Ototoxicity of Chloroquine and Hydroxychloroquine: Need for Awareness during COVID-19 Pandemic

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Dear Editor,

The debate on the efficacy of chloroquine (CQ) and hydroxychloroquine (HCQ) in the present severe acute respiratory syndrome coronavirus 2 (SARS COV-2) pandemic is still raging. Nevertheless, many organizations, politicians, and health-care professionals have propagated their use in prophylaxis and treatment of the infection resulting in many patients self-medicating and an increase in the demand for these drugs globally. Both these drugs are derivative of quinine, which is already known to be ototoxic.[1] Although there are no randomized trials, a substantial number of reports exist in the literature regarding the ototoxic potential of these drugs.

The ototoxicity related to CQ has been reported as early as 1968.[2] The symptoms experienced by the patient ranges from mild-to-severe sensorineural hearing loss, tinnitus, and even vestibular paresis.[3] The hearing loss can be both reversible and irreversible.[3] In addition to multiple case reports, over 700 adverse events linked to the ear and labyrinthine structure in the United States in the last 5 years were reported due to HCQ.[4]

A recent study by Mustafa *et al.*[5] found a significant decrease in pure tone audiometry thresholds at 4000, 6000, and 8000 Hz and transient evoked otoacoustic emissions in asymptomatic COVID-19 polymerase chain reaction (PCR)-positive cases, implying possible inner ear damage due to the infection.

The mechanism of the ototoxicity is poorly understood, and the possible hypothesizes are as follows:[1]

1. CQ gets accumulated in the inner ear tissues containing melanin leading to vascular injury and degenerative changes in the planum semilunatum and stria vascularis.
2. Another theory postulates that the drug may increase extracellular glutamate concentration leading to neuronal excitotoxicity. An overproduction of reactive oxygen species results in damage to the glial cells.
3. Drug-induced vasoconstriction leading to ischemic damage to the inner ear

Many aspects regarding ototoxicity remain unclear; for example, the reported ototoxic side effects of HCQ can be due to underlying conditions like SLE. In addition, the dose of these drugs which can cause ototoxicity is unclear. However, as the ototoxic potential still exists we recommend the following:

1. Patients on CQ or HCQ should be aware of the ototoxic potential of these drugs. They should be encouraged to report symptoms such as tinnitus imbalance and formal hearing evaluation should be done for these patients.
2. Ongoing and future clinical trials on CQ and HCQ should monitor patients for potential ototoxicity.
3. Patients who are self-administering these drugs can be educated and self-monitor their hearing with widely available validated free mobile applications.
4. Other ototoxic drugs such as azithromycin and aminoglycosides should be avoided, whereas patients are on CQ and HCQ
5. These drugs should not be used in patients with previous sensorineural hearing loss or vestibular disorders.
6. Health-care professionals should be made aware of the ototoxic potential and early referral to an otolaryngologist should be encouraged.

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Conflicts of interest
There are no conflicts of interest.

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