



Role of Antivirals in the Management of COVID-19

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The current coronavirus disease 2019 (COVID-19) is a major threat to the human civilization and poses several challenges ahead [1]. It has affected almost every country in the world and for the past fifteen months has led to huge suffering and loss of human lives. It not only has broken the back of the health care system of our country but also led to several deaths of many health care workers [2]. As of May 02, 2021, there were more than 15 million confirmed cases of COVID-19 with more than 3 million deaths. Although most of the cases are asymptomatic or have mild clinical symptoms, 20% of the hospitalized patients require intensive care unit (ICU) admission, resulting in tremendous burden on the health care system.

At present in the market, there are a lot of drugs that are being used for the treatment of COVID-19 [3]. Most of these drugs are used only after a positive RT-PCR report done for diagnosis of COVID-19 [4]. The use of these drugs on a prophylactic basis is strictly not recommended in any situation. Amidst the confusion regarding the management of the disease and when to start what drug in which stage of the disease, a rapid assessment of the currently available antiviral drugs is crucial at this juncture. At this given moment, there are more than eighty antiviral drugs available and approved for treating human viral infections. About 50% of these are used to treat HIV infection with the rest against other viral infections like influenza A and B, cytomegalovirus (CMV) and Ebola virus.

Several antiviral drugs have been under trial and are being used based on their ability to block or inhibit the various biochemical events and components in the replication cycle of the coronavirus. They include the spike protein, proteolytic enzymes and the RNA dependent RNA polymerase.

Among the various antivirals available, the Reverse transcriptase inhibitors are the most widely used. These drugs target the reverse transcription step by blocking the RdRp and therefore preventing viral replication. Remdesivir, Favipiravir and Ribavirin are the common drugs of this category. Favipiravir was first approved in 2014 in Japan to be used against non-complicated influenza infections but developed wide attention for COVID-19 treatment (mild and moderate cases) due to its large anti-viral spectrum. Studies have shown that it shortens the viral clearance time by stopping the multiplication of the virus and thus speeds up the recovery process. It is given orally at 1800 mg BD for 1st day followed by 800 mg BD for next 6 days. While prescribing drug-drug interactions must be taken into consideration. One more drug that has been in the news for all the reasons be it right or wrong is Remdesivir. The cost of this drug has reached skyrocketing prices and people are in long lines for purchasing this drug. This exponential rise in the prices of this drug is mainly due to the stocking up of this drug by medical stores and other individuals involved in black marketing. It was labelled as the wonder drug for COVID-19, but as per the latest guidelines issued by the Ministry of Health and Family welfare its use has to be approved by a medical professional and only in a hospital setting with requirement of supplemental oxygen. The recommended dose is 200 mg IV on day 1 followed by 100 mg IV OD for next four days. WHO solidarity trial which recruited 11,266 adults in 30 countries concluded that none of the drugs including Remdesivir and Lopinavir ritonavir were of any benefit as indicated by overall mortality, initiation of ventilation or hospitalization duration [5]. This led to phasing out of use of HCQ and lopinavir-ritonavir but the ACTT-1 trial showed that use of Remdesivir in hospitalized patients led to shortening of the time to recovery in adult patients [6].

The third drug is Ribavirin has been used in combination with either IFN alpha or lopinavir-ritonavir. It can be administered orally or intravenously.

Besides the above, some fusion inhibitors have also been approved for emergency use in Singapore and China. These inhibit the fusion process during the entry of the virus into the host cells. Umifenovir and Baricitinib are the two drugs which have shown promising results in some cases. They have been used to treat pneumonia due to SARS-CoV-2 in COVID-19 patients. The last group of drugs that are under investigation are the protease inhibitors like lopinavir, darunavir and atazanavir. These drugs are being used in combinations and the most common of them is lopinavir-ritonavir in a fixed dose. This combination therapy has got emergency use approval for COVID-19 in USA, Japan, Singapore, Italy and China. Darunavir-ritonavir combination has got approval for use in Italy also. In conclusion although most of these antiviral drugs have not been approved by FDA, we sincerely hope that some of these drugs can help us in this fight against the deadly coronavirus and save precious human lives.

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