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## Short Communication

## Ototoxicity prevention during the SARS-CoV-2 (COVID-19) emergency

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## ABSTRACT

Aim of this paper is to remind the risk of ototoxicity when using chloroquine and hydroxychloroquine, in particular as prophylactic agents against SARS-CoV-2, during the pandemic. Healthy subjects taking chloroquine and hydroxychloroquine as prophylactic agents against SARS-CoV-2, during the pandemic, should be screened periodically, at least by Otoacoustic Emissions (OAEs) in order to detect early manifestations of possible cochlear ototoxic damages.

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Sir,

We would like to remind about the risk of ototoxicity when using chloroquine and hydroxychloroquine, in particular as prophylactic agents against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during the current pandemic of COVID-19 (coronavirus disease 2019).

In the last months, several authors have reported chloroquine (an antimalarial drug) and hydroxychloroquine (used in autoimmune diseases) to be effective ‘in vitro’ against the novel coronavirus by inhibiting the virus interaction with the cell membrane and therefore their infection [1]. Currently, a number of clinical trials have been developed not only for therapeutic purposes but also as a prophylactic treatment against COVID-19 in healthy subjects [2]. The aim of the latter is to reduce or block virus transmission, particularly by reducing the number of asymptomatic carriers [1].

Although the ototoxicity induced by the use of chloroquine and hydroxychloroquine may be irreversible, some authors has reported that reversibility can be achieved only when the medication is stopped early and eventually adequate treatment is established [3–5]. Sensorineural hearing loss, particularly among high frequencies, tinnitus and imbalance are the main manifestations reported due to chloroquine and hydroxychloroquine

ototoxicity [3–5]. Possible mechanisms of chloroquine and hydroxychloroquine ototoxicity include: (i) damage to the stria vascularis with consequent endolymphatic poisoning; (ii) micro-circulatory damage/thrombosis; and (iii) damage to the inner ear melanocytes with induced degenerative changes in the stria vascularis [3–5]. Typically the initial damage involves the outer hair cells in the cochlear basal turn, then progressing to the apical turn [2–4]. Further damage can also occur in the inner ear-associated neural structures [3–5].

Pure tone audiometry represents the main instrument for the identification and classification of hearing impairment; however, otoacoustic emissions (OAEs) are reported to be very sensitive in evaluating early manifestations of cochlear damage [6], as ototoxic drugs typically affect primarily outer hair cells [1,3–5]. Particularly in young subjects, OAE sensitivity is greater than conventional audiometric testing in detecting initial inner ear damage [7]. Therefore, healthy subjects receiving chloroquine and hydroxychloroquine as a prophylactic agent against SARS-CoV-2 during the pandemic should be screened periodically, at least by OAEs.

Clearly, even without a fatal condition, it is important to avoid the onset of ototoxic manifestations, especially when chloroquine and hydroxychloroquine are administered with a prophylactic intent. In fact, sensorineural hearing loss, tinnitus or imbalance, when irreversible and persistent, can have a significant negative impact on communication abilities and therefore on quality of life (QoL) perception. In particular, some authors have already reported that audiovestibular symptoms

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can impact negatively on mental well-being and QoL perception and have been linked to the onset and sustaining of depression and self-isolation [7].

In our opinion, it is crucial to keep our awareness high about the potential impact of ototoxicity, especially if using ototoxic drugs in healthy subjects without defined protocols.

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#### **Competing interests**

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#### **Ethical approval**

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