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Review Article

# Effect of Hydroxychloroquine on COVID-19 Patients with Cardiac Disease: A Mini Review of the Literature

**Bader Fatani[1*], Abdulaziz Abdullah Alabood[1]**
[1]Department of medicine and dentistry, King Saud University, Riyadh, Saudi Arabia

***Corresponding Author**
**Bader Fatani**
Department of medicine and dentistry, King Saud University, Riyadh, Saudi Arabia

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**Abstract:** COVID-19 or SARS-COV-2 is a serious viral illness that has spread all over the world, this disease belongs to the group of coronaviruses. Like other coronaviruses it was transmitted to humans by animals, which is said to be an outbreak from a fish market in Wuhan (China) in December 2019. World Health Organization (WHO) has reported that COVID-19 is a pandemic on March 11, 2020 [2]. For the management of spreading of this disease, some countries forced a complete lockdown. Social distancing, hand hygiene, and isolation were considered largely effective for COVID-19 control [2]. Many medications have been reported for the treatment of Covid-19 disease. One of these medications is hydroxychloroquine/chloroquine which has gained a lot of popularity during the pandemic. This study aims to review the effect of HCQ and CQ on cardiovascular patients with COVID-19 and estimate the potential adverse effects.

**Keywords:** Covid-19, Hydroxychloroquine, Cardiac patients, Pandemic.



## INTRODUCTION

COVID-19 can spread through droplets and can be transmitted to the respiratory system by sneezing, coughing, handshaking, etc. Patients with COVID-19 can be classified from asymptomatic to critical cases which could lead to a serious respiratory failure. Elderly people, immunocompromised patients, and those with chronic diseases are at high risk of getting a fatal respiratory failure. High risk is associated with patients with an underlying cardiovascular disease [7]. Acute myocardial infarction, myocarditis, and heart failure has been reported in patients with COVID-19 [8]. This study aims to review the effect of HCQ and CQ on cardiovascular patients with COVID-19 and estimate the potential adverse effects.

### SARS-CoV-2

SARS-CoV-2 enters the cells by using the angiotensin-converting enzyme 2 (ACE2). ACE2 is a membrane protein that is extremely found in the enterocytes, lungs, and the heart and has the ability to convert angiotensin II to angiotensin-(1–7). Angiotensin-(1–7) is a vasodilator peptide that is responsible for lung protection [1]. Animal studies showed that SARS-CoV-2 can decrease the regulation of ACE2 expression, and ease the infiltration of neutrophils, which can cause further lung and myocardial damage. Many reports showed an elevation in the serum creatine kinase (CK) and lactate dehydrogenase (LDH) levels in all hospitalized COVID-19 patients [3]. Viral infections which can cause myocardial inflammation, metabolic dysfunction, and activation of the sympathetic nervous system are considered a possible factor in cardiac arrhythmia [3]. National Health Commission of China reported that some patients stated primarily CV symptoms, such as chest tightness and palpitations during the initial outbreak [3]. Adverse events from generally safe drug can be possible due to cardiac injury from COVID-19 infection [5].

### Medications used in treatment of SARS-CoV-2

A lot of medications have been introduced for the treatment of COVID-19 disease including

hydroxychloroquine, dexamethasone, remdesivir, and anti-inflammatory agents, and protease inhibitors. However, no specific therapy has been completely approved for the treatment of COVID-19. A data from China have reported that cardiovascular patients are at high risk of morbidity and mortality from COVID-19. A drug-drug interaction is possible since some of the cardiac patients are already under treatment using various kind of medications.

**Mechanism of action of hydroxychloroquine**

The use of hydroxychloroquine/chloroquine has been introduced globally for the treatment of COVID-19, because of its immunomodulatory effects which can inhibit viral fusion [1]. The use of hydroxychloroquine on the cardiovascular patient should be very cautious, with its ability to cause QT interval prolongation and possibly a lethal cardiac arrhythmia in some patients [2]. Hydroxychloroquine is a 4-amino-quinoline that is used widely for the treatment of related inflammatory and dermatological conditions and specific autoimmune disorders like rheumatoid arthritis and lupus [2,4]. This drug is now observed for the treatment of the COVID-19 infection because of its ability to inhibit ACE2 receptor-mediated entry of the COVID-19 virus due to different actions such as inhibiting lysosomal activity, increasing the intra-vesicular pH, affecting antigen processing, etc [2]. HCQ and CQ are well absorbed. In 2-3.5 hours, the serum reaches its peak concentrations, with a half-life of 22 to 45 days [4]. Measurement of QTc interval using ECG is recommended before the administration HCQ in all hospitalized COVID-19 patients. Patients can be classified into three groups (A, B, C), group A are the low-risk patients with a normal QTc interval, group B are moderate-risk patients with a little prolonged QTc interval up to 500ms, group C are the high-risk patients with a prolonged QTc interval more than 500ms [2].

**Side effects of hydroxychloroquine**

Several side effects have been associated with the use of HCQ and CQ in the long-term, such as retinal toxicity and cardiomyopathy. long-term use revealed a wide frequency of cardiac toxicity such as irreversible cardiomyopathy and conduction disorders [5]. However, with short-term use, a markedly lower risk of retinopathy and cardiomyopathy. While some concerns are related to hypoglycemia, QT prolongation, GI disturbance with an increasing risk of Torsade de Pointes (TdP) [4, 5]. These drugs should not be used for patients who have a previous history of TdP or those with congenital long QT syndrome. Both HCQ and CQ are proarrhythmic and have an anti-arrhythmic property [5]. The American Heart Association has declared these drugs as agents that can cause direct myocardial toxicity due to accumulation of glycogen and phospholipids, and lysosomal dysfunction [5, 7]. A prior study reported clinical advantages of HCQ and CQ for COVID-19 patients, resulting in decreasing in viral shedding, pneumonia severity, and hospitalization period [5]. Side effects have been reported with the use of these drugs include nausea, pruritus, and headache. However, uncommon side effects are also noticed but with serious potential harms such as idiosyncratic hypersensitivity reactions, hypoglycemia, neuropsychiatric effects, and drug-drug interactions [6]. High doses of HCQ and CQ have been reported to be associated with cardiac arrest and atrioventricular blocks [7]. HCQ and CQ also inhibit CYP2D6, which could increase the risk of bradycardia, atrioventricular block, beta-blocker exposure, and PR interval prolongation [8].

## CONCLUSION

Immunomodulatory effects of hydroxychloroquine that is associated with inhibition of viral fusion has made this medication more superior in terms of treatment of COVID-19 disease. However, their side effects such as retinal toxicity, cardiomyopathy, hypoglycemia, QT prolongation, GI disturbance and increasing risk of Torsade de Pointes has made this drug poorer in terms of treatment for COVID-19 patients.

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