Application of Different Cell Therapies in the Treatment of Covid-19

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Abstract. Covid-19, which erupted in Wuhan, China, in 2019, was highly contagious and caused panic. covid-19 has a sequelae, and the World Health Organization reports that about 10 to 20 percent of crown infections have new crown sequels, including exhaustion, overheart movement, shortness of breath, cognitive difficulties, chronic pain, sensory function, muscle weakness, etc. Research institutions such as the United States, the United Kingdom, the Netherlands and other research institutions have released a considerable number of new crown sequels in their own country, and some of the population is already unable to work. There are still no systematic treatment, only some of the symptoms proposed based on the symptoms, these traditional therapies do not treat the sequelae, so some new therapies have been proposed. This paper will revolve around cell therapy. The common methods used in clinical treatment of diseases are surgery, chemical drugs, ion exposure, plant drugs. The development of modern medical theory and technology gradually introduced cell therapy into the clinic. Cell therapy is a treatment with functional cells as the main body. Cell therapy can be used as an independent treatment or combined with the above-mentioned routine treatment. In recent years, cell therapy has shown increasing application value in the treatment of genetic diseases, cancer, tissue injury, diabetes and other diseases, and details current cell therapy and prospects.

Keywords: Covid-19; traditional therapies; cell therapy.

1. Introduction

2019 The new coronavirus (2019-nCoV) is a new coronavirus, which is the same as SARS-CoV belonging to the NEVV Coronavirus section of the beta-CoV, a single strand of strand RNA virus that is not fragmented, with a genome length of about 30,000 nucleotides. Unlike the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), 2019-nCoV is the seventh in the family of coronaviruses infected with humans [1]. In terms of gene sequence homogeneity, the 2019-nCoV genome is 80% similarity to SARS, and the 2019-nCoV gene sequence is 40% similarity to MERS-CoV. How to quickly discover effective means of treating new coronavirus is a major challenge for researchers. The existing traditional medications and treatments do not fully treat pneumonia, and they cannot cure the aftermath of the heart, lungs and kidney caused by pneumonia. More than half of patients have lung nodules, shadows, fibrosis and other manifestations, nearly one-third of non-critical cases have symptoms such as respiratory difficulties, sleep difficulties, weakness and joint pain; more than 41.7% of discharged patients have anxiety symptoms, and 37.5% of patients have depressive symptoms [2].

The survey documented the patients in great detail, with an average age of 40 to 60 years, of which 102 were only mild patients, and the remaining 18 were severely ill, and the cure of new coronavirus was extremely long and painful. But both mild and severe patients, without exception, after recovery, they are affected and injured by the new crown sequel, which also makes them delayed entering a normal life. [3]So now, cell therapy is proposed, mainly interstitiate stem cell therapy, NK cell therapy and T cell therapy. Internationally, the Abu Dhabi Stem Cell Center (ADSCC) shows development of 5,000 patients recover from the covid-19 infection because of stem cell therapy. Activation of natural killer cells (NK cells) can remove those infected with the new coronavirus and prevent infection from further expanding. NK cells are effective against viruses that produce immune escape, and NK cells kill infected cells, avoid them becoming viral culture bases and prevent more viral replication. This article will describe these cell therapies in detail.

2. Traditional Methods of Treating Covid-19

2.1. Traditional Therapies

The continuing coronavirus pandemic (COVID-19) is the most credible global crisis after World War II. Its strong infectious nature, can also affect many organ systems, severely deadly, has been classified as infectious disease. COVID-19 is a Infectious diseases are caused by the new severe acute respiratory synchronization of the drome coronavirus (SARS-CoV-2).The major threat of covid-19 is in two ways: the degree of infection, especially among health care workers, and the mortality rate of covid-19, which is much higher than the well-known mortality rate of pneumonia. Another feature of this new virus is that it is very easy to spread through aircraft. Covid-19 virus is spherical, with a diameter of about 100nm, is a single strand of the cornered RNA virus with the envelope. Infectious atypical pneumonia, also known as severe acute respiratory syndrome, is an acute respiratory infectious disease caused by coronavirus. It is spread mainly through short-distance foam, exposure to patient respiratory secretions and close contact. With fever, headache, muscle soreness, weakness, dry cough and less phlegm, diarrhea as the main clinical manifestation, severe people suffer from air push or breathing distress. Analysis of this new genome. The virus is similar to SARS-CoV and Middle East Rehelical Syndrome Coronavirus (MERS-CoV) by~79.5%. However, the highest sequence similarities of bat coronavirus were observed (~96%).

Therefore, it is speculated that COVID-19 is transmitted from Bats to humans. Recent studies have shown that a middle animal host, it may be a pangolin, or a dog. Early studies of COVID-19 have shown that the disease spreads. By releasing small spiral droplets by close contact with infected people and when coughing, sneezing or speaking. A tiny saliva or droplet released from the mouth may be carried. A large number of viruses are known to stay in the air for a long time. Therefore, it may be used as a carrier of infection. The current new crown treatment methods are generally: Effective oxygen therapy measures are given in time, including nasal catheter, mask oxygen therapy and nasal high flow oxygen therapy. Conditional treatment can be used for hydrogen-oxygen mixed inhalation (H2/O2:66.6%/33.3%).Antiviral treatment: a-interferon (pervermin (5 million u per day or equivalent dose of adult, 2 m1 of water for sterilization injection, 2 atomized inhalation per day), Romanave/Litonavi (200mg/50mg/particle for adults, 2 tablets per day, 2 sessions per day, less than 10 days), Litonavi (recommended in conjunction with interferon or ronavir/Litonavi, 2 times per day, 3 times per day for adults, 500mg per day, 3 times for the third to seventh day, 500mg per day, 3 times for the third to seventh day, 500mg per day, 3 times per day, 3 times for the third to seventh day, 500mg per day, 3 to the seventh day, 500mg per day, less than 10 days).For severe cases, high flow nasal catheter oxygen therapy or noninvasive mechanical ventilation: When patients receive standard oxygen therapy and hypoxygen is unable to remission, high flow nasal catheter oxygen therapy or nonturnal ventilation may be considered. Short time (1-2 hours).

But such a treatment does not take into account the sequelae, and on March 22, 2021, a study on the aftermath of patients with new coronavirus pneumonia was published in the medical journal Nature Medicine. A study conducted by 1733 people in China 63% of people have sequelae after recovery, and a study of 143 people in Italy showed that 53.1% of people have sequelae after recovery. The types of aftereffects are also varied, but it is certain that most human organs will generate sequelae from new coronavirus pneumonia. Natural Medicine published an article stating that lung fibrosis, sleep disorders, intestinal dysfunction, chest pain, thrombosis, kidney disease, hair loss are all possible aftermath of recovery. The outcome of any sequel can be serious for patients. Famous Canadian rapper Scarface had kidney failure just after recovery, and had to do 4 dialysis within a week. In addition to loss of smell, several common sequels of new coronavirus pneumonia include impairment of male fertility, poor clotting, brain damage, heart muscle damage, etc. On February 13, 2020, Suzhou Hospital, affiliated with Nanjing Medical University, was preprinted on this website a paper published on MedRxiv says infection is new. After the coronavirus, vascular tension conversion enzyme 2 (ACE2) in the kidneys and testicles may cause kidney and testicles damage. That is, infecting a new coronavirus can affect the fertility of men. Researchers at the National Institutes of

Health also published a paper on Preprint platform on Feb. 21, saying that the new coronavirus infection could suppress reproductive-related functions of targeted cells, thereby failing male fertility. In addition to affecting fertility, the new crown. Pneumonia may also cause patients to have poor blood clotting ability after the patient. On April 10, 2020, the United States began to dissect the bodies of the first person in the country to be killed by new coronary pneumonia. Vander Hyde of the Center for Health Sciences at Louisiana State University in New Orleans found the dead were successful after the anatomy. Hundreds of miniature thrombosis have also been present in the bodies of the autopsy since then. One possible explanation is that the new coronavirus may increase the incidence of blood clots. As a separate living body, cells have strong vitality, proliferation differentiation ability and function plasticity.

2.2. Disadvantages of Traditional Therapies

The mechanism of cell therapy for treating diseases is mainly divided into two main categories: one is the direct role of the cell, directly using its specific biological activity to repair damaged tissues and organs; or plays a specific/non-specific killing effect; the other is the indirect role of cells, such as secretion-related factors or active molecules to regulate the proliferation and functional activity of the patient's own cells [2]. The immunometric effects of intermediate-semen stem cells help suppress immune storms and lung inflammation, is expected to become one of the most ideal treatments for treating new coronavirus pneumonia; the potential of NK cells to play toxic effects on infected cells and induce other immune responses to make NK cells a candidate for treatment of new coronary pneumonia cells; when the antibody immune response fails, T cell immune response can still effectively defend Omicron, T-cell-based treatment also has potential therapy prospects.These therapies are also meaningful for treatment of sequelae [4].

3. Cell Therapies for Covid-19

3.1. Intermediate-filled Stem Cell Therapy

Mesenchymal stem cell, MSC is a multi-potential stem cell that can differentiate from cartilage tissue, bone tissue, muscle, tendon, ligament, fat and other types of tissue. Intermediate-metastatic stem cells (MSCs), also known as pluripotent matrix cells, are a type of pluripotent stem cells belonging to the middle embryo, mainly in the placental and other tissues, amniotic membrane, cord blood, etc. Intermediate-semocytes have low immunogenicity, and there will be no immune rejection reaction after entering the human body, and the side effects are very small, even without side effects.

This stem cell from the newborn cord tissue, with the potential of self-replication and multidirectional differentiation, has broad application prospects in medicine and is a very valuable resource.

Because of this, in recent years, more and more parents have children, save this stem cell for future needs.Intermediate-form stem cells have a powerful function, inseparable from their extremely strong vitality.

Intermediate-septic stem cells can play blood-forming support, immunometry and tissue repair regeneration and tissue repair biological functions such as homeling, secretion of a series of cytokines and growth factors, and secretion of exosomes.

After the new coronavirus infection, the virus enters the body, by producing a large number of inflammatory factors that induce immune storms, attacking important organs such as our lungs. Serious patients often suffer severe damage to lung tissue, which can lead to lung solid change, large numbers of lung tissue cells necrosis, and reduced immune tissue cells.

In early 2020, a study reported a patient with acute COVID-19 in China who had significantly improved CT images after 21 days of treatment with intercord metamorphosis stem cells; another 65-year-old woman who had been treated with stem cells with other therapies, had relieved lungs and transferred from a severe ward after two days of treatment with stem cells. These studies have

preliminarily confirmed that intermediate stem cells treat COVID-19 infected patients are safe and effective [4].

Since then, a clinical trial of patients with new coronavirus pneumonia was conducted in Beijing, with seven patients receiving transplantation treatment for intermediate stem cells. The results showed that all patients treated had significantly relieved symptoms after 2 days of stem cell treatment. The findings reaffirm the safety of stem cell therapies, and in this study, it also confirms that stem cell therapy can be used in patients with critical condition and reduce their risk of death.

Studies have shown that intermediate stem cells can significantly reduce lung damage after the new coronavirus infection.

Beijing Yuan Hospital recruited seven patients with neo-coronavirus pneumonia (2 cases of mild disorder, 4 cases of severe illness, 1 case of critical disease) to receive single intervein methanomorphic stem cell treatment within 14 days of transplantation, the results showed that the treatment of intermediate-heterogeneous stem cells significantly improved the lung function of seven patients, and there was no significant adverse reaction [5].

It is worth mentioning that within 2 days of intermediate-semocyte stem cell treatment, all patients have significantly improved lung function and symptoms; within 2-4 days of treatment, all patients have all symptoms including: high fever, weakness, shortness of respiration, low blood oxygen saturation, and resting blood oxygen saturation ≥95%. Two patients with mild disorder and one severely ill patient were discharged from hospital within 10 days of treatment.666666

In February 2022, Wang Fusheng's team announced the results of a year-long follow-up of patients with new coronary severe disease using human umbilical cord stem cells, published in the Lancet journal EBioMedicine. The results show that the human cord intermediate-cord prescription stem cell administration has long-term benefits for lung lesions and symptoms recovery in patients with coronavirus pneumonia, and the patient's symptoms are lighter and better quality of life, sleep difficulties, daily activities and digital rating scale scores have been significantly improved.

A large number of studies have confirmed that intermediate-semocytes can be nested to the lungs, differentiated into the lung epithelial cells and the pulmonary vascular endothelial cells, thus playing its protective role. At the same time, the cytoplasm stem cells can repair the epithelial cells of the lung bubble and increase the secretion of surfactant substances of the lung bubble. Improve bronchial lung maldevelopment, reduce lung damage, restore lung structure and vascular density, reduce lung fibrosis, reduce lung structure and function, improve lung structure and function, effectively improve pulmonary fibrosis and lung damage, block the expression of pro-inflammatory factors of lungs, reduce lung inflammation levels, and eventually reverse the fibrosis process and restore normal lung structure [6].

3.2. NK Cell Therapy

NK cells are the core cells of the immune system, the first line of defense of human immunity, which mediates the immune response in part of anti-tumor and various types of viral infection, and is a "natural barrier" in the human immune system.[4]

NK cells have a strong immune surveillance function, can detect and start immune defense function in the first time, rapidly kill the lesion/cancer cells, efficiently identify and clear the body's aging and apoptosis cells, thus maintaining the stability of the environment in the body, delaying aging, preventing the occurrence of aging-related diseases.

Unlike T cells, NK cells can kill tumor cells without relying on antigen presentation, and therefore are not subject to the main tissue-compatible complex (MHC). Tumor cells often downplay MHC I expression to avoid T cell cracking, but this is not useful in NK cells, and when tumor cells downplay their MHC Class I molecules and upgrade the activated ligands, NK cells trigger cell-mediated cracking. This phenomenon is called the "lost self" response.Compared with healthy individuals, there are more NK cells expressing NKG2A proteins in NKG2A proteins in NKPneumonia patients, but the number of NK cells and effect function molecules expressing CD16 (such as interferon, letin 2, etc.), and NKG2A proteins present on the surface of certain NK cells, helping NK cells distinguish

between normal cells, healthy cells and abnormal cells. CD16 is expressed as indicating the level of activation of NK cells and the level of readiness to eliminate abnormal cells.

There are fewer mature CD57-positive cells in severe cases than in mild cases and survivors, a class of NK cells involved in immune responses [7].

Single-cell RNA sequencing analysis found that NK cell phenotypes in severe new coronavirus cases were exhausted.

The above observations of the type, number and exhaustion of NK cells suggest that NK cells may not cause severe inflammation of new coronavirus pneumonia. Therefore, NK cell immunotherapy may be beneficial to treating new coronavirus infections.

On January 4, 2023, Smith D M, Schafer J published an article on Scientific Translational Medicine published an article that NK cells are a natural weapon for antiviruses. Immunotherapy of NK cells are being explored for treating infectious diseases, including viral infections. The researchers discussed evidence of NK cells 'response to different viruses, elaborated on ongoing clinical work and the current state of clinical research on NK cells for a variety of infections, including HIV, influenza virus, giant cell virus, and new coronavirus. Numerous studies have found that NK cells change rapidly during the acute stage of new coronavirus infection. For example, the total number of NK cells in new crowns has decreased significantly and even depleted compared to healthy individuals; and in patients who recovered after treatment, the number of NK cells has not yet been able to recover to the proportion of pre-infection, suggesting that NK cells 'function depletion is associated with neo-coronavirus infection. The study found that NK immune cells change rapidly during the acute stage of new coronavirus infection [7]. For example, the total number of NK cells in new coronavirus patients has been significantly reduced and even depleted compared to healthy individuals; while the number of NK cells recovered in patients who recovered after treatment; this suggests that NK cells 'exhaustion is associated with new coronavirus infections.

Overall, NK cells produce rapid and powerful antiviral immune responses that can quickly and powerfully resist viral infection by destroying infected cells, producing chemicals to fight viruses and affect the adaptive immune system. Since antiviral drugs are usually taken after symptoms have appeared, they have not prevented early viral replication and related mortality, NK cell infusion is an attractive potential treatment for acute viral infections, including lower respiratory viral infections. Other scientific studies have shown that patients with plenty of NK cells and better active, with viral loads falling faster, symptoms or lighter.

3.3. T-cell Therapy

Integritin is a class of a-B isodimer cell surface adhesive receptor. A4 integrin and B2 integrals are expressed specifically on the lymphocyte surface. Integritin binds to its ligands by identifying two types of conservative tripeptide sequences, Arg-Gly-Asp (RGD base) and Leuflle-Asp/Glu-Val/Ser/Thr (LDV base).The receptor binding domain of the new crown S protein (S-RBD) has three potential integrative binding bases: RGD (Arg403-Gly404-ASP405), LDS (Leu441-ASP442-Ser443) and LDI(Leu585-ASP586-Ile587) [8].

This means that the new coronavirus is likely to enter lymphocytes through these combinations.

The new coronavirus is likely to promote its entry with T cell death. The study found that coronaviruses such as coronaviruses infected the human body, which may cause lymphocytes to decrease, lymph nodes to atrophy or even deplete. The world's first new coronavirus pneumonia pathological anatomy report in The Lancet revealed that the number of patients 'peripheral blood T lymphocytes was significantly reduced.

And of course, there may be more than T cells. As is known from the first graph, B cells, plasma cells, NK cells and neutrophils barely express the known SARS-CoV-2 receptors.

T cells can play a major role in the immune response in the new coronavirus, helping to clarify the important role of the body's immune response in virus clearance, and also to realize the strong security of T cells for body health. Therefore, T-cell-based therapies are expected to be another option for new crown therapy [8].

On May 23, 2023, research team from Shenzhen Bay Laboratory, Tsinghua University, the Institute of Medical Biology of the Chinese Academy of Medicine and Fudan University and other institutions published a research paper entitled "An mRNA-base T-cell-inducing antigen strengthens COVID-19 vaccine against SARS-CoV-2 variants" in Nature Communications, which aims to improve immune protection effect of the new coronavirus immunity and effectively respond to the immunity of the coronavirus mutation [9].

3.4. Disadvantages of Cell Therapy

But cell therapy is still problematic [10].

Increased intravenous input efficiency. In fact, is very dangerous, reaching only a small part of the target organ. Stem cell exosomes are about 50-70 nanometers and can be injected. But this is a mixture, and cell-in-vitro culture and other things change its composition.

The problem of exotic exclusion is of course. A large number of experiments have also shown that the same type of foreign MSC cannot function properly in the body, which is also to be clarified.

Traditional cultivation does not guarantee stable genetic traits.

4. Conclusion

Overall, the best therapies for coronavirus are, of course, developing drugs that can be effective antiviruses, but other therapies based on scientific cognition are also viable options for the future, such as stem cell therapies.

In recent years, the application of intermediate-form stem cells in disease treatment has become more and more widely used, and has become a popular track for disease treatment. Many early clinical trials of semocytes have proven safety and effectiveness, scientific publications on intermethamphetamine stem cells exceed 100,000, in addition, according to the National Clinical Database data Clinicaltrils.gov, the world's ongoing intermediate stem cell clinical trials, more than 1,000, in various indicator fields are involved. The potential of NK cells to toxically influence infected cells and induce other immune responses can make NK cells a candidate for treatment of new coronavirus pneumonia cells; when the antibody immune response fails, T cell immune response still effectively defends Omicron, T-cell-based treatment also has potential therapy prospects.

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