UMBILICAL CORD MESENCHYMAL CELLS FOR TREATMENT OF COVID-19

INTRODUCTION

Coronavirus may have the ability to stimulate a cytokine storm in the lung. The cytokine storm is resulted from the production of a large number of inflammatory factors due to over activation of the immune system. This will lead to dysfunction of air exchange, acute respiratory distress syndrome (ARDS) and secondary infection and multiorgan failure. Therefore, the avoidance of the cytokine storm may be the potential key treatment for COVID-19 patients. The mesenchymal stem cells (MSCs) are reported to have the ability to inhibit the over activation of the immune system. At a cellular level, mesenchymal stem cells would appear to have natural immunity to the coronavirus from their immunomodulatory effects. They may also have beneficial effects in preventing or attenuating the cytokine storm by secreting powerful antiinflammatory factors.[1,2]

EVIDENCE on EFFECTIVENESS and SAFETY

There was no article retrieved from the scientific databases such as Medline, EBM Reviews, EMBASE via OVID, PubMed and from the general search engines [Google Scholar and US Food and Drug Administration (USFDA)] on umbilical cord mesenchymal stem cells for treatment of COVID-19. However, two relevant articles were retrieved from scientific databases on mesenchymal stem cells for treatment of COVID-19. There were three clinical trials that have been registered to date on umbilical cord mesenchymal stem cells for treatment of COVID-19 and nine clinical trials on mesenchymal stem cells for treatment of COVID-19.[3]

Leng Z et al. (2020) conducted a study aim to investigate whether MSCs transplantation improves the outcome of patients with COVID-19 pneumonia. The study was conducted in Beijing YouAn Hospital, Capital Medical University, China from Jan 23, 2020 to Feb 16, 2020. From this study, an intravenous MSCs transplantation was performed on seven patients (n=7) with COVID-19 infected pneumonia. Seven confirmed COVID-19 patients, including one critically severe, four severe and two common conditions were enrolled. All patients (aged from 18 to 95 years) were confirmed by the real-time reverse transcription polymerase chain reaction assay of COVID-19 RNA in Chinese Center for Disease Control and Prevention. The clinical grade MSCs (intravenous injection) were supplied, for free, by Shanghai University, Qingdao Co-orient Watson Biotechnology group co. LTD and the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences. The cell product has been certified by the National Institutes for Food and Drug Control of China.[2]

The immunomodulating function of MSCs contributed to the main efficacy outcome and the transplantation of MSCs showed impressive positive results in reducing the symptoms of fever, weakness, shortness of breath, and low oxygen saturation. In the critically severe patient, the plasma C-reactive protein level decreased from 105.5 g/L (Jan 30) to 10.1 g/L (Feb 13), which reached the highest level of 191.0 g/L on Feb 1, indicating that the inflammation status was alleviating quickly. The secondary outcomes were also improved in the critically severe patient

where the lymphopaenia was significantly improved after the cell transplantation and improvement of the chest imaging. The authors concluded that administration of intravenous injection of MSCs significantly improved the inflammation situation in severe COVID-19 patients. The patients with severe COVID-19 pneumonia survived the worst condition and recovery due to unique immunosuppression capacity, the serum levels of pro-inflammatory cytokines and chemokines were reduced significantly.

A case report by Liang et al. (2020) reported on the use of allogenic human umbilical cord mesenchymal stem cells (hUCMSCs) in a 65 years old female critically ill COVID-19 patient in China. The allogeneic hUCMSCs which were produced under GMP condition were administered intravenously for three times (5×107 cells each time) with antibiotics and thymosin α1 were given to the patient. No obvious side effects were observed after first administration. Several improvements that has been reported which include the gradual reduction of serum bilirubin, CRP, ALT/AST, white blood cell count and neutrophil count to the normal level, the lymphocyte count and the counts of CD3+ T cell, CD4+ T cell, and CD8+ T cell were also remarkably increased to normal levels. The chest CT images showed that the pneumonia was relieved. The throat swabs were reported to be negative 8 days after the administration of hUCMSCs .The authors concluded that adoptive transfer therapy of hUCMSCs might be an ideal choice to be used or combined with other immune modulating agents in COVID-19 patients.[4]
In terms of safety, Yip HK et al. (2020) in a prospective phase I clinical trial investigated the safety, feasibility and possible adverse events of single-dose human umbilical cord-derived mesenchymal stem cells in patients with moderate-to-severe acute respiratory distress syndrome (ADRS). A total of nine ARDS patients were enrolled prospectively in this phase I clinical trial. In-hospital mortality was 33.3% (3/9), including two with recurrent septic shock and one with ventilator-induced severe pneumomediastinum and subcutaneous emphysema. Transient desaturation, dyspnoea, and hypotension at 10–15 minutes after cell infusion were observed in two cases. One case presented with generalised skin rash that appeared a few hours after cell therapy and was persistent for about 2 days. However, all these adverse events did not cause any life-threatening condition and these patients were recovered smoothly.[5]

CONCLUSION

Limited evidence suggests that mesenchymal stem cells may have potential to be used for treatment of COVID-19. However, the safety and effectiveness of umbilical cord mesenchymal stem cells in COVID-19 patients is still inconclusive as there is insufficient evidence to support its use or treatment of COVID-19. The results from several ongoing clinical trials may provide more information in the future. As use of umbilical cord mesenchymal stem cells in COVID-19 are still investigational, it should be used under research environment.

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