

CELL-BASED THERAPY FOR MS PATIENTS DURING COVID-19 PANDEMIC PRACTICAL RECOMMENDATIONS FOR CLINICAL TRIALS

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INTRODUCTION

COVID-19 causing by SARS corona virus type 2 is a pandemic infection since December 2019 and more than 2 million related mortalities reported all over the world. Underlying issues including pulmonary diseases, older age, obesity and high BMI, chronic inflammation, and being under immunosuppression treatment are predisposing factors in COVID-19. Modeling this disease can promote research in order to find practical solutions in this condition [1].

Nowadays, many patients suffering from chronic neuroinflammatory and neurodegenerative diseases such as multiple sclerosis (MS) who receive disease-modifying therapies (DMTs). These patients may be at higher risk of becoming infected with the coronavirus, especially those with older age and more disability.

DISCUSSION

Stem cell therapy might be a novel therapeutic choice for some of these patients [3]. The safety and efficacy of different methods of cell-based therapy in MS patients have been reported in many clinical trials. Hematopoietic and mesenchymal stromal cells (HSCs & MSCs) are two types of stem cells which have been used for treatment of MS patients in different trials [4].

Since some MS patients may be candidate for cell-based therapies during COVID-19 pandemic, some recommendations in translational clinical practice should be highlighted here:

1) Although HSC transplantation is one of the most effective approaches for treating MS patients [4], particularly in the aggressive active form of disease. This therapeutic option has some adverse events including pancytopenia, febrile neutropenia, and possibility of infections [3].

Innate and also adaptive immunity are necessary for defending against coronavirus infection [5]. Regarding to bone marrow suppression in the first step of HSC transplantation (HSCT) in order to reconstitute the immune system [3], these patients are

in higher risk of infection with COVID-19 due to the loss of their immune function. Therefore, this is a high risk procedure for such a high risk patients during the current pandemic and it is reasonable to postpone any HSCT for MS patients who were assigned as HSCT candidate. We also recommend patients who have already had HSCT, to be isolated as much as possible and pay attention to essential health recommendations. The health care givers should be aware of any signs and symptoms of COVID-19 in these patients. Follow-up should be done regularly and the treatment should be performing as soon as possible. It seems that administration of convalescent plasma of people who have recovered from COVID-19 is a proper prophylactic option in these patients [6, 7]. Moreover, we recommend to consider early COVID-19 vaccination in these group of MS patients as well as other aged or frontline health care workers [8]. However, because of immunosuppressive properties of HSCs, the immunogenicity of COVID-19 vaccination may be variable at different stages of the therapy [9].

2) Mesenchymal stromal cell (MSC) therapy, particularly for MS patients during the COVID-19 pandemic, sounds to be a safe procedure. There are many clinical trials which have used MSCs as a therapeutic option in advanced and disabled MS patients such as MESEMS trial which is the largest multicentric trial in this field. The preliminary results presented in ECTERIMS 2019 have shown that MSC therapy is feasible and safe in these patients [10]. In MSC-based therapy, there is no need of using immunosuppressive medications for patients [11], so their immune system won't be manipulated in terms of immune reconstitution. Therefore, they might not be more prone to any infection compare to other MS patients. Thus we can perform MSC therapy in MS patients by considering some crucial cautions; such as injecting in the clean and isolated hospital ward or a green clinic. We also recommend following them up more closely after injection and for the monitoring of any sign of infection after discharge from the hospital or clinic. Furthermore, COVID-19 vaccine in these patients sounds to be safe [8].

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One of the advantages of MSC therapy is suppression of some inflammatory cytokines including IL-6 [12] which have an important role in COVID-19 complications such as ARDS, and storming of these cytokines is associated with poor prognosis [13]. Accordingly, immune modulation by MSC therapy could be protective in COVID-19 patients, the subject that should be investigated and proved in the clinic. One of the other advantages of MSC therapy (compare to HSCT) is a single IV dose of 1×10^6 cells/kg infusion [14] and also the fact that the patients can be easily discharged four hours after cell transplantation, so the admission in the hospital is short [15]. COVID-19 vaccination is recommended for all MS patients treated with this cell type regardless of time of injection. It is assumed that mesenchymal stem cells have no negative effect on immunogenicity of the vaccines.

CONCLUSION

Finally, as we know, the most common clinical symptoms of COVID-19 are fever in up to 90%, cough in 70%, myalgia and fatigue in about half of patients. Dyspnea and chest pain are also common symptoms in these patients. Some uncommon signs and symptoms like headache, diarrhea and anosmia have also reported [16, 17]. A smart system or tele monitoring in which minimum signs and symptoms of COVID-19 or any history of contact with the infected/ suspicious person in MS patients who are under cell therapy, should be implemented. Moreover health care providers should do a rapid diagnostic test for COVID-19 in these MS patients.

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