Role of antimalarials in COVID-19: observational data from a cohort of rheumatic patients

The potential role of chloroquine (CQ) and hydroxychloroquine (HCQ) in the management of COVID-19 is certainly of relevance in this health emergency scenario. For this reason, we read with great interest the letter published by Romão and colleagues highlighting the need for more definite evidence on the role of antimalarial drugs in both preventing severe acute respiratory syndrome coronavirus-2 infection and making COVID-19 clinical course milder.[1] While several ongoing clinical trials are progressively providing controversial data about the real efficacy and safety of antimalarials in the treatment of overt COVID-19,[2–4] rheumatological patients already taking CQ or HCQ for the treatment of chronic inflammatory diseases are an excellent bench for testing the potential effect in preventing the contagion.[5] Being operative in the Research Center for Adult and Paediatric Rheumatic Diseases of the ASST Gaetano Pini-CTO in Milan (Lombardy), we had the opportunity to deal with a large cohort of rheumatic patients living in one of the regions most affected by the outbreak.[6] In the period between 25 February and 16 April 2020 we circulated among our patients a survey designed to investigate the incidence of COVID-19 (defined as nasopharyngeal swab positivity) and symptoms consistent with viral infection, and to clarify how our patients had changed their treatment and behaviour due to the outbreak. The survey was administered face-to-face to all patients evaluated during an outpatient visit or by telephone to those who missed a scheduled appointment during the period under review. The rate of non-responders to the survey was very low (1.85%) and unlikely to significantly affect the overall results. The final study population included 914 patients stratified in HCQ-users (n=112) and non-HCQ-users (n=802), whose demographic and clinical characteristics are detailed in table 1. Briefly, mean age, mean disease duration and prevalence of comorbidity were overlapping in the two groups. Conversely, significant differences were observed in the distribution according to gender (female prevalence was greater in HCQ-users) and diagnosis (rheumatoid arthritis and connective tissue diseases were more frequent in HCQ-users, whereas spondyloarthritis in non-HCQ-users). Moreover, the prevalence of concomitant biological/targeted synthetic drugs was higher in non HCQ-users, while corticosteroids were more frequently reported in HCQ-users. The vast majority of patients in both groups had strictly adhered to the norms for the prevention of contagion (use of masks and gloves, social distancing, home-working) since the beginning of the epidemic. The frequency of definite contact with COVID-19 positive subjects was similar in both groups. In the overall population, six patients with COVID-19 positive swab were observed, five of whom had a complete recovery (four required hospitalisation with low-flow oxygen therapy), while a 32-year-old woman suffering from systemic sclerosis with lung involvement (taking HCQ) died. The incidence of COVID-19 positive subjects was comparable in the two groups (0.89% in HCQ-users vs 0.62% in non HCQ-users; p=0.64). This result did not change either by broadening the definition of COVID-19 to include patients who had not had access to the swab but who presented symptoms consistent with COVID-19 (at least one between fever >37.5°C, cough, or dyspnoea of recent onset), or were living in a highly endemic area (COVID-19 incidence ≥1%), according to WHO criteria (16% HCQ users vs 14.6% non-users; p=0.67). In conclusion, our preliminary data does not appear to support the use of antimalarials as prophylactic therapy for COVID-19, although the lack of a complete matching between the two groups under analysis does not allow definitive conclusions to be drawn.

Table 1 Demographic and clinical characteristics of study population

	HCQ users (n=112)	Non-HCQ users (n=802)	P value
Age (mean±SD)	57.3±14.2	54.5±16	0.06
Female	96 (85.7%)	528 (65.8%)	<0.0001
Disease duration (mean±SD)	11.4±10	13.4±9	0.07
Diagnosis			
Rheumatoid arthritis	79 (70.6%)	401 (50%)	<0.0001
Spondyloarthritis	8 (7.1%)	307 (38.2%)	<0.0001
Connective tissue diseases	21 (18.7%)	52 (6.5%)	<0.0001
Other	4 (3.6%)	42 (5.3%)	0.64
Concomitant bDMARD	50 (44.6%)	605 (75.4%)	<0.0001
Concomitant corticosteroids	70 (62.5%)	253 (31.5%)	<0.0001
Comorbidities (≥1)	39 (34.8%)	302 (37.6%)	0.60
COVID-19			
Contagion prevention	93 (83%)	700 (87.2%)	0.23
Treatment discontinuation	4 (3.6%)	42 (5.2%)	0.54
Definite contact with COVID-19 positive subjects	2 (1.8%)	14 (1.7%)	0.90
COVID-19 positive swab	1 (0.89%)	5 (0.62%)	0.64
Respiratory symptoms (no swab)	18 (16%)	117 (14.6%)	0.67

P value was calculated by using Fisher's test for categorical variables and t-test for continuous variables. Respiratory symptoms, at least one between fever >37.5°C, cough, or dyspnoea of recent onset.
bDMARD, biologic disease-modifying antirheumatic drugs; HCQ, hydroxychloroquine.

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