Original Article

SARS-CoV-19 treatment with weakened immune systems and why children do not have acute conditions in SARS-CoV-19

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Abstract

In the new SARS-CoV-19 virus disease that cause death of thousands of people all around the world. It named hidden death means, lung infections that cased by SARS-CoV-19 virus. In this disease the reaction of body is inflammation that cause death. As a result of inflammation, the fluid that fills the air sacs becomes concentrated due to glycogen, called fibrinogen, so, it cannot move, and as a result, the Alveolus lose the ability to exchange gas, resulting in death. In this method, TNF alpha is the factor that targeted and prevented it from connecting to the main receivers that located on the cell surface.

Keywords: SARS-CoV-19, inflammation and (TNF alpha)

Introduction

The SARS-CoV-19 virus was first transmitted from animal to human, and human-to-human transmission occurs when we come in contact with a person with a SARS-CoV-19 virus. For example, it can be transmitted from coughing, sneezing and any physical contact between the person with the SARS-CoV-19 virus to the others. The rate of transmission of this virus to some extent that one person with the virus can infect a country [1, 2]. Symptoms do not always occur in sick people, depending on the individual's immune system. But researches have shown that the virus has little effect on children. Symptoms include high fever, shortness of breath and dry cough [3, 4]. Researches show that the virus is similar to the SARS virus and therefore provides more stability in cold and dry climates, and it is hoped that the virus will be eliminated in hot conditions [5]. This virus because of Sheath to chord is not resistant. The best way to prevent SARS-CoV-19 is to keep the distance at least 1 and a half meters. Since, this virus is heavy and cannot stay in the air for a long time. These viruses have the largest viral genome. Washing hands properly with soap and water prevents them from spreading widely.

Immunosuppressive drugs are used to treat the disease, and one of the new drugs found is Hydroxychloroquine, that is a drug for malaria and rheumatoid arthritis and also it is an Immunosuppressive drug [6]. Although in general, all of them do the same thing, but if we look more closely, the mechanism of action of all of them is different. Another new method is plasma therapy, which uses antibodies in the serum of people who had SARS-CoV-19 but have recovered [7, 8]. In addition, the virus is so difficult to grow in the laboratory and the process of making it is difficult and time consuming. From the moment we get the vaccine, we see the catastrophes of human death and the disruption of the economy. Therefore, the treatment of this disease until the vaccine is made will have a huge change on the planet. So my goal in this article is to reduce the symptoms of SARS-CoV-19 to make it a simple disease. Most people think that the causes of this disease is the virus, while this idea is wrong, the cause of this disease is the body itself. In other words, the body's non-specific and inflammatory response, cause death. SARS-CoV-19 virus stays on plastic or steel surface for up to three days, up to 24 hours on paper, and up to 3 hours in air. SARS-CoV-19 viruses are a large family, and include many viruses, like colds and seven of them effect the respiratory system [9].

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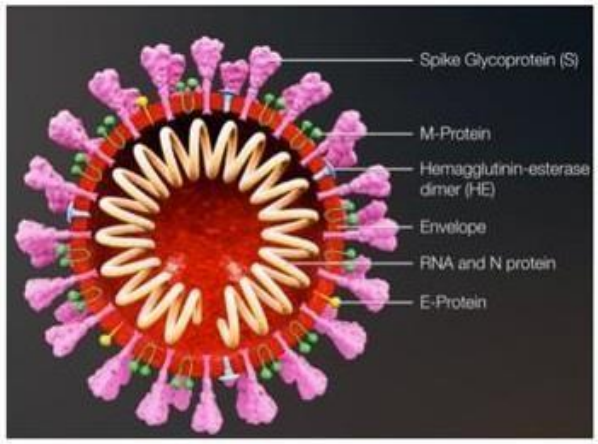
In 2002, new coronavirus was discovered in China caused by a genetic mutation in viruses. This coronavirus, called SARS, has also spread to 17 countries. Its origin is not fully defined yet, but it is possible transferred from bat to human. It is also as acute respiratory illness because it causes respiratory illness and it is very similar to the new SARS-CoV-19. In 2012, an other coronavirus was discovered in Saudi Arabia caused by a genetic mutation in the coronaviruses. The virus affects not only the respiratory system but also other organs in the body, including the liver and kidneys, killing people all around the worldThese viruses have crown-like appendages and therefore called MERS-COV [10]. Electron microscopy is used to observe coronaviruses. These viruses have crown-like appendages and therefore called corona. These viruses are from RNA viruses. They are with positive polarity (ss RNA (+)), Their RNA contains proteins called N, which together with RNA form a helical structure. Their protein production is similar to the Toga viruses. These viruses are among the lipid sheath viruses. They have two types of proteins on their membrane surface and there are two glycoproteins on the sheath surface, glycoprotein E1 and glycoprotein E2. The glycoprotein E2 in the body are the target of antibodies that also help to penetrate into the cell. The glycoprotein E1 are membrane-passing proteins. The encoding genes of all three types of proteins are present on the RNA virus, but they take their lipid sheath from the host cell. [11, 12]

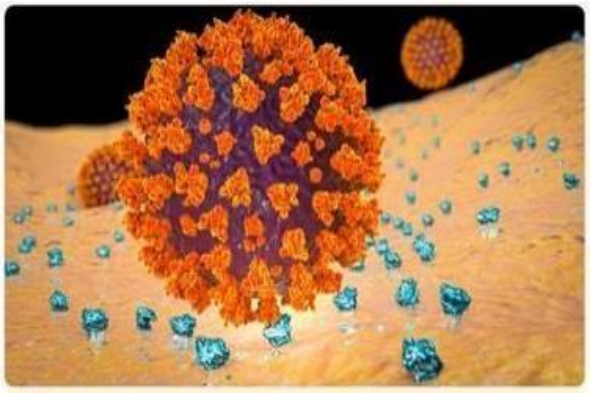
In 2019, the latest type of SARS-CoV-19 virus was found Covid-19 or SARS2 or the new SARS-CoV-19 in Wuhan, China, and spread around the world, killing thousands of people and still killing people. This Virus is very similar to SARS virus, the rate of multiplication is much faster than SARS, but it's weaker than SARS. It affects the respiratory system, first the upper respiratory tract (nose and nasal cavity and sinuses, larynx), then affects the lower respiratory tract (trachea, bronchioles, bronchus and lung (part of the larynx)). [13]

After Rhino viruses, many colds caused by SARS-CoV-19 viruses. Laboratory tests: are used to diagnose SARS-CoV-19 viruses through respiration and to use RT-PCR and RNA samples in the teeth and if tested positive for SARS or Covid-19, it will be tested more accurately at a virology laboratory. [14]

The virus has just been discovered, but it has a special feature, which is that in most cases children do not develop acute conditions and are often considered carriers. According to the researchers, the reason why children show fewer symptoms than adults is because children have a better immune system to fight the virus, which is why most people at risk are people with chronic diseases such as type 2 diabetes or have high blood pressure, heart disease, and people over the age of 65 [15]. In this disease, the rate of deaths and mortality is higher than SARS and Mers because the transfer routes are much easier and faster.



SARS-CoV-19 virus, with the help of ACE2 enzymes linked to E2 or s receptors, convert Exo peptidase angiotensin 1 to 9-1 or angiotensin 2 to 7-1. E1 or M proteins are membrane proteins, and N proteins along with RNA have a helical structure.



The receptor of this virus in the body is ACE2, as a result of connecting to it, triggers immune responses. In the first line of defense, there is a non-specific defense that causes the production of biotech ins, as a result, the inflammatory response occurs. [16, 17]

Methodology

In SARS-CoV-19 disease, Pneumonia is the cause of death. Inflammation is a physiological response of the body to any tissue damage. This response is non- specific and acts equally against all external factors, including viruses, fungi, and bacteria. Inflammation is dangerous in most cases because it can cause diseases such as cancer and heart disease. Of course, in autoimmune diseases, the cause of inflammation is inflammatory factors. Inflammation also plays a role in Asthma. From here, we can conclude that, non-specific inflammation is inappropriate or excessive, not only does not help the body, but it also causes inflammatory diseases. [18]

Another response of the body that acts against the foreign agent is a specific response that includes lymphocytes and acts more carefully against the foreign agent. The body's first response is a non- specific response that acts in the same way against all factors. In the second step, there is a specific

answer. In inflammation, the site of infection or redness becomes inflamed and warmer than elsewhere. [19]

Inflammation of the damaged tissue is isolated from other parts so that the infection does not spread. In inflammation, the goal is to separate the affected area from other parts of the body and prevent it from spreading. In inflammation, the cause of the damaged tissue is that the body recognizes the inflammatory tissue as an external factor and tries to destroy the site of inflammation, that is, the inflammatory site begins to apoptosis, which is the planned death of the cell. The mechanism of inflammation is that in the first step, old phagocytes present in the interstitial fluid migrate to the site of infection, especially mast cells. Mastocytes secrete histamine, histamine stimulates dilation and increases the permeability of blood vessels (By increasing the distance between endothelial cells of the blood vessel). As a result, red and white blood cells go to the site of infection, and the cause of the redness and warmth of the damaged tissue is the same. Inflammation has many factors, including interleukin 1, interleukin 6, and TNFalpha.[20]. For the treatment of SARS-CoV-19, most of the time anti-interleukin 6 drugs are used, and hydroxychloroquine is also used as an anti-interleukin1 drug. In this article, the goal of the alpha necrosis factor is TNFalpha.

Immunoglobulin E: One of the antibodies in the blood. This antibody cannot cross the plasma. Therefore, this antibody is not present in infants during the embryonic period. It is 90 international units in adults and may be up to 800 in some cases. For example, those with asthma or urticarial, or those with severe infections, also have increased antibody levels [21]. In fact, it is an antibody that binds to a foreign agent that secretes histamine and triggers inflammation, so it can be concluded that SARS-CoV-19 disease patients with acute inflammatory conditions can be given the anti-immunoglobulin E drug. These include XOLAIR, an anti-immunoglobulin E drug that reduces the effects of this antibody or, in other words, reduces inflammation.

XOLAIR: An anti-antibody drug. Used in Urticarial and severe Asthma. One of the characteristics that children have compared to adults is that the amount of this antibody in children is less than in adults, and perhaps this is why the acute conditions of SARS-CoV-19 in children are less than in adults. And not accurate, yet. But by comparing the amount of this antibody in children and adults and knowing its mechanism of action, we can conclude that the cause of fewer symptoms is the lower amount of immunoglobulin E in them. [22]

In this paper, by reducing the effect of the alpha necrotizing factor, the amount of inflammation caused against the new SARS-CoV-19 virus is also reduced, thereby reducing the acute conditions and mortality. Alpha-necrotizing antifungal drugs include infliximab, Adalimumab, and etanercept. The mechanism of action of infliximab is that by binding to the alpha necrotizing factor, prevents it from binding to its receptor, thereby reducing the amount of interleukins 1, 6 and the alpha necrotizing factor and is used to reduce inflammation.

Alpha necrotizing factor: This inflammatory agent is produced from lymphocytes, lethal cells, macrophages, endothelial cells and astrocytes, smooth muscle cells and so on. The most important effect of this alpha necrosis factor is related to the immune system. This necrotizing factor causes endothelial cells to secrete the selectin molecule, and neutrophil cells and leucocytes can travel to the site of infection. This necrotizing factor has 2 glycoprotein receptors on the cell surface. Named TNFR1, TNFR2. The tendency of alpha necrotizing factor to its type one receptor is higher.

Initially, it was known as an anti-tumor factor, but today it has been linked to diseases such as cancer and neurological diseases. In addition, this factor secretes glycogen protein called fibrinogen. [23, 24]

Fibrinogen: is a glycoprotein that is secreted by the liver. It is one of the most important blood coagulation factors. In inflammatory conditions, under the influence of necrotizing factor, alpha secretion increases and causes clots in the tissue fluid of the affected area, and thus the tissue fluid loses its movement and stays in the site of inflammation, thereby, Separates the damaged tissue, that is the reason causes death in SARS-CoV-19 disease. In this way, the alpha necrosis factor is secreted from the mast cells and other cells mentioned, and then stimulates the secretion of fibrinogen, and this fibrinogen enters the fluid that fills the sac, and then causes clots, followed by fluid. Alveolus fillers lose their mobility and cannot move, so the Alveolus cannot normally exchange gas and cause problems for the person. [25]

In addition, alpha necrotizing factor is resistant in comparison with insulin and also interferes with insulin-sensitive tissues, so it can also be involved in the development of type 2 diabetes. Therefore, it can be concluded that this factor also causes obesity. [26]

In some heart patients, the cause of clogged arteries and valves is blood clots, which cause blood clots due to fibrinogen. The cause of fibrinogen secretion in some cases is the alpha necrosis factor. It can be concluded that increasing the amount of alpha necrosis factor can also cause a heart attack. [27]

This is why most patients with type 2 diabetes also have heart disease, because type 2 diabetes has a high blood necrosis factor. For this reason, these two groups of people are more at risk for acute SARS- CoV-19 disease, and of course, people with Asthma are also at risk due to high levels of immunoglobulin E. So, these antibodies E secrete histamine, then histamine triggers the inflammatory response. However, by binding histamine to its type 1 receptor, it triggers an anti-inflammatory response by inactivating an intracellular

enzyme called TACE, which removes the necrotizing factor from the cell surface and then enters the bloodstream. It can be connected to the alpha necrosis factor and prevents it from connecting to its main receiver. So histamine has both inflammatory and non-inflammatory properties, depending on which receptor it binds to.

From the above explanations, it can be concluded that by reducing this necrotizing factor of alpha or reducing its action, a big step can be taken against SARS-CoV-19. This alpha necrotizing factor is normally present in the blood as normal, and its presence is essential. What makes it harmful and dangerous is its high amount. This necrotizing factor of alpha increases in infectious conditions and in diseases such as Asthma, and in this disease, its amount is very high and causes tissue damage, so by reducing its effect, the amount of inflammation and response can be reduced .This alpha necrosis factor shows its effect when it binds to its receptors. The necrotizing factor has two receptors that are normally located on the cell surface, which the tendency of the alpha necrotizing factor to type1 receptor is greater.

Because the over-the-counter response is harmful, the body has anti-inflammatory responses against the inflammation. For example, it secretes anti-inflammatory factors such as interleukin 10, and for alpha necrotizing factor, it has a unique anti-inflammatory response to alpha necrosis factor. Thus, as mentioned earlier, the body produces a non-specific inflammatory response against the external agent, which secretes histamine. When histamine binds to its type 1 receptor, it activates an intracellular enzyme called TACE, by activating this enzyme, receptor type 1 isolates the alpha receptor necrotic factor from the cell surface and enters the bloodstream. As it enters the bloodstream, it binds to the alpha necrotizing factor and prevents the alpha receptor necrosis factor from binding to its main receptors. Because The alpha necrosis factor has not been able to bind to its receptor, therefore cannot show its effect, means it cannot cause inflammation. [28]

From the above, we found that increasing the amount of alpha-necrotizing factor in the blood makes the condition more difficult in SARS-CoV-19 disease. In this study, the main purpose is to reduce the effect of alpha necrosis factor by using its receptors. [29]

In this research, the method is in this way that in the first laboratory conditions, by giving histamine to laboratory animals, we cause the histamine in the animal's body to bind to its first type of receptor, and then histamine activates the TACE intracellular enzyme. The type 1 alpha necrotic factor is removed from the cell surface and enters the bloodstream. In this case, by extracting these receptors from the blood and injecting these receptors to the SARS-CoV-19 patients that we took from the blood of animals, we cause the alpha necrotizing factor, which is elevated in the bloodstream, to bind to these receptors and not bind to its main receptors, so it cannot show its effect (or the infliximab drug can also be used). In this way, we reduce inflammation and as a result we reduce mortality.

So, in fact, in this method, we first extracted the receptors and then injected them into the patients and then reduced the body's non-specific response, which is inflammation. Currently, the best way to deal with SARS-CoV-19 is to reduce the amount of inflammation because the virus has just been found and finding antiviral methods is a bit time consuming and difficult.

In this disease, the main defense system is against dedicated defense system, so in this method, we only weaken the non-specific immune system. Dedicated defense systems include B and T lymphocytes. B lymphocytes have two types of antigens. Protein antigens and non-protein antigens. B lymphocytes need to act alone to bind to non-protein antigens. They bind to antigens and secrete antibodies. They secrete antibodies but require T lymphocytes in the protein antigen.

Discussion and Conclusion

The main cause of death in people with SARS-CoV-19 disease is inflammation of the body itself, not the Covid-19 virus, so our goal here is to reduce the body's response and bring it to normal. In this disease, the methods used for treatment, such as, suppress the immune system. Current treatments include anti- interleukin 6 drugs and the use of hydroxychloroquine, an anti-malarial drug targeting interleukin-1. In this study, the goal is alpha necrosis factor (as a result, both interleukin 6 and interleukin 1) that in order to reduce its action, we use its own receptors (or Infliximab) to prevent this alpha necrotizing factor from its main receptor, which is located on the cell surface, that is, in this way, we reduce its effect as much as possible. To do this, in the laboratory conditions, we extract the first type of alpha necrotizing factor and inject it into SARS-CoV-19 patients, and reducing inflammation in the body and thus reducing mortality.

Another conclusion that can be drawn is that the reason why children are less likely to die is that they have low antibodies, and since this antibody is the cause of allergies, i.e. inflammation, it is low in children. So children are less at risk for death in this disease, but people with heart disease, diabetes or any chronic illnesses such as Asthma are at higher risk. In very severe cases, when the patient is dying, the target can be enlarged and the main cause of the inflammation can be targeted, and the main cause of the inflammation, the interleukin, can be targeted and reduced, which can be treated with XOLAIR. XOLAIR is an anti-pneumonia drug used to treat severe allergies in people over the age of 12, but it should also not be used simultaneously with allergy medications. It can also be used in acute conditions.

By injecting histamine into laboratory animals, histamine binds to its first receptor, h1, then activates the TACE intracellular enzyme, separates TNFR1 receptors from the cell surface, and then enters the bloodstream, where these TNFR proteins can be extracted and injected to the SARS-CoV-19 patients to reduce inflammation by binding to TNFalpha.

References

1. Sars-cov- THC. Systematic Comparison of Two Animal-to-Human Transmitted Human Coronaviruses: SARS-CoV-2 and SARS-CoV. 2014
2. Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic Transmission of SARS-CoV-2-Singapore. Morb Mortal Wkly Rep. 2020;69:411–5.
3. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: An overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. Pediatr Infect Dis J. 2020;39:355–68.
4. Zheng J. SARS-coV-2: An emerging coronavirus that causes a global threat. Int J Biol Sci. 2020;16:1678–85.
5. Chin AWH, Chu JTS, Perera MRA, Hui KPY, Yen H-L, Chan MCW, et al. Stability of SARS-CoV-2 in different environmental conditions. The Lancet Microbe. 2020;1:e10. doi:10.1016/s2666-5247(20)30003-3.
6. Fox RI. Mechanism of action of hydroxychloroquine as an antirheumatic drug. Semin Arthritis Rheum. 1993;23:82–91.
7. Cheng Y, Wong R, Soo YOY, Wong WS, Lee CK, Ng MHL, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. Eur J Clin Microbiol Infect Dis. 2005;24:44–6.
8. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U S A. 2020;117:9490–6. doi:10.1073/pnas.2004168117.
9. Patients L, Taylor D, Lindsay AC, Halcox JP. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med. 2020;:0–3.
10. Cheng VCC, Lau SKP, Woo PCY, Kwok YY. Severe acute respiratory syndrome coronavirus as an agent of emerging and reemerging infection. Clin Microbiol Rev. 2007;20:660–94.
11. D A Brian , R S Baric . Coronavirus Genome Structure And Replication. 2005;287:1-30
12. Ahmed SF, Quadeer AA, McKay MR. Preliminary identification of potential vaccine targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies. Viruses. 2020;12.
13. Lirong Z, Feng R, Mingxing H, Lijun L, Huitao H, Zhongsi H. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. 2020;382:1175–7.
14. Richardson SE, Tellier R, Mahony J. The laboratory diagnosis of severe acute respiratory syndrome: emerging laboratory tests for an emerging pathogen. Clin Biochem Rev. 2004;25:133–41.
15. Jordan RE, Adab P, Cheng KK. Covid-19: Risk factors for severe disease and death. BMJ. 2020;368 March:1–2
16. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med. 2020;46:586–90.
17. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020;581:215–20.
18. Yu J. Inflammatory mechanisms in the lung. J Inflamm Res. 2008;:1.
19. Libbey JE, Fujinami RS. Adaptive immune response to viral infections in the central nervous system. Handb Clin Neurol. 2014;123:225–47.
20. Punchard NA, Whelan CJ, Adcock I. The Journal of Inflammation. J Inflamm. 2004;1:1–4.
21. Amarasekera M. Asia Pacific allergyImmunoglobulin E in health and disease. Asia Pac Allergy. 2011;1:0–3.
22. Ruíz AAB. No 主観的健康感を中心とした在宅高齢者における健康関連指標に関する共分散構造分析Title. 2015;3:54–67.
23. Wen-Ming Chu . TUMOR NECROSIS FACTOR.Cancer Lett.2013 jan 28;328(2):222--225
24. Baugh JA, Bucala R. Mechanisms for modulating TNFα in immune and inflammatory disease. Curr Opin Drug Discov Dev. 2001;4:635–50.
25. Kattula S, Byrnes JR, Wolberg AS. Fibrinogen and Fibrin in Hemostasis and Thrombosis. Arterioscler Thromb Vasc Biol. 2017;37:e13–21.
26. Akash MSH, Rehman K, Liaqat A. Tumor Necrosis Factor-Alpha: Role in Development of Insulin Resistance and Pathogenesis of Type 2 Diabetes Mellitus. J Cell Biochem. 2018;119:105–10.
27. Dunlay SM, Weston SA, Redfield MM, Killian JM, Roger VL. Tumor necrosis factor-α and mortality in heart failure: A community study. Circulation. 2008;118:625–31.
28. Bahia MS, Silakari O. Tumor necrosis factor alpha converting enzyme: An encouraging target for various inflammatory disorders. Chem Biol Drug Des. 2010;75:415–43.
29. Strieter RM, Kunkel SL, Bone RC. Role of tumor necrosis factor-α in disease states and inflammation. Crit Care Med. 1993;21 10 SUPPL.