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Special Article - COVID-19

Use of Iron Chelators to Reduce the Severity of COVID-19

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Short Communication

Iron is an essential factor for humans because of its essential role in immunity to help the body resist infection and inflammation by its role in activating macrophages that consider the first line of body defense against viral or bacterial attacks [1]. Additionally, iron is the main part of the hemoglobin component that is the main oxygen carrier for various body tissues [2]. Balanced iron levels promote immune response and general health. Still, high levels of iron do more harm to the body during inflammation and infection besides the transferrin receptor that can be used as an entrance to cells by viruses [3]. Iron chelators of different types such as (Deferoxamine, Deferiprone, Deferasirox) may help in preventing that by binding to excess iron and precipitating it to excreted in the urine. Also, part of the chelators back to the liver and bind to excess hepatic iron to be secreted in bile, these chelators also able to absorb accumulated iron in cardiac muscle cells directly [4].

Deferoxamine may cause significant toxicity (Ophthalmological and Auditory), but it is the only form of chelators that can be given SC and IV. Other types are available in oral form only. Deferiprone can cause agranulocytosis, neutropenia, and arthralgia; however, it is considered the most effective type in cardiac iron excretion [5].

Effects of iron chelators on COVID-19

Recent studies show that viruses (including family coronaviruses) require iron-containing enzymes to complete their replication. Besides, poor prognosis occurred in cases of hepatitis B/C (HBV/HCV) virus. However, treatment with iron chelators as deferiprone has shown that patients with Acquired Immunodeficiency Syndrome (AIDS) have increased their survival. Limiting iron thus constitutes a promising adjuvant strategy in the treatment of viral infection [6]. Increasing efficient hemoglobin and reducing iron both will improve patient condition through enhancement of tissue oxygenation (that is a leading cause for COVID-19 morbidity and mortality) and also through deprivation of the virus from iron essential for its replication [7].

Effect of erythropoietin (EPO) administration on critically ill COVID19 patients

A study was performed on an 80-year-old reported case of COVID-19, which, following treatment with recombinant human erythropoietin (rhEPO) due to extreme anemia, showed primarily unexplained rapid relief of symptoms and viral regression. During a 9-day course of therapy, rhEPO was administered at a dose of 300IU/kg divided into five doses of 4000 IU subcutaneous injections daily. Both the severity of anemia and the symptoms of the patients improved dramatically within eight days [8]. In addition to antivirals, rhEPO was administered due to his extreme anemia. After that, a very rapid response was observed in both anemia correction (from Hb: 6.7 to Hb: 9) and COVID-19 symptom relief, considering his age and previous medical history, which could not be elaborated merely as a result of anemia correction.

Erythropoietin (EPO) is a hormone/cytokine primarily released by the kidneys via the hypoxia-inducible factor-2 as its primary transcription factor, which increases red cell mass by inhibiting RBC precursor apoptosis. The EPO has other beneficial cytoprotective effects, including anti-ischemic, regenerative, and antiapoptotic effects on various tissues, including the lung, kidney and cardiac muscles, nervous system, retina, pancreas, and endothelial cells. Protective effects are carried out by a particular receptor; EPOR-βcR following injuries and in critically ill patients [9,10].

Does COVID19 affect the iron level?

A study was performed on 99 patients confirmed with COVID-19, and the report reflected the abnormal phenomenon of hemoglobin-related biochemical indices in patients. This report demonstrates that the hemoglobin and neutrophil counts of most patients have decreased, and the index values of serum ferritin, erythrocyte sedimentation rate, C-reactive protein, albumin, and lactate dehydrogenase of many patients increase significantly [11]. This trace means that the patient's hemoglobin is declining, and the heme is rising, and the body will accumulate too many harmful iron ions, which will cause inflammation in the body and increase C-reactive protein and albumin. Cells respond to stress due to inflammation by producing high amounts of serum ferritin to bind iron-free ions to minimize damage.

Hemoglobin composed of four subunits, 2-α and 2-β, and each subunit has an iron-bound heme; the structure without iron is called porphyrin [12]. When iron is divalent, hemoglobin can release carbon dioxide and capture oxygen atoms in alveolar cells, and iron is oxidized to trivalent. When hemoglobin is accessible in the body to the other cells through the blood, it can release oxygen atoms and capture carbon dioxide, and iron is reduced to divalent. Therefore, it is believed that combining viral proteins and porphyrins will cause a series of human pathological reactions, such as a decrease in hemoglobin.This study has shown that the novel coronavirus proteins (such as ORF8 and surface glycoproteins) have a function of combining with porphyrin to form a complex. At the same time (ORF1ab, ORF10, ORF3a) co-ordinately attack heme to dissociate the iron to form the porphyrin. This mechanism of the virus inhibited the normal metabolic pathway of heme and caused people to show symptoms of the disease [13].

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References

1. Rosário C, Zandman-Goddard G, Meyron-Holtz EG, D'Cruz DP, Shoenfeld Y. The hyperferritinemic syndrome: macrophage activation syndrome, Still's disease, septic shock and catastrophic antiphospholipid syndrome. BMC medicine. 2013; 11: 185.

2. Chen W, Dailey HA, Paw BH. Ferrochelatase forms an oligomeric complex with mitoferrin-1 and Abcb10 for erythroid heme biosynthesis. Blood. 2010; 116: 628-630.

3. Cureton DK, Harbison CE, Cocucci E, Parrish CR, Kirchhausen T. Limited transferrin receptor clustering allows rapid diffusion of canine parvovirus into clathrin endocytic structures. J Virol. 2012; 86: 5330-5340.

4. Cui HJ, He HY, Yang AL, Zhou HJ, Wang C, Luo JK, et al. Efficacy of deferoxamine in animal models of intracerebral hemorrhage: a systematic review and stratified meta-analysis. PloS one. 2015; 10.

5. Bauchner H, Fontanarosa PB, Golub RM. Evaluation of the Trial to Assess Chelation Therapy (TACT): the scientific process, peer review, and editorial scrutiny. JAMA. 2013; 309: 1291-1292.

6. Liu W, Zhang S, Nekhai S, Liu S. Depriving Iron Supply to the Virus Represents a Promising Adjuvant Therapeutic Against Viral Survival. Curr Clin Microbiol Rep. 2020: 1-7.

7. Geier MR, Geier DA. Respiratory Conditions in Coronavirus Disease 2019 (COVID-19): Important Considerations Regarding Novel Treatment Strategies to Reduce mortality. Med Hypothes. 2020: 109760.

8. Hadadi A, Mortezazadeh M, Kolahdouzan K, Alavian G. Does recombinant human Erythropoietin administration in critically ill COVID-19 patients have miraculous therapeutic effects? J Med Virol. 2020.

9. Nekoui A, Blaise G. Erythropoietin and nonhematopoietic effects. Am J Med Sci. 2017; 353: 76-81.

10. French C. Erythropoietin in critical illness and trauma. Crit Care Clin. 2019; 35: 277-287.

11. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395: 507-513.

12. Kazazian Jr HH, Woodhead AP. Hemoglobin A synthesis in the developing fetus. New Eng J Med. 1973; 289: 58-62.

13. Liu W, Li H. COVID-19 Disease: ORF8 and Surface Glycoprotein Inhibit Heme Metabolism by Binding to Porphyrin. ChemRxiv. 2020.