



Infusion of Mesenchymal Stem Cells: A Promising Treatment for Severe Covid-19

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Introduction

Over 8 million people around the world, to the present date, were reported to have the disease provoked by SARS-CoV-2 virus infection, COVID-19 [1]. This virus belongs to the same genus as SARS-CoV and MERS-CoV, Betacoronaviruses that have triggered previous epidemic outbreaks, causing respiratory infections. The most commonly reported symptoms of COVID-19 are fever, cough, and fatigue, shortness of breath, nausea and diarrhoea. Age has been identified as a major risk factor, as well as comorbidities, such as cardiovascular disease, diabetes, obesity and hypertension, regardless of age group [2]. The initial mechanism of infection occurs through the binding of the virus spike protein to the angiotensin-converting enzyme 2, which is present on the surface of several cell types, especially of epithelial cells [3].

A subgroup of COVID-19 patients develops the cytokine storm syndrome [4], which is associated with increased tissue and plasma content of cytokines, including interleukin (IL) -1, IL-10, IL-13, IL-17, macrophage inflammatory protein-1, interferon (IFN)- and tumour necrosis factor (TNF) -. In the lungs, this results in alveolar oedema, oxygenation impairment and acute respiratory distress syndrome (ARDS), which may be lethal [3,5]. So far, despite all efforts, there is no established drug therapy capable of totally reverting the symptoms of COVID-19 [4].

About the Study

Mesenchymal stem cells (MSC) have shown safety and efficacy in clinical trials that include inflammatory conditions as Crohn's disease and cardiomyopathy [6] and in ARDS and sepsis treatment, in preclinical models [6], suggesting that these cells may be employed in the treatment ARDS, due to their ability to promote paracrine signalling [6,7]. MSCs are non-hematopoietic stromal precursor cells, considered to be multipotent, as they are able to differentiate into various cell types of mesodermal origin, depending on the stimulus received [8]. Moreover, MSCs can be isolated from several tissues, such as the bone marrow, adipose tissue, dental pulp, placenta, umbilical cord blood and matrix [9].

MSCs display several characteristics that render them excellent candidates for employment in the treatment of acute diseases. These cells can undergo extended expansion without detriment to their multipotency or self-renewal properties [10], and show low tumorigenicity [11], while being considered non-immunogenic, owing to low constitutive expression of the major histocompatibility complex (MHC) class I and to the absence of co-stimulatory molecules of MHC class II (allowing allogeneic transplantation without the need for human leukocyte antigen matching or immunosuppression) [9].

MSCs have immunomodulatory and anti-inflammatory effects on host tissue, partly through the release of paracrine factors [6]. Several preclinical studies, as reviewed by Johnson et al. [12], have demonstrated that in sepsis and acute lung injury/ARDS models,

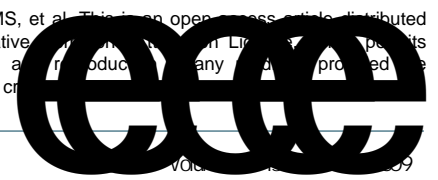
MSCs exposure resulted in a decline of the expression and secretion of pro-inflammatory cytokines, including IL-1, IL-1, IL-6, IFN-,

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umbilical cord stem cells, 7 trials with adipose tissue stem cells, and