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Letter to the Editor

COVID-19: Wait for a novel drug or act with the age old drug – Do we have a choice?



With the limited options available, countries like India completely rely upon the World Health Organization (WHO) guidelines and supportive management in treating the SARSCoV2 infection/COVID-19 [1]. The premier research institute of India, the Indian Council For Medical Research (ICMR) has rolled out its protocol or the standard operating procedure (SOP) for the collection and testing of the samples of suspected cases of SARS-CoV2 [2]. In a recent notification, the ICMR has confirmed the isolation of 11 isolates from the patients of SARS-CoV2 [3]. They have commented that it will take another one and a half to two years to develop a vaccine against the novel coronavirus which will require the mandatory field trials.

In a recent scientific report, the scientists from China, the epicenter of COVID-19, have tried their hands on the age-old antimalarial drug, chloroquine in the treatment of COVID-19 [4]. Recently, the doctors from one of the best medical college hospitals in Rajasthan, India have treated a COVID-19 patient, a tourist from Italy with 3 groups of drugs: the anti-HIV drugs Ritonavir and Lopinavir, the anti-influenza drug, Oseltamivir, and the anti-malarial drug, the Chloroquine [5]. According to the doctors, the patient has been tested negative after the treatment with their protocol. The patient's husband, who also tested positive for coronavirus is under non-invasive ventilatory support is also being treated with the same regimen and he is stable according to the treating physicians. The delay in the recovery of this patient was suspected to be due to the already existing lung pathology.

The Government of India is taking all the efforts in keeping the situation under control by spreading awareness on COVID-19 through mass communication to the public. The government is also keen on finding out an effective treatment modality to treat the COVID-19 patients. Hence the option of using the already available drugs like lopinavir, ritonavir, oseltamivir, and chloroquine would be the best choice. On 13th March 2020, The ICMR has released a protocol for public health emergency which includes lopinavir and ritonavir [6]. They have given a set of inclusion criteria to whom this regimen can be used, the inclusion criteria include high-risk patients, such as patients who are >60 years of age, patients with hypertension, diabetes mellitus, renal failure, chronic lung disease, and immunocompromised persons. These high-risk patients have been included in the inclusion criteria as these are the patients who may succumb to the COVID-19 due to their co-morbid conditions. We also know the fact that this regimen cannot be generalized to treat all the patients of COVID-19 without proper

scientific evidence. The antiviral properties of ritonavir, lopinavir, oseltamivir, and chloroquine are already known with scientific evidences. The antiviral properties are proved in vitro from many studies starting long back from 1969 to till recent times [7–11].

Chloroquine, the age-old anti-malarial drug possesses anti-viral properties. Many in vitro and in vivo studies have shown various mechanisms by which chloroquine exerts antiviral activity on various viruses like the Zika virus, avian leucosis virus, the HIV-1, H5N1 virus by changing the endosomal pH, inhibiting the viral gene expression, changing the glycosylation pattern of HIV-1: (HIV-1) gp120 envelope and inhibit the replication of the HIV virus in CD 4+T cells, inhibiting the autophagy and reducing the alveolar epithelial damage in the lungs of avian influenza H5N1 mice, inhibiting the Zika virus-induced autophagy. Animal experiments have shown that the vertical transmission of Zika virus from the mother to the fetus can be cut off by Chloroquine. In a study conducted by Keyaerts et al. in 2004 (7), it was observed that chloroquine inhibits the replication of SARS-CoV in Vero E6 cells. In a recent study by Xu et al. in January 2020 [12], it was observed that the SARS-CoV2 and the SARS-CoV shared an identical structural identity and similar Van der Waals and electrostatic properties.

Vincent et al. [13] stresses that chloroquine can even be considered as prophylaxis for people traveling to the affected area due to the easy availability and cost-effectiveness of chloroquine and may be considered to treat and prevent coronavirus infection. In addition to the anti-viral activity, chloroquine also possesses an anti-inflammatory property which can be used to reduce the virus-induced inflammation [14]. More than 10 clinical trials are registered and are underway in China and other parts of world to prove the efficacy of chloroquine in the treatment of COVID-19 [15]. A recent study in China that included more than 100 patients demonstrated that “chloroquine was superior to the control treatment in inhibiting the exacerbation of pneumonia, improving the lung Imaging findings, promoting a virus-negative conversion and shortening the disease course” [16].

Chloroquine has certain advantages to itself being an age-old drug. First and foremost is that it is almost available everywhere in the world, making it easy to acquire. Secondly, it is very cost-effective. Thirdly the adverse drug reaction profile of the drug is well known so that the drug–drug interactions or drug–disease (other co-morbid conditions) interactions may be avoided.

Another drug, Hydroxychloroquine, a 4 aminoquinoline, has also given promising results in the treatment of COVID-19. The US-

FDA has issued an Emergency Use Authorisation (EUA) on March 28, 2020. According to the EUA, chloroquine, and Hydroxychloroquine are to be donated to the Strategic National Stockpile (SNS) to be distributed to hospitals where they can be used to treat certain COVID-19 patients [17]. In a non-randomized study conducted by Gautret et al., a combination of hydroxychloroquine and Azithromycin has caused a significant reduction or disappearance of the viral load in COVID-19 patients [18]. Another prospective study from China with 30 patients randomly allocated to hydroxychloroquine with 400 mg daily for 5 days in addition to other supportive care, injection interferon beta and available antivirals vs standard care alone. Even though there was no statistical difference in virologic clearance a trend was seen in hydroxychloroquine with support with “86.7% vs. 93.3% viral clearance” [19]. More than 50 clinical trials are registered and are underway in China and other parts of world to prove the efficacy of hydroxychloroquine in the treatment of COVID-19 and its complication [20]. The ICMR has rolled out a protocol for using Hydroxychloroquine as a prophylaxis in the Health care workers (HCW) and the close contacts of the suspected or COVID-19 positive patients [21].

To conclude, with the daily increase in the number of newly detected COVID-19 cases and the number of deaths increasing at a faster pace, waiting for the newer drug with questionable efficacy in different races seems to be unethical. Drugs with known efficacy and toxicity profile will be a good strategy in developing countries. So a combination of antiviral, antimalarial and anti-flu drugs will be a good strategy until the newer drugs are developed. Today's off label maybe tomorrow's alternate drug of choice. These drugs, the chloroquine, and hydroxychloroquine are not without their own adverse effects. Hence, vigilance should be mandatory in using this drug for treatment purposes of confirmed cases of COVID-19. Misuse as a prophylactic drug will create massive failure of these drugs for their respective indication they have been introduced especially for Chloroquine and Hydroxychloroquine.

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