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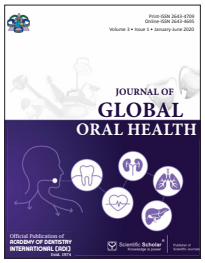

Opinion Piece Articles

Human dental pulp stem cells based therapy for COVID-19

Saravana Priyan GL[1]

[1]Department of General Dentistry, Balaji Dental and Craniofacial Hospital, Chennai, Tamil Nadu, India.

***Corresponding author:**
Dr. Saravana Priyan GL, Department of General Dentistry, Balaji Dental and Craniofacial Hospital, Chennai, Tamil Nadu, India.

drsaravanapriyangl@gmail.com

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ABSTRACT

The incidence of COVID-19 as a global pandemic led many researchers from various fields to find solutions to manage the spread and treat patients suffering from the disease. This led to the discovery of various vaccines which greatly reduced the spread of COVID-19. However, stem cell therapy was also proposed to be a suitable option in treatment of the same, due to its immunomodulatory properties. There are various ongoing clinical trials with various approaches for the prevention and treatment of COVID-19.

Keywords: Human dental pulp stem cells, Mesenchymal stem cells, SARS-CoV-2, COVID-19

INTRODUCTION

The global pandemic of 2019, Coronavirus disease (COVID-19) was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19, a cause of severe viral pneumonia, has resulted in over 52,00,267[1] deaths worldwide and over 4,68,790[2] deaths in India as of November 28, 2021. Stem cells are clonogenic cells capable of self-renewal and multi-lineage differentiation. Mesenchymal stem cells (MSCs) have broad clinical applications in regenerative medicine due to their immunomodulatory properties. MSCs inhibit the cell-mediated inflammatory response induced by SARS-CoV-2 and reduce acute lung injury. Human dental pulp stem cells (HDPSCs) have various applications in regenerative medicine. Dental pulp stem cells (DPSCs) are considered as neural crest cells having higher regenerative potential than bone marrow-derived MSCs. They have an immunomodulatory function, multipotency, and self-renewal capacity. DPSCs are clonogenic, highly proliferative, and are capable of differentiating into odontoblasts, adipocytes, neural cells, and various other cells.[3]

COVID-19 PATHOPHYSIOLOGY

The pathophysiology of COVID-19 can be divided into three stages based on the pathological findings of the infected respiratory tract.[4] In the first asymptomatic stage, the main receptor expressed in the respiratory epithelium is Angiotensin-Converting Enzyme II using which the coronavirus binds to the epithelial cells in the nasal cavity.[5] The polymerase chain reaction from nasal swab samples is used to diagnose the infection rate. In the second airway response stage, clinical symptoms are exhibited as the virus spreads downward the respiratory tract, along the conducting airways, eliciting a vigorous innate immune response. In stage three, the alveolar cells continue to undergo apoptosis due to viral infection, and the patient develops pulmonary

infiltration, hypoxia, thereby resulting in very severe disease.

The immune-mediated inflammation markers, monocyte chemo attractant protein-1, interleukin-2, 6, 7, and tumor necrosis factor alpha, play a significant role in the pathogenesis of COVID-19. These inflammatory cytokines in the lung tissues causes edema, lung dysfunction, and acute respiratory distress syndrome (ARDS), eventually leading to possible death.[6] COVID-19 is accompanied by an increase in neutrophil numbers and a reduction in the lymphocytes. The number of B cells, natural killer cells, and T cells decreases in patients with severe infection.[7]

HDPSCs AND LUNG INJURY

The main characteristics of ARDS includes loss of alveolar structures and accumulation of inflammatory cells followed by fibrosis.[8] M1 macrophages release pro-inflammatory cytokines thereby increasing tissue fibrosis.[9] Managing macrophages can be a valuable strategy to treat ARDS. Wakayama *et al*. showed that intravenous (IV) infusion of SHED (Exfoliated Deciduous Teeth) and their DPSC-Conditioned Medium (CM) assessed in chemically induced acute lung injury (ALI) in a mouse model. The results proved that the regeneration and survival rate improved after the administration of SHED or DPSC-CM. The M2 macrophages were also activated that upregulated the anti-inflammatory effect.[10] The clinical studies in COVID-19 used the IV injection of MSCs as a less invasive method. The MSCs injected intravenously are trapped mostly in the lungs and to a lesser extent in other tissues;[11] thus suggesting that IV administration of DPSCs will be localized to the lung tissues.

DPSCs are available in abundance, easy to harvest, and have effective therapeutic abilities. They can be easily isolated from discarded teeth and comply with ethical considerations. *In vitro*, the DPSCs show a high proliferative ability. They also provide sufficient cell numbers in a very short time frame. They also demonstrate a multi-differentiation potential. They are considered to be a good choice for numerous cell-based approaches for immune and inflammation related diseases.[12]

CLINICAL TRIALS OF DPSCs IN PROGRESS

A randomized clinical trial with 20 participants is in progress to evaluate the safety and efficacy of allogeneic Human Dental Pulp Mesenchymal Stem Cells (HDPMSCs) in the treatment of severe pneumonia caused by COVID-19 and its role in reducing mortality and improving clinical prognosis. The study involves IV injection of 3.0 × 10e7 HDPMSCs solution about (30 ml) on days 1, 4, and 7, respectively, based on the routine treatment of COVID-19. The study aimed to discover a new therapeutic strategy for COVID-19 using allogeneic HDPMSCs.[13]

An interventional clinical trial with about 24 participants is in progress to the evaluation of Coronavirus induced severe pneumonia treated by DPSCs.[14]

CONCLUSION

COVID-19 is a global pandemic which requires the simultaneous development of effective therapy and vaccine. The cytokine storm in the lungs of a severely impacted COVID-19 patient can be inhibited by HDPSCs through their immunomodulatory and regenerative capacity. They can be obtained safely and easily without morbidity and raising any ethical concerns; however, the challenge of understanding the mechanisms underlying the therapeutic effects of HDPSCs in the treatment of COVID-19 requires more research.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflict of interest.

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