Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Psychosomatic Research 135 (2020) 110159

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores

Letter to the editor

Drug treatment of SARS-Cov2: Potential effects in patients with substance use disorders (SUD)

ARTICLE INFO

Keywords:
SARS-CoV2
Treatment
Substance use disorders

Severe acute respiratory syndrome- Coronavirus 2 (SARS-CoV2) has presented an unprecedented challenge of finding therapeutic agents. Presently hydroxychloroquine (HCQ), lopinavir-ritonavir combination (LR), remdesivir, and favipiravir are candidate medications. Patients with substance use disorder (SUD) are especially susceptible to develop COVID-19 owing to underlying comorbidities, immune-suppression, and socio-economic circumstances of drug use [1]. Moreover, the SARS-CoV2 pandemic has met with a pre-existing epidemic of Opioid use disorders. Given the susceptibility and magnitude of both the conditions, co-occurrence seems to be commonplace. Therefore, exploring the effects of candidate medications (for SARS-CoV2) among patients with SUD warrant clinical attention.

HCQ may lower seizure threshold with reports of tonic-clonic seizures among patients with systemic lupus [2]. Abruptly stopping alcohol use may lower seizure threshold warranting caution before starting HCQ. Both alcohol and HCQ may affect proximal muscles and peripheral nerves, hence patients with alcohol-induced neuro-myopathy need close monitoring, especially those with comorbid hepatic dysfunctions [3]. HCQ, azithromycin combination, are arrhythmogenic, and co-administration of methadone may increase the risk of QT_C prolongation [4]. Hence close ECG monitoring is advisable. Moreover, methadone and HCQ are substrates for CYP2D6 and CYP3A4a; methadone's serum level may increase with resultant risk of overdose. Tobacco smokers had lower HCQ response rates (in malaria) compared to non-smokers (possibly due to induction of CYP450 enzyme system in smokers and nicotine-blockade of HCQ uptake inside lysosomes) [5]. Therefore, smokers might necessitate dose adjustment of HCQ.

LR may have clinically significant interactions with medications used for SUDs and with drugs with misuse potential. Lopinavir is an inducer of methadone metabolism, leading to sub-therapeutic level of methadone and the emergence of opioid withdrawal symptoms (which overlap with symptoms of COVID-19) within a week of LR initiation [6]. However, no clinically significant interaction was reported with buprenorphine, another medication treatment for opioid use disorders. Administration of LR inhibits CYP3A-mediated *N*-demethylation of oxycodone, leading to significant increase in plasma concentrations of oxycodone, consequently increasing risk of overdose [7]. Concurrent use of LR and bupropion for smoking cessation, may lead to reduction in bupropion concentration, possibly due to induction of CYP2B6 and glucuronidation [8]. Liquid (not the capsule) formulation of LR contains 42.4% ethanol. Its co-administration with disulfiram (for treatment of alcohol dependence) could result in ethanol-disulfiram reaction; it should be avoided.

Remdesivir (RDV) is an investigational pro-drug with potential hepatotoxicity, and caution should be exercised among subjects with alcohol or opioid dependence and comorbid liver dysfunction [9]. Ribavirin is unlikely to have any specific clinical concern in patients with SUD. Finally, favipiravir, a viral RNA polymerase inhibitor, is hypothesized to have a moderate antiviral effect against COVID-19. Favipiravir is not a CYP450 substrate but is a possible CYP2C8 inhibitor. Therefore, co-administration with CYP2C8 substrates such as buprenorphine may pose a risk for increased serum levels and the effects of buprenorphine. Favipiravir inhibits acetaminophen metabolism, too, increasing the risk of toxicity in doses more than 3 g. Drugs of misuse, such as tramadol and tapentadol, are sold as fixed-dose combinations with acetaminophen. High dose misuse of these drugs with favipiravir might increase the risk of acetaminophen toxicity [10].

Therefore candidate medications for COVID, when administered in patients with SUD, have potential poor tolerability, reduced efficacy, and increased side effects. It is essential to raise clinician's awareness of these interactions and continue to enhance screening for SUDs.

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Received 8 May 2020; Received in revised form 20 May 2020; Accepted 20 May 2020

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