

Treatment of COVID-19 Pneumonia using Hydroxychloroquine, Azithromycin and Tocilizumab

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INTRODUCTION

The global pandemic caused by a novel coronavirus [severe acute respiratory syndrome (SARS)-CoV-2] and its disease, COVID-19, has led to infection in over 15.8 million individuals and more than 640,000 deaths as of July 25, 2020. As there are no approved treatments, management of COVID-19 is largely supportive. One empirical treatment for COVID-19 which has received attention is hydroxychloroquine, an antimalarial drug repurposed in recognition of its anti-inflammatory properties in the treatment of autoimmune conditions. Hydroxychloroquine its analogue, chloroquine, demonstrate suppression of SARS-CoV-2 replication in vitro, with hydroxychloroquine demonstrating greater potency. Studies from the original SARS-CoV virus suggest a mechanism of action involving impairment of the terminal glycosylation of angiotensin converting enzyme 2 (ACE2), inhibition of SARS-CoV viral entry, and rapid elevation of endosomal pH that prevents endosome-mediated viral entry. The immunomodulatory effects are thought to be due to the accumulation of the drug in lymphocytes and macrophages leading to reduction of proinflammatory cytokines, including type I interferons, tumor necrosis factor alpha, and interleukin-6. Other anti-inflammatory effects may be related to inhibition of signaling pathways.

Recently tocilizumab has been introduced to treat patients with COVID-19 and researchers are investigating further the efficacy of this drug for different are patients. Hydroxychloroquine has been touted as a potential COVID-19 treatment. Tocilizumab, an inhibitor of IL-6, has also been proposed as a treatment of critically ill patients. According to a protocol-based treatment algorithm, among hospitalized patients, use of hydroxychloroquine alone and in combination with azithromycin was associated with a significant reduction in hospital mortality compared to not receiving hydroxychloroquine.

Two known zoonotic coronaviruses, SARS-CoV and MERS-CoV, have been reported to damage the respiratory tract and cause severe outbreaks in the past decade. Common symptoms at the onset of the disease include fever, cough, myalgia, fatigue, dyspnea and diarrhea. Most of the patients developed pneumonia, which

can rapidly worsen into respiratory failure and develop Acute Respiratory Distress Syndrome. Higher susceptibility and mortality was observed in elderly and patients with low immune function.

Researchers are discovering new drugs to treat this emerging virus. So far about 30 drugs have been introduced to treat patients with COVID-19 such as lopinavir, ritonavir, oseltamivir, and ganciclovir. There is a classification of used drugs to treat respiratory infections from COVID-19 and stratified into three categories: immune system enhancement, Chloroquine phosphate, Antiviral components. Tocilizumab (a humanized anti-IL-6 receptor antibody) is one of drugs discussed for the treatment of these patients.

Tocilizumab is prescribed to treat moderate to severe active arthritis in adults, Giant cell arthritis, Polyarticular juvenile idiopathic arthritis and cytokine release syndrome in patients 2 years of age older with active disease. The recommended dose of Tocilizumab is 4–8 mg/kg administered as a single 60-minute intravenous infusion every 4 weeks. Individuals with active infections should not be treated with Tocilizumab. There are no adequate studies of Tocilizumab in the pregnant women. Also, it is not known whether Tocilizumab is excreted in breast milk.

Tocilizumab inhibits IL-6- receptor, witch as described above is a key cytokine leading to an inflammatory storm which may result in increased alveolar-capillary blood-gas exchange dysfunction, especially impaired oxygen diffusion, and eventually lead to pulmonary fibrosis and organ failure. Based on some reports, tocilizumab can be a suitable and effective drug for COVID-19 patients. Tocilizumab demonstrated a trend association towards reduced mortality among ICU patients.

Tocilizumab may have a positive effect on improving immune damaging, lung functional injuries and arterial oxygen saturation. Researchers, who had the successful experience of using this drug for treating inflammation lungs diseases, hope it will make effective and promising treatment to improve lung tissue inflammation in patients with fatal COVID-19 virus. However, further accurate clinical trial studies are needed to determine its efficacy in patients with specific characteristics such as age, level of IL-6, and different clinical symptoms.

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Received: February 12, 2021; **Accepted:** February 26, 2021; **Published:** March 05, 2021

Citation: Shetty P (2021) Treatment of COVID-19 Pneumonia using Hydroxychloroquine, Azithromycin and Tocilizumab. J Clin Res Bioeth. 12:e124

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