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BENEFIT OVER RISK OF USING CHLOROQUINE AND HYDROXYCHLOROQUINE IN COVID – 19 PATIENTS

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ABSTRACT

The increasing mortality rate across the world lead the medical professionals to find alternatives to curve down the deceased rate and the spread the novel coronavirus pandemic however the potential vaccination for the said virus might need some more time to develop. Recently many studies were conducted on the benefit of chloroquine and hydroxychloroquine in the prevention and management of COVID-19. Moreover the evidence of safety profile of these drugs in COVID-19 patients is very weak due to lack of clinical trials. However, most studies did not address the clinically associated side effects and toxicity associated with both the drugs. This article provides a brief note on its potential side effects that might arise during the medical therapy of the COVID-19 patients.

KEYWORDS: coronavirus, chloroquine, hydroxychloroquine, COVID-19.

INTRODUCTION

It was in the late year of 2019 where a latest global outbreak of unknown etiology was firstly reported to the World Health Organization on 31st December about a cluster of pneumonia originated in china precisely from the animal and meat market in the city of Wuhan. Later it was identified and reported that the causative organism for the global outbreak was β-coronavirus and was named as 2019-novel coronavirus (2019-nCoV) on 12 January 2020 by World Health Organization (WHO). The International Committee later proposed to rename the 2019-novel coronavirus (2019-nCoV) as severe acute respiratory syndrome coronavirus (SARS-CoV-2) on 11 February 2020. This novel coronavirus created havoc that lead to

spread to every nook and corner of the globe within a very little spare of time.[1] The emergence of the spread of the disease is increasing day by day which reported to have 13, 47, 803 confirmed cases worldwide with having 2, 27, 807 recovered patients including 58, 937 death toll. The scenario of the disease prevailing in India is not different from the rest of the world with 2, 902 confirmed cases including 3981 active cases, 324 recovery and 114 death as reported on 7th April, 2020 at 09:00 hr.[2] The increasing rate of death has now become a big concern for the states for an immediate medical therapy to curb and control the mortality rate without any specific drug. The WHO recommended only clinical management which includes the supportive care of supplementing oxygen therapy and ventilator support to the severe complication of the patients.[3]

However handful of other antiretroviral drugs are used as prophylaxis to the infected COVID-19 patients to decrease the viral load which uses Oseltemavir[4], protease inhibitor drug includes Lopinavir, Ritonavir[5], Remdesivir which are under the trail for their efficacy.[6, 7] Recently the US-FDA allowed the use of chloroquine and hydroxychloroquine to treat the COVID-19 pandemic as an emergency use authorization that marked the first EUA for a drug related to COVID-19 without a relevant data about the safety profile for mass usage.[8] Therefore it is urgent necessary to know the safety and toxicity profile of chloroquine and hydroxychloroquine for the severe acute respiratory syndrome coronavirus (SARS-CoV-2) patients.[9]

GEMONIC CHARACTERIZATION OF 2019 NOVEL CORONAVIRUS

Novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) is a single – stranded, polyadenylated, positive sense RNA genome with 26 – 32 Kb in length.[10, 19] The family of Coronaviridae is divided four genera: alpha-coronavirus, beta-coronavirus, gamma-coronavirus and delta-coronavirus. However, there are six human coronaviruses (HCoVs) has been isolated and identified, which includes the alpha - CoVs HCoVs - NL63 and HCoVs - 229E and the beta - CoVs HCoVs - OC43, HCoVs - HKU1, Middle East respiratory syndrome - CoV (MERS - CoV).and severe acute respiratory syndrome-CoV (SARS - CoV).[11] These coronaviruses possess spike glycoprotein on their surfaces that play an important role for its binding to the receptor domain and these spike protein are also responsible for the trans- membrane fusion in the host cell in which the S1 spike glycoprotein is responsible for its binding to the receptor on the contrary S2 spike glycoprotein helps in the fusion with the cell membrane.[12] However, it is pertinent to note that the receptor binding

properties of novel SARS-CoV-2 was similar to SARS-CoV which led to the hypothesis that the newly immerged β-coronavirus uses angiotensin-converting enzyme 2 (ACE2) as a cell receptor.[10, 12]

USE OF CHLOROQUINE AND HYDROXYCHLOROQUINE IN SARS-CoV-2 PATIENTS

Chloroquine is one of the 4-aminoquinoline antimalarial drugs and hydroxychloroquine is the hydroxyl derivative of chloroquine used as rapidly acting antiprotozoal drugs for suppressive and acute treatment of malaria, it also possess modest DMARD activity. They are indicated for treatment of rheumatoid arthritis and systemic lupus erythematosus for its immunomodulatory action.[13] Usage of chloroquine has been surged in SARS-CoV-2 due to its antiviral activity. Chloroquine is weakly basic in nature which accumulates in the acidic vacuoles and has the property to change the pH of the cell membrane to slightly basic thus prevents the entry of the virus into the host cell and prevents antigen processing and MHC class II-mediated autoantigen presentation to T cells and ultimately inhibits the replication of virus and acts a fusion inhibitor.[14, 18] This antimicrobial drug interferes with the lysosomal activity inside the cell which destabilizes the cell membrame and interferes with the signaling pathway of the cell moreover this drug also has the property to inhibit the nucleic acid replication, release of progeny of the virus and the transcriptional activity.[15] Thus prevents the glycosylation of spike proteins present on the virus surface with the angiotensin-converting enzyme (ACE) 2 receptor leading to decrease in the viral load.[16,17]

SAFETY AND TOXICITY OF CHLOROQUINE AND HYDROXYCHLOROQUINE

Chloroquine and hydroxychloroquine possess good oral, intramuscular and subcutaneous absorption with large volumn of distribution and extremely sequestered in the liver, spleen, kidney, lungs and has the capacity to pass the blood brain barrier (BBB) and in the spinal cord. It moderately binds with the plasma protein and undergoes hepatic biotransformation and slowly excreted in urine.[20]

Chloroquine and its metabolite has high affinity for melanin and the nuclear chromatin, concentrated in the various tissues of the body and selectively accumulates in the retina that is responsible for the ocular toxicity and moreover, the drug also requires a close cardiac monitoring while treating COVID-19 associated pneumonia due to its ability to prolong QTc interval, which may lead to fatal arrhythmia and torsade de points in COVID – 19 patients.[16]

The toxicity of chloroquine is low with mild side effects includes anorexia, nausea, vomiting, headache, itching, myalgia, and arthralgia, anemia, epigastric pain and blurred vision. Parenteral administration of chloroquine and hydroxychloroquine can cause hypotension, convulsions, cardiac depression, arrhythmias and CNS toxicity to the patients. However prolonged use of these medication may cause loss of vision due to retinal damage due to deposition of the drug in the retina that might lead to loss of vision, photo allergy, myopathy, mental disturbances, rashes and phototoxicity can occur to the patients on long term use moreover upon administration in pregnancy this drug has shown some teratogenic effects.[21, 22, 23]

CONCLUSION

Chloroquine being the board spectrum antimicrobial drug extensively used as a prophylactic and for the treatment of mild to complicated malaria its antiviral activity drew a lot of attention for the treatment of severe acute respiratory syndrome coronavirus (SARS-CoV-2). Several studies suggests that chloroquine and its derivative were effective in reducing the viral load in-vivo.[24]

However, regular blood testing must be conducted on the patient to check the development of leucopenia, thrombocytopenia, renal and hepatic dysfunction and monitoring of serum electrolyte balance moreover cardiac functions were to be examined on a regular interval for the development fatal arrhythmia and torsade de points.[25]

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