LETTER TO THE EDITOR

Hydroxychloroquine and "off-label" utilization in the treatment of oral conditions

To the Editor:

In response to President Trump's remarks made on March 19, 2020, concerning the potential of chloroquine and hydroxychloroquine (HCQ) as treatment for the novel coronavirus-19 (COVID-19) infections: "The U.S. Food and Drug Administration (FDA) swiftly issued a statement to clarify that, no, these drugs are not approved as treatments for COVID-19, the disease caused by the coronavirus SARS-CoV-2. Both drugs are approved to treat malaria, lupus, and rheumatoid arthritis but must still be assessed in clinical trials before being declared a safe and effective COVID-19 treatment. Doctors in the United States have wide latitude to prescribe drugs "off-label," meaning for conditions beyond their initial FDA approval."[1] HCQ may or may not pan out to be a successful therapeutic agent in the treatment for COVID-19 infections. However, it appears likely that many health care providers may begin using this drug without knowledge of accepted dosage regimens and toxicity.

HCQ is a drug specifically approved for the prevention and treatment of malaria. However, it is utilized extensively by both physicians and dentists (oral medicine clinicians) in the treatment of rheumatologic conditions, such as systemic lupus erythematosus, Sjogren syndrome, rheumatoid arthritis, chronic ulcerative stomatitis, immune thrombocytopenia purpura, lichen planopilaris, and oral lichen planus. In the realm of treatment of autoimmune secretory and oral mucosal conditions, HCQ has been deemed safe and effective for such oral conditions as Sjogren syndrome, chronic ulcerative stomatitis, and oral lichen planus.[2-9]

A noted possible negative effect of HCQ is drug-induced conjunctivitis. This toxicity is typically addressed by advising the patient to see his or her ophthalmologist at least once yearly.[10] Recently, it has been noted that there is a rare complication related to HCQ use, that is, sudden death resulting from a particular cardiac arrhythmia. Torsade de pointes arrhythmia is associated with prolonged QT duration secondary to high-dose HCQ administration.[11,12] However, as reported by O'Laughlin et al.,[13] HCQ-related QT interval prolongation and secondary arrhythmia are extremely rare and may be related to higher dosage regimens.

Danielsson et al.[14] reported that the results of their recent study on sudden death in older patients indicated an increased risk of torsade de pointes arrhythmia with the use of the selective serotonin reuptake inhibitor citalopram. Therefore, there appears to be the possibility of additive drug interactions when prescribing HCQ to patients already taking citalopram and other drugs that significantly prolong the QT duration and increase the risk of a torsade de pointes arrhythmia.[15]

Over 20 years ago, it was noted that the antihistamine H1 blocker terfenadine was cardiotoxic in higher doses and that particular drugs used in dentistry, such as ketoconazole and erythromycin, and even grapefruit juice could result in a drug−drug interaction and potentially lethal serum values, with the possible result of cardiotoxicity (specifically the torsade de pointes arrhythmia) and death. The danger of this sudden death condition resulted in the eventual removal of terfenadine as a clinical therapeutic agent worldwide.[16-19]

At rheumatologic therapeutic dosage levels, HCQ has been regarded as a reasonably safe therapeutic agent. However, oral medicine clinicians and other health care providers should be advised of the potential issues with the use of HCQ, such as drug−drug interactions, the additive toxicity of QT duration prolongation, and the association with sudden death, in the treatment of older patients.

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