LETTER TO THE EDITOR

World War against COVID-19: How strong is our armamentarium?

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Dear Editor,

As the Coronavirus disease (COVID-19) pandemic continues its rampage all over the globe, it turns out that, it is nothing short of a world war declared by SARS-CoV-2 against the human race. Apart from being a monumental threat to global health, the pandemic has also seriously impacted the economy of most nations.

The prevention strategies against COVID-19 are limited to quarantine, isolation, and infection-control measures and management choices are limited for those who become ill. With no vaccine and efficient treatment option available, the current need of the hour is a specific 'magic bullet', which can optimally treat the infected, decrease the viral shedding and ward off subsequent transmission.

Scientists all over the world are racing against time to come up with strategies to combat this exponentially spreading disease. In the interest of time, repurposing of drugs that are already approved for use and with known safety profiles is considered the smart strategy rather than identifying and evaluating a new drug molecule from scratch. There are several clinical trials underway all over the world wherein, more than twelve treatment options are being evaluated.

A nucleotide analogue prodrug, remdesivir, previously evaluated against Ebola, Severe Acute Respiratory Syndrome (SARS-1) and Middle East Respiratory Syndrome (MERS) viruses has been used on hundreds of patients in the United States of America (USA), Japan and Europe on 'compassionate basis' and reportedly shown benefits.[1] Preliminary results from a National Institute of Health (NIH) sponsored clinical trial in USA have indicated faster recovery and survival benefits among COVID-19 patients who received remdesivir.[2] Further evidence-based results are awaited from various ongoing clinical trials.

A combination of lopinavir-ritonavir, a protease inhibitor drug used in treatment of human immunodeficiency virus (HIV) infection, is being evaluated in various clinical trials, though a recent study involving 199 confirmed COVID-19 cases in China found no difference in the clinical outcome when compared to standard care alone.[3]

Chloroquine and hydroxychloroquine, affordable and easily available drugs used for treating malaria and other autoimmune conditions have received wide attention based on the promising results from various *in vitro* studies and smaller clinical trials. An open label non-randomised control trial from France, evaluating hydroxychloroquine along with azithromycin has reported significant reduction in viral load in COVID-19 patients.[4] However, there have been concerns on the side effects of chloroquine, hydroxychloroquine and azithromycin and increased risk of association with cardiac death.

With increasing evidences from several studies indicating a 'cytokine storm' with release of interleukin-6 (IL-6), IL-1, IL-12, tumour necrosis factor-alpha and other immunological mediators in the pathogenesis of COVID-19, IL-6 inhibitors such as sarilumab and tocilizumab are being evaluated in various trials.[5] Passive antibody administration through transfusion of convalescent plasma has been used successfully as a treatment option during the outbreaks of coronaviruses like SARS-1 and MERS. Early and limited data from China have indicated radiological resolution, reduction in viral loads and improved survival upon transfusion of convalescent plasma to COVID-19 patients.[6]

Considering the need for speed and scale in the clinical trials to combat COVID-19, World Health Organization (WHO) has launched an international clinical trial known as 'Solidarity'. The Solidarity trial, working together with over 100 countries, evaluates four treatment options including remdesivir, lopinavir/ritonavir, lopinavir/ritonavir combined with interferon beta-1a and chloroquine/hydroxychloroquine against standard of care to rapidly assess their relative effectiveness against COVID-19. While randomised clinical trials normally take years to design and conduct, the WHO expects that this trial will reduce the time taken by 80%.[7] by the collective effort of enrolling patients in one single randomised trial to facilitate rapid comparison of treatment options worldwide. In addition, this strategy also overcomes the risk of multiple small trials not generating the strong evidence needed to determine the relative effectiveness of potential treatments.

With all the concerted efforts of scientists worldwide, hope we can effectively build up and fortify our armamentarium with more treatment options to efficiently combat this pandemic.

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