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COVID-19: therapeutics and their toxicities

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The COVID-19 pandemic has presented an unprecedented public health and critical care challenges worldwide. Every day there seems to be a new "magic bullet" drug therapy in the news headlines and another pre-print of a drug trial fast-tracked into publication. The death and disability from COVID-19, combined with the lack of approved treatments, have created an unmet need for efficacious therapies.

As researchers and pharmaceutical companies race to develop vaccines and antivirals, some have turned to remedies with little to no supporting evidence. This article will discuss some therapeutic options against SAR-CoV-2 to understand the mechanism and toxicity of each agent.

What are the side effects of hydroxychloroquine?

Chloroquine and hydroxychloroquine have been used as antimalarials and for rheumatic disease treatment for many years with much success. They have been used in the setting of COVID-19 because they inhibit endosomal acidification required for virus-host cell fusion. In overdose, these drugs can cause

- hypotension
- hypokalaemia
- QRS and QT prolongation
- atrioventricular block
- arrhythmias
- Coma.

What are the adverse effects of Azithromycin?

Azithromycin is a macrolide antibiotic that has been used in conjunction with hydroxychloroquine for the management of COVID. Azithromycin and chloroquine are both known to prolong the QT interval. However, the ventricular tachycardia episodes were not due to Torsades des Pointes, in which patients are at increased risk with prolonged QT.

Does ivermectin have side effects?

Ivermectin is an anti-parasitic agent used to treat conditions such as pinworm, threadworm, whipworm infection, head lice, and lymphatic filariasis. Recently, there has been intense media interest in a study showing in vitro inhibition of COVID-19 with ivermectin.

Some side effects that may be associated with ivermectin include:

- painful joints or muscles
- unusual tiredness or weakness
- skin rash or itch
- headache
- nausea, vomiting, stomach discomfort
- dizziness
- swelling of the face or the legs
- Worsening asthma.

What are the side effects of remdesivir?

Remdesivir has been used previously to treat Ebola and has recently been prescribed to a small cohort study of COVID-19 patients. Side effects noted included elevated aminotransferase enzymes, diarrhea, rash, and renal impairment.

What are the adverse effects of lopinavir/ritonavir?

The lopinavir/ritonavir combination has shown in vitro activity against severe acute respiratory syndrome (SARS) previously. Side effects include gastrointestinal upset and liver injury. In the setting of overdose, lactic acidosis renal injury, central nervous system depression,

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seizures, and cardiac arrhythmias have been reported previously

Does tocilizumab have side effects?

The cytokine storm,as a result of COVID-19, can result in severe multi-organ dysfunction and death. Interleukin-6 (IL-6) plays a key role in cytokine release syndrome. Tocilizumab is a recombinant monoclonal antibody used against IL-6 and has previously been used to treated rheumatoid arthritis. Side effects with therapeutic use include headache, elevated liver enzymes, myelosuppression, hemorrhage and pancreatitis, and convulsions.

What are the side effects of Nitazoxanide?

Nitazoxanide, traditionally an antihelminthic agent, has broad antiviral activity and a relatively favorable safety profile. Nitazoxanide has demonstrated in vitro antiviral activity against MERS and SARS-CoV-2. Although in-vitro studies indicate that there might be a potential role of Nitazoxanide in the management of COVID-19, there is no clear evidence that it might be useful in the clinical setting. It is generally well-tolerated, and side effects include gastrointestinal disturbances, transaminitis, elevated creatinine, and enlarged salivary glands

What are the adverse effects of Favipiravir?

The drug gets converted to its active form by host enzymes and has exhibited considerable activity in influenza. In a small clinical trial of COVID-19 patients, when compared to another potential drug, arbidol, it showed a faster clinical recovery rate at day seven and a more effectively reduced incidence of fever and cough. The dosing used in the study was 1600 mg twice daily on the first day and 600 mg twice daily on day 2 to day 14. Side effects include raised serum uric acid levels, psychiatric symptoms, and gastrointestinal disturbances.

Mention the side effects of Niclosamide?

Niclosamide is a chlorinated salicylamide used for the treatment of infection with trematodes. Niclosamide has potential activity against coronaviruses based on in vitro studies alone, but there is a lack of data for the efficacy of this drug on SARS-CoV-2. Use of Niclosamide is associated with mild and infrequent side effects that include gastrointestinal disturbances, malaise, pruritus, and lightheadedness.

Conclusion:

The data on these drugs are increasing every day. It is tempting to try these drugs in the name of safety or ease of availability. Some initial studies showed benefit in early viral clearance. Subsequent studies failed to show such benefits. However, their effectiveness in early COVID is debatable. Till the time the data on these drugs come from well-conducted clinical trials are available, judicious and well-informed use is the need of the hour.

Further Reading:

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