Hydroxychloroquine reduces the risk of covid-19 in patients with rheumatic diseases: myth or reality?

We read with great interest the article by Figueroa-Parra et al illustrating whether patients with rheumatic diseases are at higher risk of the coronavirus disease 2019 (covid-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In this study, the authors mentioned the potential benefit of antimalarial drugs for patients with rheumatic diseases in the context of covid-19 pandemic. At present, that is the really pivotal question, whether the antimalarial drugs could reduce the risk of SARS-CoV-2 infection in patients with rheumatic diseases.

Hydroxychloroquine (HCQ) and chloroquine, as antimalarial drugs for more than 70 years, have been successfully used to treat variety of rheumatic diseases, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis. Both drugs have a flat aromatic core structure and share nearly identical mechanism of action, but HCQ has replaced chloroquine in most countries due to its much better safety profiles. In vitro and in vivo assays, chloroquine treatment was found to be effective against coronavirus infections, including SARS-CoV-2 and has been recommended as an antiviral therapy in the latest Chinese guideline for the management of covid-19. Regarding the HCQ, Yao et al first confirmed HCQ was found to be more potent than chloroquine in SARS-CoV-2 inhibition in vitro. In humans, an open-label non-randomised clinical trial reported HCQ treatment (600 mg/day for 10 days) is efficient for virus elimination and its effect is reinforced by azithromycin. Meanwhile, a randomised clinical trial (ChiCTR2000029559) of 62 covid-19 patients also suggested the use of HCQ (400 mg/day for 5 days) could significantly shorten time to clinical recovery and promote the absorption of pneumonia. On the contrary, a prospective study of 11 patients (600 mg/day for 10 days) and a pilot study of 30 patients (400 mg/day for 5 days) failed to replicate the significant efficacy of HCQ. For patients with rheumatic diseases, previous clinical researches showed median blood HCQ concentration in patients with cutaneous lupus erythematosus and SLE who received HCQ 400 mg/day is 758 (2.26) and 917 (2.73) ng/mL (μM), respectively. In vitro, HCQ was found to decrease the viral replication in a concentration-dependent manner, with EC50 values of 6.25 and 6.14 µM at 24 hours before or after SARS-CoV-2 exposure, respectively. However, HCQ has a wide distribution in lung where HCQ concentration reaches hundred times more than that in the blood, and this unique property might lead to enough high concentration necessary for inhibitory effects on the lung compartments. Although lung is the major organ to be injured during SARS-CoV-2 infection, it should be noted that SARS-CoV-2 receptor is widely expressed in various organs or tissues (heart, kidney and bile ducts) and definite effect of HCQ on SARS-CoV-2 infection among patients with rheumatic diseases and treated with HCQ 400 mg daily is not unequivocal.

Notably, despite the proven favourable safety, HCQ may cause several serious adverse events in patients with rheumatic diseases at a higher daily or cumulative dose, such as retinopathy and cardiotoxicity, especially in those with primary heart disease or liver dysfunction. Therefore, rheumatologists are advised to fully consider the risks and benefits before initiating the HCQ therapy or increasing HCQ daily dose and patients with rheumatic diseases should not take, stop or change the dose of HCQ without healthcare provider’s permission.

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