REVIEW ARTICLE

UMBILICAL CORD BLOOD DERIVED MESENCHYMAL STEM CELL THERAPY IN NOVEL CORONA VIRUS INFECTION – A REVIEW

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ABSTRACT

The 2019 Novel Coronavirus has become a threat to the humanity at present affecting many countries over the world. Coronaviruses (CoV) are enveloped single-stranded RNA virus causing mostly respiratory illness in the humans. The envelope anchored Spike protein (S) of CoV facilitates the attachment of the CoV to the host cell membrane Angiotensin-converting enzyme 2 receptor thereby infecting the host cell. If a huge number of cells are infected together at a time, huge amount of proinflammatory cytokines are released which results in "Cytokine Storm". To prevent the cytokine storm and pulmonary damage, umbilical cord blood derived mesenchymal stem cells may be an important therapeutic measure in fighting the CoV infection.

KEY WORDS

Corona virus ; COVID; cord blood; stem cell

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INTRODUCTION

Corona viruses (CoV) are enveloped single-stranded RNA virus[1]. Most of the corona viruses cause respiratory illness or intestinal infections in the animals and humans. Some of the common types of corona virus infecting animals are porcine respiratory CoV (PRCoV), canine CoV(CCoV), bovine CoV(BCoV); and those infecting humans are HCoV-229E, HCoV-NL63, Severe Acute Respiratory Syndrome-associated CoV(SARS-CoV) and Middle East respiratory syndrome virus (MERS-CoV). The newest of the CoV infecting humans is the 2019 novel corona virus (2019-nCoV) causing symptoms ranging from mild flu to severe acute respiratory illness.

These corona viruses family are divided into four major genera – Alpha corona virus, Beta corona virus, Delta corona virus and Gamma corona virus[2].The 2019 novel corona virus (2019-nCoV) belong to the Beta corona virus family.

The Coronavirus genetic material usually synthesizes five types of protein viz., Spike protein (S), Envelope protein (E), Membrane protein (M), Nucleocapsid protein (N) and haemagglutinin-esterase (HE) protein[3]. The haemagglutinin-esterase (HE) protein may not be found in all types of coronavirus.

The structure of CoV reveals the presence of an outer envelope consisting of M protein, S protein and HE protein whereas the inner nucleocapsid consists of N protein and genetic material i.e. RNA.

The envelope anchored Spike protein (S) of CoV facilitates the attachment of the CoV with the host cell membrane receptor followed by fusion between the viral and host cell membrane[4-7].This interaction between the S protein of CoV and host cell receptor is important for anchorage of the virus with the host there by causing the infection.

AIMS AND OBJECTIVES

This review article will enable the readers to gather a brief idea about the CoV family of viruses with special emphasis on the 2019 novel corona

virus (2019-nCoV) structure and its pathogenesis. Besides that, recent concept of treatment of CoV affected patient with Mesenchymal Stem Cells has also been reviewed in this article.

DISCUSSION

Pathogenesis of CoV infection

The Spike protein (S) of CoV contains a specific receptor-binding domain (RBD) which specifically identifies and attaches to the host receptor Angiotensin-converting enzyme 2 (ACE2)[8,9]. CoV RBD contains a receptor-binding motif (RBM) which usually binds to the receptor ACE2 at its outer surface[10].

The receptor (ACE2) is normally present on the cell membrane of various cells located in lungs, liver, heart, kidneys and also in almost all the endothelial cells as well as smooth muscle cells. After attachment of 2019 novel CoV receptor-binding motif (RBM) with ACE2 receptor, both of it fuses together to constitute a conduit through which the genetic material of CoV i.e. viral RNA is introduced inside the human cell cytoplasm. Then the viral RNA utilizes the human cell machinery to replicate and induces to produce its various components such as Spike protein (S), Envelope protein (E), Membrane protein (M), Nucleocapsid protein (N). The different components of the virus assemble together within the host cell. Those host cells get distended containing fully assembled CoV and finally bursts. Thus numerous viruses are released outside by destroying the host cell. Those released CoV further infects and destroys more and more number of host cells. As the host cells are destroyed, an inflammatory response develops by the release of numerous proinflammatorycytokines. As a result of these cytokine release, the cells near the vicinity die there by creating a barrier between those of living host cells and the CoV infected cells with an attempt to localize the infection. If a huge number of host cells are infected together at a time, huge amount of proinflammatory cytokines are also released which results in "Cytokine Storm". Such cytokine storm paves the pathway for destruction of huge number of host cells. Slowly the COVID-19 immunocompromised patients develop multi-organ failure. In case of immunocompetent patients, the immunological response as mediated by the T cells and B cells can control the viral multiplication and prevent complications.

Treatment of COVID patients with Umbilical Cord blood derived Mesenchymal Stem Cells

The main stay of 2019 novel CoV infected patients is symptomatic, though some antimalarials, antiretrovirals are being used in day to day practice. As till date, there are no FDA-approved drugs or vaccines to treat and prevent Novel Coronavirus infection, FDA has approved clinical trials for the same. Even if a drug or vaccine is discovered in near future, it will take many months to become available in the market.

The main goal to the treatment of CoV infection should be the prevention of Cytokine storm. Many countries like China, Italy have started trials with Umbilical cord blood derived mesenchymal stem cells (MSCs) to treat COVID patients with a hope of not only reducing the number of patients to be transferred to ICU but also a relatively quicker recovery of ICU admitted COVID patients[11].

The first umbilical cord blood stem therapy in a COVID patient was reported from China. A sixty-five-year-old female COVID patient suffering from pneumonia, respiratory distress and multiorgan failure and under mechanical ventilatory support was treated with three doses of allogenic cord blood stem cells at an interval of three days. Each and every dose contained about 50 million allogeneic cord blood mesenchymal stem cells. Patient responded to the therapy well and there was marked improvement in several parameters [12].

The mode of action of MSCs in the treatment of COVID infection and prevention of cytokine storm is discussed here. After intravenous infusion of MSCs, numerous number of MSCs gets deposited in the lungs thereby improving the pulmonary micro environment and protecting the lung alveolar epithelial cells. This helps in prevention of pulmonary fibrosis and favours the improvement of lung function[13-15]. MSCs also have immunomodulatory effects and play a positive role in promoting host immune response against the viral pathogens as well as by promoting phagocytic activity. Expression of indoleamine 2,3-dioxygenase (IDO), Interleukin (IL)-17 and Antimicrobial peptides (AMPs) like cathelicidin LL-37, hepcidin, human β-defensin-2 (hBD-2), lipocalin-2 (Lcn2) are mediated by MSCs which helps in fighting the novel corona virus[16-18]. Thus MSC therapy play a critical role in management of COVID patients by preventing development of complications and maintaining normal lung integrity and pulmonary function.

CONCLUSION

The 2019 Novel Coronavirus has become a threat to the humanity at present affecting many countries over the world. Without the absence of any definite curative therapy, supportive treatment remained the only option. MSCs derived from umbilical cord blood showed some positive results in treatment of critically ill COVID patients. However, further trials are needed for establishing MSCs to be the first line treatment of COVID patients.

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