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RESEARCH ARTICLE

HCQS IN MANAGEMENT OF COVID-19: HOAX OR BOON

Abhimanyu Sharma¹, Prachi Garhia², Pranav Kapoor³, Anunay Gupta⁴ and Jyoti Ahlawat⁵

1. SRA Oral & Maxillofacial Surgery ESIC Dental College, New Delhi.
2. BDS ESIC Dental College, New Delhi.
3. MDS Orthodontics, Professor, ESIC Dental College.
4. PG Resident Orthodontics, PGI Dental College, Rohtak.
5. MDS Endodontics, Senior Consultant, New Delhi.

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Abstract

Scientist around the world are still working day and night to find out a definite vaccine against the Pandemic COVID-19. Many trials had their peaks and failure but there is a drug which was constantly resonating all this while - Hydroxychloroquine. We performed a systematic review of the PubMed, Google Scholar and EMBASE database to find out information on the efficacy of hydroxychloroquine in patients infected with SARS CoV-2. Our efforts are revealing a promising role of this drug, if not as a definitive measure, then as a supportive and prophylactic medicine to reduce the impact of SARS CoV-2. We believe that along with the search for vaccine against SARS CoV-2, more specific trials should take place to determine the role of Hydroxychloroquine in dealing with the same.

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Introduction:-

In December 2019, the world witnessed the outbreak of an emerging disease (COVID-19) due to a novel coronavirus (named SARS-CoV-2 later), which started in Wuhan (Hubei province), China, but rapidly spread to other parts of the world.¹⁻² WHO declared the COVID-19 as a public health emergency of international concern on 30th January, 2020, and as a pandemic on 11th March, 2020. By 12th May, 2020, around 4,88,848 confirmed cases with 283,153 deaths had been reported by the World Health Organisation.³

SARS-CoV-2 is a novel strain of the coronavirus family that has not been identified in human beings prior to this. Studies suggest that this particular strain might have emerged from the zoonotic cycle, further spreading rapidly via human to human transmission.⁴ So far, respiratory droplets have been deemed as the main route of transmission, along with aerial droplets and close contact.⁵ Direct transmission occurs when an infected person sneezes or coughs, and the released droplets are inhaled by somebody who is in close proximity, thus entering his/her respiratory system. On the other hand, the mode of transmission is referred to as indirect when the infected droplets are accidentally touched by a healthy person, who then proceeds to touch his/her nose, mouth or eyes, and in the process, infects himself/herself. It has been studied that the virus can survive on inanimate objects for a period of hours to days. In some recent studies, live SARS-CoV-2 has been detected in the stool sample of patients, which justifies the gastrointestinal symptoms, probable recurrence, and transmission of the virus via the feco-oral route.⁶ However, it is not yet proven that the consumption of virus-contaminated food might lead to infection and transmission.⁷

Corresponding Author:- Abhimanyu Sharma

Address:- SRA Oral & Maxillofacial Surgery ESIC Dental College, New Delhi.

The initial symptoms include fatigue, low grade intermittent fever, dry cough, shortness of breath, which usually tends to improve with early detection and conservative treatment. In a few cases, especially immunocompromised patients and the population belonging to the extreme age group range, it can worsen, causing dyspnoea and productive cough, further progressing to complications such as bilateral pneumonia, ARDS, sepsis and septic shock, secondary infections, etc.⁸ While majority of the affected individuals tend to be asymptomatic, approximately 15% of the patients have been seen to contract the severe form of the disease.

Till date, there is no pharmacological treatment that has been approved by the regulatory agencies for the treatment of this particular infection. However, a few in-vitro studies have suggested that chloroquine and its analog, hydroxychloroquine, can inhibit SARS-CoV-2 transmission.⁹⁻¹¹ We performed a systematic review of the PubMed, Google Scholar and EMBASE database ranging back as far as the earliest publications to 10th April, 2020, to find out information on the efficacy of hydroxychloroquine in patients infected with SARS CoV-2. The databases were screened independently by three authors, followed by extraction of useful information. A systematic review protocol was not set due to the limited availability of resources on this particular topic.

Results:-

The preliminary database search resulted in over 200 sources, which were narrowed down to six, following screening of titles and abstracts. These included one book series, one observational study, one in-vitro experiment, one clinical trial, and two systematic reviews.

Discussion:-

Towards the end of 2019, a new disease emerged in Wuhan city, Hubei province, China, which caused pneumonia-like symptoms and lung fibrosis.⁸ Within the next few months, this highly contagious virus rapidly spread to multiple countries all over the world, wreaking havoc. Till date, no drug has been approved for the treatment and prophylaxis of this infection. According to the World Health Organisation (WHO), there is not enough evidence that can be extracted from randomised clinical trials to advocate an anti-nCoV therapy for suspected or confirmed cases. However a number of FDA-approved drugs that are being tested have shown promising antiviral activity in cell cultures as well as animal models.¹²

Chloroquine, and its analog hydroxychloroquine, have been used since decades to treat malaria as well as autoimmune conditions such as lupus and rheumatoid arthritis. While both of these drugs have the same mechanism of action, a more tolerable safety profile makes hydroxychloroquine a better choice. In addition, it is a cheap and easily available drug. In-vitro studies have shown that hydroxychloroquine can inhibit SARS-CoV-2 transmission via alkalisation of intracellular phagolysosome, preventing virion fusion and uncoating, thus, interfering with the spread of the virus.¹³⁻¹⁴ Apart from its antiviral effect, its immunomodulatory properties might also play a role in patients with cytokine storm. In some patients, the immune response to the SARS-CoV-2 virus results in an increase in the levels of cytokines IL-6 and IL-10¹⁵⁻¹⁶, which may eventually result in a cytokine storm, followed by multi-organ failure and potentially death. Hydroxychloroquine can help suppress the increase in immune factors¹⁷⁻¹⁸, and prevent the progression to a life-threatening state.

According to a study done in Beijing, comparing the in-vitro antiviral activities of chloroquine and hydroxychloroquine, the latter was found to be more potent in inhibiting SARS CoV-2. The researchers recommended a loading dose of 400 mg of oral hydroxychloroquine sulphate twice daily, followed by a maintenance dose of 200 mg twice daily for 4 days. It has been seen that hydroxychloroquine decreases the replication of the virus particles in a concentration-dependent manner.¹⁹

The results of a clinical trial conducted across various centres in South France suggested that hydroxychloroquine showed efficiency in clearing the nasopharyngeal carriage of the virus particles in majority of the COVID-19 patients within three to six days. 200 mg of oral hydroxychloroquine sulphate was administered three times per day during ten days. This study also suggested the synergistic effect of administering azithromycin along with hydroxychloroquine as this combination would act both as an antiviral therapy, as well as prevent any bacterial super-infections.²⁰

In a second Chinese trial done on 62 patients, Chen et al showed that hydroxychloroquine administration resulted in a shorter recovery period as compared to the placebo group.²¹

While these studies do seem to portray hydroxychloroquine as a promising drug treatment for COVID-19 patients, they have their own limitations, ranging from small sample size, selection bias, and patient dropout to poorly described inclusion and exclusion criteria to absence of long-term follow-ups. It is imperative to conduct clinical trials on a large-scale with proper criteria, randomisation, placebo group allocation, and long-term follow-ups.

Conclusion:-

With the current exponential rise in cases worldwide, it is the need of the hour to find an effective drug to treat the symptomatic cases as well as reduce the duration of virus carriage so as to limit community spread. Hydroxychloroquine seems to be a promising pharmacological agent for the treatment of SARS CoV-2 virus owing to its superior antiviral and immunomodulatory properties, in addition to being easily available and affordable. However, it is crucial to have future trials with an aim to elucidate the role of hydroxychloroquine in treatment of critically ill COVID-19 patients.

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