derived from mesoderm, which widely distributes in connective tissue and organ stroma, such as bone marrow, adipose tissue, Wharton's jelly, umbilical cord blood, placenta, menstrual blood, dental pulp, and several other tissues. Evidence from preclinical and clinical studies have confirmed that MSCs has the characteristics of self-renewing, differentiation potential, low immunogenicity, and inherent tumor or inflammatory tropism. Notably, MSC also has strong anti-inflammatory and immunomodulatory functions.

MSCs can regulate inflammation through a series of mechanisms, including promoting the recruitment of regulatory T lymphocytes, such as CD4+CD25+FoxP3+ T lymphocytes and CD8+CD28- T lymphocytes, inhibiting excessive proliferation and differentiation of B lymphocytes, the maturation of dendritic cells, and promoting macrophages to anti-inflammatory phenotypic polarization<sup>3</sup>. Therefore, the immunomodulation function of MSCs may be the key to reduce the occurrence of CSS in COVID-19 patients. In addition, MSCs transplanted intravenously can quickly reach the lungs. Radwan et al<sup>4</sup> indicate that adipose tissue-derived MSCs can inhibit NF-κB signal pathway, reduce the expression of pulmonary pro-inflammatory factors, alleviate pulmonary inflammation, and finally reverse the process of amiodarone-induced pulmonary fibrosis in rats.

**Table I.** Clinical trials using MSCs treatment for COVID-19.

Trial identifier	Title	Phases	Conditions	Interventions	Locations	Study start
NCT04269525	Umbilical Cord (UC)-Derived-Mesenchymal Stem Cells (MSCs) Treatment for the 2019-novel Coronavirus (nCoV) Pneumonia	2	Pneumonia, Viral; Pneumonia, Ventilator Associated	UC-MSCs	Wuhan, China	February 6, 2020
NCT04288102	Treatment with Mesenchymal Stem Cells for Severe Corona Virus Disease 2019 (COVID-19)	1,2	Corona Virus Disease 2019 (COVID-19)	MSCs; Saline containing 1% Human serum albumin (solution of MSC)	Wuhan, China	March 5, 2020
NCT04313322	Treatment of COVID-19 Patients Using Wharton's Jelly-Mesenchymal Stem Cells	1	Use of Stem Cells for COVID-19 Treatment	WJ-MSCs	Arabia Amman, Jordan	March 16, 2020

Both preclinical and clinical data seem to indicate the feasibility and safety of utilizing MSCs in clinical treatment. Several previous studies have confirmed the efficacy of MSCs in the treatment of acute respiratory distress syndrome, acute lung injury, and other lung diseases, and it has been reported<sup>5</sup> that umbilical cord derived MSCs (UC-MSCs) can significantly reduce H5N1 virus-related acute lung injury and prolong survival. At present, SARS-Cov-2 is rampant all over the world, and clinical trials based on MSCs for severe COVID-19 patients have been carried out one after another (Table I).

Collectively, MSCs has great advantages in anti-inflammation and injury repair, and has better safety in clinical use. Therefore, on the basis of ensuring the survival rate and activity of MSCs, it is worth a bold attempt to utilize MSCs transplantation to treat severe COVID-19 to curb the progression of critically ill patients and reduce the mortality.

#### Conflict of Interest

The Authors declare that they have no conflict of interests.

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