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Editorial

Drug Drug Interaction Risk in COVID-19 Management – The Issue to be Addressed

At present the world is facing the wrath of COVID-19 pandemic and its post COVID-19 complications. Many patients are elderly and thus more prone to morbidity due to various comorbid factors. Moreover, these patients are exposed to many medicines and for this there is a strong probability of drug drug interactions in these patients .As we know that many repurposed drugs like ivermectin ,chloroquine ,remdesivir ,dexamethasone ,monoclonal antibodies and more to add have been the arsenals to treat COVID-19 clinicians involved in the management of COVID-19 must not ignore the importance of drug drug interactions issues. They must compile, as a component of good clinical practice, a current list of all the medications taken by the patients. Though all drug drug interactions (DDIs) are not clinically significant knowing the importance of implications of DDIs in the management of COVID-19 would help clinicians to identify the avoidable adverse effects of drugs prescribed.

COVID-19 patients' immune response plays pivotal role in the pathogenesis with cytokine reaching the peak in severe cases. This hyperinflammatory state sparks significant imbalances in transporters and drug metabolic enzymes, and subsequent alteration of drug pharmacokinetics resulting in unexpected therapeutic response. The present scenario has accounted for the requirement for therapeutic opportunities to relive and overcome this pandemic. Despite the diminishing developments of COVID-19, there is no drug still approved to have significant effects with no side effect on the treatment for COVID-19 patients. Based on the evidence, many antiviral and anti-inflammatory drugs have been authorized by the Food and Drug Administration (FDA) to treat the COVID-19 patients even though not knowing the possible drug-drug interactions (DDI). Remdesivir, favipiravir, and molnupiravir are deemed the most hopeful antiviral agents by improving infected patient's health. Dexamethasone is the first known steroid medicine that saved the lives of seriously ill patients. Monoclonal antibodies are also being used. A recent review paper summarizes medication updates to treat COVID-19 patients in an inflammatory state and their interaction with drug transporters and drug-metabolizing enzymes. It gives an opinion on the potential DDI that may permit the individualization of these drugs, thereby enhancing the safety and efficacy[1].

Another recent review paper pointed out the possibilities of risk of drug interaction of mentioned drug in tackling COVID-19. The inflammatory response enforces changes in the expression and activity of transporters and drug metabolizing enzymes (DMEs). Disposition of medicines used to treat COVID-19 infection involves drug metabolism by Cytochrome P450 enzymes (CYPs) and drug transported by ABC('ATP-Binding Cassette') and solute carrier (SLC) transporters. However, it is already known that ABC and SLC transporters play a central role in the disposition of mostly antiviral drugs and can participate in many drug-drug interactions. Most importantly, the involvement of CYPs in used drugs in COVID-19 infection, drug-drug interaction has been comprehensively known, but some drugs are still unknown. That's why in COVID-19 conditions, inflammatory responses play a crucial role in disease-drug or drug-drug interactions. Alteration in the transporters and DMEs can lead to changes in the pharmacokinetic parameters of the drug used. Hence, inflammation might play an essential role in drug efficacy and

toxicity. The risk of drug interactions should not be prohibited since they are frequently manageable and convenient. Lopinavir/ritonavir (LPV/RTV) is being used in combination with other drugs. HCQ (hydroxychloroquine) in combinations with azithromycin and with LPV/RTV has been used in COVID-19 patients. These medications have been classified as having a risk of developing torsades de points (TdP). Moderate to severe QTc prolongation was observed during these pharmacological treatments. The ATV-RTV (atazanavir /ritonavir)has shown new options among clinically approved drugs and should be considered an effective treatment option. Another combination of remdesivir with baricitinib has shown severe side effects even though this combination has shown promise for COVID-19 with accelerating clinical status improvement. The consumption of a single drug may possibly not be more effective but, during co-medication of multiple medications, the risk of drug interaction are increased[2,3].

To assist clinicians in identifying risks associated with the combined use of two drugs, drug-interaction books and searchable drug-interaction databases are available. These resources exhibit varying degrees of sophistication and accuracy, and both include some interactions that have never been validated by controlled clinical trials. The potential of drug-drug inter-action or disease-drug interaction is an important consideration when identifying optimal treatment regimens for individual patients[4]. Therefore, the clinicians dealing CVOID -19 patients must not show any sign of complacency on DDIs importance or it might spell disaster for patient's health.

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References

1. Kumar D, et al . Disease-drug and drug-drug interaction in COVID-19: Risk and assessment. Biomed Pharmacother . 2021 Jul; 139.
2. Zequn Z, Yujia W, Dingding Q, Jiangfang L. Off-label use of chloroquine, hydroxychloroquine, azithromycin and lopinavir/ritonavir in COVID-19 risks prolonging the QT interval by targeting the hERG channel Eur J Pharmacol. 2021 Feb 15;893:173813.
3. Carlotta Sciaccaluga et al; COVID-19 and the burning issue of drug interaction: never forget the ECG; Postgrad Med J . 2021 Mar;97(1145):180-184.
4. Kenneth Bachmann. Pharmacology Principles and Practice2009; 303-325.

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