



Can iron chelation as an adjunct treatment of COVID-19 improve the clinical outcome?

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Dear Editor;

A recent bioinformatic study showed that one of the important pathogenic effects of coronavirus disease 2019 (COVID-19) is through the direct damage of haemoglobin molecules by the novel coronavirus (SARS-CoV-2) [1]. The haemoglobin molecule consists of four globulin subunits: two beta chains and two alpha chains [1]. Each subunit attaches to heme which has two main components: iron and porphyrin [1]. SARS-CoV-2 attacks one of the beta chains of the haemoglobin which leads to dissociation of iron from heme [1]. This leads to increased free iron level in the body, which could explain why most patients with COVID-19 have very high ferritin level [2]. Although the result of this study has not been fully validated, it might explain multiple aspects of the pathogenesis of COVID-19. Increased iron level in the body generates reactive oxygen species which causes oxidative stress and damage to the lung, leading to subsequent lung fibrosis and decline in the lung function [3, 4]. There is evidence shows that iron overload increases viral replication, which might have a role in the severity of the infection [5]. Infection with SARS-CoV-2 causes diffuse endothelial inflammation which leads to widespread microvascular thrombosis, organ ischemia and multi-organ failure [6]. Interestingly, an *in vitro* study showed that iron had a similar effect by inducing the release of endothelial inflammatory cytokines, such as IL-6 [7]. Through its iron chelation effect, deferoxamine reduces iron availability in serum and body tissue which could prevent lung injury and fibrosis following COVID-19 infection. An *in vitro* study showed that deferoxamine decreased the level of viral replication of some RNA viruses, such as HIV-1. Moreover, when it was combined with an antiviral drug, it led to a synergistic effect on reducing the viral replication cycle [8]. This might

suggest that deferoxamine could be beneficial in adjunction with anti-viral drugs to treat Covid-19. In addition, deferoxamine decreased the level of IL-6 and endothelial inflammation *in vitro*, which could reduce the severity of COVID-19 infection as endothelial inflammation is one of the important factors which leads to multi-organ damage and failure [7]. Interestingly, deferoxamine has immunomodulatory effect. It improved the immune response against enteroviral infection in infected mice by inducing upregulation of B cells and increasing the level of neutralising antibody titre [9]. Therefore, deferoxamine could ameliorate the pathogenic effect of COVID-19 caused by viral-induced lymphopenia.

In conclusion, iron chelation drugs, such as deferoxamine, can be used as a supportive treatment to improve the clinical outcome and to reduce the severity of COVID-19 infection. However, multiple randomised control studies are required to test their efficacy and safety.

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Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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