Drug interactions: a review of the unseen danger of experimental COVID-19 therapies

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As global health services respond to the coronavirus pandemic, many prescribers are turning to experimental drugs. This review aims to assess the risk of drug-drug interactions in the severely ill COVID-19 patient. Experimental therapies were identified by searching ClinicalTrials.gov for 'COVID-19', '2019-nCoV', '2019 novel coronavirus' and 'SARS-CoV-2'. The last search was performed on 30 June 2020. Herbal medicines, blood-derived products and in vitro studies were excluded. We identified comorbidities by searching PubMed for the MeSH terms 'COVID-19', 'Comorbidity' and 'Epidemiological Factors'. Potential drug-drug interactions were evaluated according to known pharmacokinetics, overlapping toxicities and QT risk. Drug-drug interactions were graded GREEN and YELLOW: no clinically significant interaction; AMBER: caution; RED: serious risk. A total of 2378 records were retrieved from ClinicalTrials.gov, which yielded 249 drugs that met inclusion criteria. Thirteen primary compounds were screened against 512 comedications. A full database of these interactions is available at www.covid19-druginteractions.org. Experimental therapies for COVID-19 present a risk of drug-drug interactions, with lopinavir/ritonavir (10% RED, 41% AMBER; mainly a perpetrator of pharmacokinetic interactions but also risk of QT prolongation particularly when given with concomitant drugs that can prolong QT), chloroquine and hydroxychloroquine (both 7% RED and 27% AMBER, victims of some interactions due to metabolic profile but also perpetrators of QT prolongation) posing the greatest risk. With management, these risks can be mitigated. We have published a drug-drug interaction resource to facilitate medication review for the critically ill patient.
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