International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

IVIG (Immunoglobulin) as an Adjuvant Therapy in COVID-19

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Abstract

COVID-19 viral disease appeared in China in December 2019 and then spread around the world, affecting millions and causing the death of thousands of people. Its danger in simple and easy infection transmission methods. Some believe that it has moved from the bat to the human and its symptoms are high temperature, dry cough and difficulty breathing, and symptoms vary from person to person, as they may not appear on some and be severe in others. Laboratory, in COVID-19 the rate of D-dimer increase so we recommended using of Enoxaparin sodium to raise the level of liquidity in the blood, thereby reducing the chance of thrombosis and reducing the value of D-dimer. In COVID-19 also we find the PO2 decrease in arterial blood gas analysis, increase liver enzyme levels, increase ferritin value and decrease the No of lymphocyte. Low percentage of lymphocytes is one of the predictions for infection with COVID-19 virus. Lymphocytes originate from the bone marrow and include B cells, T cells, and natural killer cells. COVID-19 binds to lymphocyte receptors and destroys them. In this case, we recommend using immunoglobulin to maintain these cells as an adjuvant therapy in COVID-19.

Keywords: COVID-19; coronavirus; Immunoglobulin; lymphocytopenia; pneumonia.

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1. Introduction

COVID-19 viral disease appeared in China in December 2019 and then spread around the world, affecting millions and causing the death of thousands of people. Its danger in simple and easy infection transmission methods [1, 2]. Laboratory, in COVID-19 the rate of D-dimer increase so we recommended using of Enoxaparin sodium to raise the level of liquidity in the blood, thereby reducing the chance of thrombosis and reducing the value of D-dimer. In COVID-19 also we find the PO2 decrease in arterial blood gas analysis, increase liver enzyme levels, and increase ferritin value. The COVID-19 virus causes also decrease in the number of lymphocytes and causes lymphocytopenia [3]. Low percentage of lymphocytes is one of the predictions for infection with COVID-19 virus. Lymphocytes as type of WBCs, it so important immune system's cells against COVID-19. The Lymphocytes comes from the bone marrow and found in the blood and lymph tissue [4]. The normal ranges of lymphocytes in children less than 10 years old are almost twice that of adults and decrease as age increases. Lymphocyte levels changing according to a person's race, lifestyle habits, location, and gender. The normal range of lymphocyte in adults is between 1,000 and 4,800 lymphocytes in one microliter (µL) of blood. The normal range of lymphocyte in children is between 3,000 and 9,500 lymphocytes in one microliter µL of blood. The type of lymphocytes known as B lymphocytes (B Cells) and T lymphocytes (T Cells) and natural killer cells (NKC), The B cells and T cells are originating from stem cells in the marrow. The function of B cells is the formation of antibodies, B cells protein produced by the immune system to kill foreign substances called antigens, and each one of B cell is tuned to form one specific antibody, this antibody corresponds to an antigen, then, the antigen is marked for devastation, But T cells control the immune response to foreign substances, by the way of killing cells in the body that have been taken over by COVID-19 viruses. The 3rd type of lymphocyte is called as natural killer (NK) cells, Natural killer (NK) cells respond fastly to several foreign substances and are specialized in killing COVID-19 virus-infected cells [5, 6].

2. The possible reasons for lymphopenia in COVID-19 patients

- Lymphocytes carry ACE2 receptors for the COVID-19 virus, which makes them a clear target for it. They infected with this virus directly and the result is the death of lymphocytes [6, 7].
- The virus may cause acute lymphatic dysfunction by directly infecting the lymph organs such as the thymus and spleen [7].
- Inflammatory cytokines continued to be disordered, perhaps decrease the No of lymphocyte. Some of basic researches confirmed that tumor necrosis factor (TNF) α, interleukin (IL)-6 and other pro-inflammatory cytokines may be reason of lymphopenia [8].
- Lymphocytes frustration by metabolic molecules produced by metabolic disorders, like hyper lactic acidemia. The severe cases of COVID-19 patients had high blood lactic acid levels, which may prevent the spread of lymphocytes. Multiple mechanisms mentioned above or later may work together to cause lymphocytosis [9].

3. Immunoglobulin

Immunoglobulin treatment is called as (NHIG) normal human immunoglobulin, (NHIG) is the use of mixing of antibodies (immunoglobulin) to treat a number of health conditions that include immune thrombocytopenic purpura, primary immunodeficiency, chronic inflammatory demyelinating polyneuropathy, Kawasaki disease, Guillain-Barre syndrome, certain cases of HIV/AIDS and measles and in certain other infections when a more specific immunoglobulin is not available [10, 11]. No of specific immunoglobulin combinations are also available including for varicella infection, hepatitis B, tetanus, rabies, and Rh positive blood exposure [12, 13,14].

4. Mechanism of action of immunoglobulin

The right mechanism by which immunoglobulin treatment may curb harmful inflammation is multifactorial. It has been reported that immunoglobulin treatment can deny Fas-mediated cell death. Perhaps the most common theory is that the immunosuppressive effects of immunoglobulin therapy are mediated by binding to glycosylate in IgG [14, 15], and by binding to receptors on antigen presenting cells, IVIG can increase the expression of the inhibitory Fc receptor and shorten the half-life of self-interacting antibodies. Immunoglobulin therapy's ability to depend on preventing pathogenic immune responses through this mechanism is based on the presence of a sialylated glycan at position CH2-84.4 of IgG. In particular, de-sialylated preparations of immunoglobulin lose their therapeutic vigor and the anti-inflammatory impact of IVIG can be recapitulated by sialylated IgG1 Fc. There are many other proposed mechanisms of action and the actual initial targets of immunoglobulin therapy in autoimmune disease are still being clarified. Some suggested that immunoglobulin treatment may work through a multi-step model whereby the injected immunoglobulin first forms a type of immune complex in the patient. When these immune complexes are formed, they can interact with Fc receptors on dendritic cells that mediate anti-inflammatory leverages helping to reduce the severity of the autoimmune disease or inflammatory state, and some proposed mechanisms include the possibility that donor antibodies may bind directly with the abnormal host antibodies, stimulating their removal; the possibility that IgG induces the host's complement system, leading to promoted removal of all antibodies, including the harmful ones; and the ability of immunoglobulin to block the antibody receptors on immune cells (macrophages), leading to decreased damage by these cells, or regulation of macrophage phagocytosis. Indeed, it is becoming clearer that immunoglobulin can bind to a number of membrane receptors on T cells, B cells, and monocytes that are pertinent to auto reactivity and induction of tolerance to self [13, 14, 15]. A recent report stated that immunoglobulin application to activated T cells leads to their decreased ability to engage microglia. As a result of immunoglobulin treatment of T cells, the findings showed reduced levels of tumor necrosis factor-alpha and interleukin-10 in T cell-microglia co-culture. The results add to the understanding of how immunoglobulin may affect inflammation of the central nervous system in autoimmune inflammatory diseases [15].

5. Conclusion

IVIG (immunoglobulin) being can join to a number of receptors on T cells and B cells (lymphocyte) that are relevant to auto reactivity and induction of tolerance to self, being immunosuppressant, anti-inflammatory and it

can remove abnormal antibodies through complement system. We recommend IVIG as an adjuvant therapy in COVID19 management protocol.

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