Chloroquine and Hydroxychloroquine are Available Treatment Options to Fight with COVID-19: A Literature Review

Abstract:

The pandemic Covid-19 disease is caused by SARS-CoV-2, a virus belonging to the corona virus family. At present there is no vaccine or drug approved by FDA to treat Covid-19 patients. The significant mortality rate and extreme fast spreading of disease in the community make researchers to invent possibleqalialali_75@gmail.comqalialali_75@gmail.com therapeutic inventions a global priority. Recent studies suggested that Chloroquine (CQ) and Hydroxychloroquine (HCQ) can be used for the treatment of Covid-19 patients. In-vitro tests suggest CQ and HCQ have good efficiency towards SARS-CoV-2 virus. In this report, we have reviewed latest literature information about CQ and HCQ drugs to use for the treatment of this pandemic.

Introduction:

The epidemic of carona virus was declared in December 2019 in Wuhan city of China. This is caused by a new type of virus called SARS-CoV-2. On 7th January, 2020, there was an official announcement from Chinese health officials related to discovery of carona virus. By this time the new virus SARS-CoV-2 affected 11 million people in the Wuhan metropolis city. Later on 30th January 2020 the World Health Organization (WHO) officially declared public health emergency of worldwide concern. Later WHO gave name to disease caused by the new virus as Covid-19. Due to the exponential increase of virus effected patients globally the WHO upgraded the situation epidemic to pandemic on 11th March 2020 [1,2].

In Covid-19 patients, the SARS-CoV-2 virus main target is lower respiratory tract which cause cold, cough and throat infections. Serious symptoms such as difficulty in breathing or shortness of breath and chest pain appeared in the Covid-19 patients. On average it takes 5-6 days to observe the symptoms from when someone is infected with the virus; however it can take up to 14 days. It is notable that adult patients with Covid-19 in early stage, observed with a keen decrease in CD^{4+} and CD^{8+} T-cell subsets [3,4]. Accordingly the patients suffered with acute respiratory distress syndrome for 7 to 10 days after infected with Covid-19 due to the swift growth of virus in the body. The virus replication in the body also increase the pro-inflammatory cytokines as well as chemokine response and inflammatory cell infiltrates [4,5]. The vague incubation period of SARS-CoV-2 oscillating between 2 and 14 days make it very difficult to diagnose early and control the community infection as well as to initiate treatment in early stages [5,6].

Epidemiology of carona virus:

After an epidemic breakout in China in January of 2020 the epidemic status has been advanced globally with the rapid growth in South Korea, Singapore and Japan. Soon after we noticed rapid growth of Covid-19 affected patients in Italy and Iran. In the above countries it is witnessed as a community transmission with the persons came from China. The number of Covid-19 patients reached to peak after two months the virus appeared in China. In March first week the Chinese officials announced that the number of new cases are decreasing sharply in country and government reopened the public places. However by that time all the European countries are badly affected with the corona virus [1], precisely Italy, Span and France countries. By the March 16th the WHO announced almost as many cases appeared in China are appeared worldwide with 81,077 Covid-19 patients in China and 86,438 patients rest of the world which includes 143 countries. The WHO announced that as of May 11th 2020, there were 4,088,848 confirmed Covid-19 cases and 283,153 deaths.

Treatment options:

The center of Disease control and prevention (CDC) on 21st March 2020 in a public document informed that there is no vaccine or specific drugs for SARS-CoV-2 [7]. The rapid outbreak of this virus worldwide and the distressing more number of deaths encouraged the scientific community accelerates the invention of all possible and innovative controlling methods of this disease[8]. Several interventional treatment options come up for controlling Covid-19 disease with indefinite efficiency and safety measures [9]. Recent studies recommended a well known anti malarial drug Chloroquine (CQ) and its derivative Hydroxychloroquine (HCQ) for the treatment of Covid-19 patients. These FDA approved drugs are used for the treatment of malaria and specific inflammatory conditions at present. In this epidemic situation WHO lists CQ and HCQ as essential medicines, meaning it should be have affordable price and available through all times. Both CQ and HCQ drugs showed in-vitro activity against SARS-CoV, SARS-CoV-2, and other corona viruses. It is reported that the HCQ is having relatively high potency than CQ against SARS-CoV-2 virus [13-14].

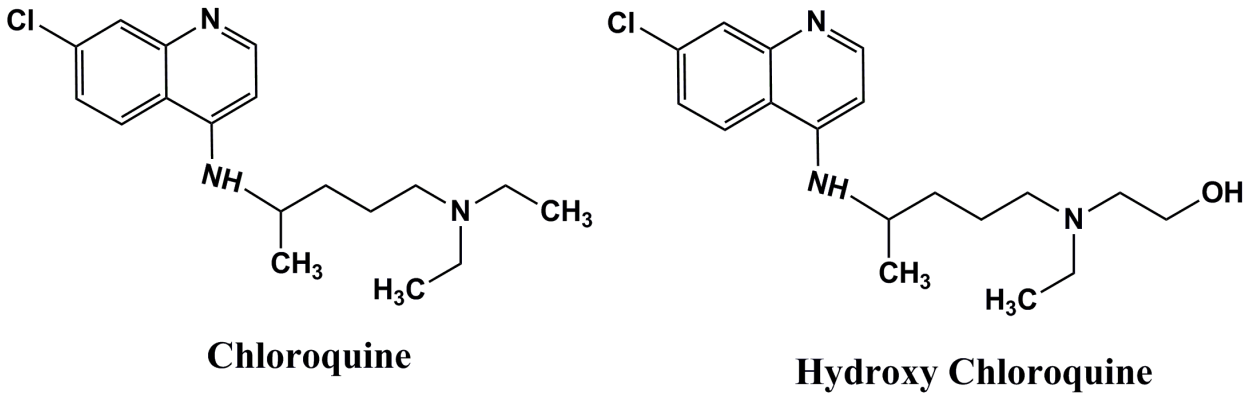

Figure 1: The chemical structures of Chloroquine and Hydroxychloroquine

Chloroquine and hydroxychloroquine antiviral activities against COVID-19

The CQ and HCQ have chemical structure similarities and they are approved by FDA for anti malarial and anti rheumatic treatment. For the literature these drugs also known for their antiviral activity with various mechanisms [15-17]. In this epidemic outbreak, CQ and HCQ have been proposed as anti-SARS-CoV-2 drugs as CQ inhibited the virus in cell culture experiments [18-19] and they also emerge to decrease virus growth in Covid-19 patients in an open label non-randomized trail [20]. These drugs are showed excellent anti-viral properties in-vitro, with its effect on early stage of virus replication through inhibiting virus-endosome fusion, by increasing endosomal pH [21]. SARS-CoVs were shown to be able to enter target cells through pH-dependent mechanism, where lower pH of the lysosome leads to fusion of the viral and endosomal membranes resulting in viral particle uncoating and subsequent release of viral nucleic acid into the cytoplasm [22]. The CQ also damages the post translational alterations of viral proteins by interfering with prolytic processes [23]. CQ also shows inhibition of glycosylation through inhibiting sugar modifying enzymes or glycosyltransferases [24]. It's known that CQ molecule known to inhibit entry of SARS-CoV into cells by interfering with the glycosylation of its cellular receptor angiotensin converting enzyme 2 receptor (ACE2). Recent literature reveals that SARS-CoV-2 also enters into the human body through ACE2 receptor. This suggests that a possible similar effect of CQ on SARS-CoV-2 at this viral replication step [25]. On the other hand, because of its anti-inflammatory activity CQ and HCQ drugs are used to treat multiple diseases where inflammation is effect such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and osteoarthritis [26]. In this regard, the central symptom of COVID-19, the virus causes an acute inflammation in the lungs can be an advantageous effect of CQ and HCQ due to its anti-inflammatory activity. It is encouraging, the difference of treating inflammation of COVID-19 vs SLE or RA is the presence of an infectious agent i.e., SARS-CoV-2.

Efficacy and Toxicity

The CQ drug in-vitro tests on Vero E6 cells infected by SARS-CoV-2 showing the EC_{90} of 6.90 μM, is became a promising choice of using CQ in clinical treatment of SARS-CoV-2 as completely off-label [27]. On the other hand, HCQ drug is significantly more potent than CQ was observed in-vitro results as the EC_{50} values of HCQ is 0.72 μM and CQ is with 5.47 μM, and HCQ has lower efficiency for drug-drug interactions than CQ. Further, physiologically based pharmacokinetic models demonstrate that hydroxychloroquine sulfate is significant superior (5 days in advance) to Chloroquine phosphate in inhibiting SARS-CoV-2 in vitro [28].

The most common adverse effects of CQ and HCQ are gastrointestinal symptoms such as nausea, vomiting and abdominal discomfort [29], and uncommonly worrisome fulminant hepatic failure [30], toxic epidermal necrolysis (TEN) [31] and cardiotoxicity that could manifest with QT abnormality [32-34]. Nevertheless, over the years CQ and HCQ have maintained a good safety profile when used in several chronic diseases such as RA and SLE. Despite some animal experiments suggesting that HCQ is probably less toxic than CQ, there is a lack of high quality evidence from clinical trials supporting this claim [35-38]. These toxicities could be related to the very long half-life and the large volume of distribution of both drugs.

Conclusion:

As researchers are working in the direction of finding a specific drugs and vaccines, the CQ and HCQ became life savior drugs for the pandemic SARS-CoV-2 in recent times. The *in-vitro* anti viral activity tests suggests that the HCQ is more potent, prominent and safe in comparison with CQ. The lack of high quality clinical trials, the dosage quantity may be varies and it may be higher in comparison with regular dose of systemic lupus and rheumatoid arthritis. In the view of the present condition the prescribed doses and the side effects of the CQ and HCQ should shared with in health professionals to minimize the risk of usage, and a deeper research.