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Letter to the Editor

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Don't forget ototoxicity during the SARS-CoV-2 (Covid-19) pandemic!

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Abstract

Aim of this communication is to remind clinical professionals to be aware of ototoxic side effects of several specific drugs proposed for the treatment of the new virus SARS-CoV-2 (Covid-19). In particular, chloroquine and hydroxychloroquine, azithromycin, as well as antiviral drugs such as remdesivir, favipiravir and lopinavir can all present potential ototoxic side effects. The data in the literature do not offer specific information on their potential synergetic effects nor on their interactions.

Keywords

chloroquine, favipiravir, hydroxychloroquine, lopinavir, ototoxicity, remdesivir, SARS-CoV-2 (Covid-19) pandemic

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Dear Editor,

In this particular time where the SARS-CoV-2 pandemic has been reported to all clinical realities globally, we would like to remind clinical professionals to be aware of ototoxic side effects, a well-known issue back in vogue, due to the recent use of specific drugs against the new virus. Ototoxicity not only contributes to sensorineural hearing loss, tinnitus, or imbalance, but potentially impacts considerably the quality of life (QoL). In fact, it is well documented that hearing loss, tinnitus, and persistent imbalance retain a negative effect on mental well-being and QoL, having a strong association with the onset and the sustaining of depression and self-isolation.[1]

Ototoxicity is a feature shared among some of the drugs proposed for the SARS-CoV-2 treatment. In particular, chloroquine and hydroxychloroquine have been widely promoted and used during the pandemic;[2,3] however, in the past, data in the literature have suggested that in many treated cases side effects such as sensorineural hearing loss, tinnitus, and/or persistent imbalance were common. Unfortunately, the latter are rarely reversible especially if developed after a drug usage of weeks or months.[4]

Azithromycin, a macrolide, has been administered often in combination with hydroxychloroquine, reinforcing its action, in SARS-CoV-2 patients. It has also been reported to cause both reversible and irreversible sensorineural hearing loss and tinnitus.[5]

Remdesivir and favipiravir are antiviral adenosine nucleotide analogues which are reported as

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possible useful treatments against SARS-CoV-2. However, ototoxicity has been reported among the possible side effects of the adenosine nucleotide analogues;[5,6] specifically, data in the literature report that patients may develop irreversible unilateral or bilateral hearing loss and tinnitus due to the use of these drugs, usually after a few weeks of administration.[7,8]

Lopinavir, a nucleoside reverse-transcriptase inhibitor, proposed in the treatment of SARS-CoV-2 infections, has been related to the onset of sensorineural hearing loss,[9] after several weeks of administration. Data in the literature also verify the ototoxic effects of lopinavir in vitro.[10]

In case of ototoxicity, the severity of hearing loss, tinnitus, or imbalance are usually influenced by the dose, the duration of the therapy, and other factors related to the patient (i.e. concomitant diseases and use of other medications). In most cases, the ototoxic effects develop after the persistent use of a medication over weeks or months. The etiology of the ototoxicity, the precise mechanisms which mediate inner ear hair cell damage, still remain unknown in many cases. Furthermore, the data in the literature do not offer information on the possible ototoxic synergetic effects, when treatments are administered in combination or consecutively. Currently, ototoxicity as a result of the interaction of the aforementioned specific drugs has not been fully investigated.[11]

Another major drawback is the difficulty of monitoring hearing threshold shifts, while maintaining social distancing, during the pandemic. Since SARS-CoV-2 patients are completely isolated when sick, there is no possibility of monitoring their hearing level accurately as in an audiometric setting. Possible solutions (i.e. remote hearing level measurements) could relate to a tele-audiology model, but this technology is not adequately and widely developed so far.[11]

Finally, it is necessary to consider that SARS-CoV-2 could potentially target directly the inner ear, as many other viruses, that is, HSV and VZV.[12] The data in the literature offering information on this topic are rather scarce.[13,14]

Furthermore, cochlear hair cells have a high metabolic activity and are particularly vulnerable to hypoxic or ischemic damage.[15] This scenario is also probable in the SARS-CoV-2 patients where the inner ear can be damaged indirectly, due to the presence of persistent hypoventilation and hypoxygenation.

In conclusion, it is necessary to strictly monitor the use of such drugs, since the ototoxic hearing loss and/or tinnitus can be irreversible.

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