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Can hydroxychloroquine be useful in the prevention of COVID-19? An Italian survey in dermatologic and rheumatologic patients already under treatment

To the Editor: The World Health Organization declared the coronavirus disease 2019 (COVID-19) a pandemic on March 11, 2020. To date, there is an urgent need for effective drugs against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Chloroquine and hydroxychloroquine (HCQ) have been shown to inhibit SARS-CoV-2 in vitro, and HCQ seems more effective than chloroquine.[1,2]

The aim of our research was the evaluation of HCQ preventive effects on the acquisition of SARS-CoV-2 infection. We conducted an observational retrospective study through a telephone survey among patients in treatment with HCQ for chronic dermatologic or rheumatologic diseases referring to the Dermatologic and Rheumatologic Clinics of the University of Naples Federico II, Italy. The survey and its results are summarized in Tables I-III.

We reviewed 66 patients, 30 dermatologic patients (8 men and 22 women; median age, 55.5 years; medium duration of HCQ treatment, 14.2 months; range, 3-36 months) and 35 rheumatologic patients (5 men and 30 women; median age, 46.1 years; medium duration of HCQ treatment, 50.1 months; range 2-240 months). Overall, 65 of the 66 patients (98.4%) in treatment with

Table I. Questions asked in the telephone survey and dermatologic patients' answers

Patient	Age, y	Dermatologic diagnosis	HCQ dose, mg/d	Duration (ongoing?)	History of respiratory symptoms or fever*	Exposure to people with respiratory symptoms or fever*	Exposure to established COVID-19 cases	HCQ-related toxicity
1	58	LPP	200	18 mo (yes)	No	No	No	None
2	57	LPP+FFA	200	30 mo (yes)	No	No	No	None
3	17	LPP	200	7 mo (yes)	No	No	No	None
4	60	LPP	200	12 mo (yes)	No	No	No	None
5	59	LPP	200	24 mo (yes)	No	No	No	None
6	58	LLP	200	12 mo (yes)	No	No	No	None
7	31	LLP	600	18 mo (yes)	No	No	No	None
8	64	LLP	200	12 mo (yes)	No	No	No	None
9	65	LLP	200	12 mo (yes)	No	No	No	None
10	47	LLP	200	15 mo (yes)	No	No	No	None
11	62	LLP	200	7 mo (yes)	No	No	No	Visual decline
12	66	LLP	200	3 mo (yes)	No	No	No	Visual fogging
13	58	LLP	200	12 mo (yes)	No	No	No	None
14	74	LLP	200	12 mo (yes)	No	No	No	None
15	56	LLP	200	12 mo (yes)	No	No	No	None
16	61	LLP+AGA	200	15 mo (yes)	No	No	No	None
17	85	FFA	200	12 mo (yes)	No	No	No	None
18	62	LLP	200	6 mo (yes)	No	No	No	None
19	48	LLP	200	5 mo (yes)	No	Yes, a son with fever	No	None
20	55	LLP	200	5 mo (yes)	No	No	No	None
21	68	LLP	200	12 mo (yes)	No	No	No	None
22	60	LLP	200	11 mo (yes)	No	No	No	None
23	70	LLP	200	14 mo (yes)	No	No	No	None
24	72	LLP	200	14 mo (yes)	No	No	No	None
25	29	LLP	200	15 mo (yes)	No	No	No	None
26	56	LLP	200	12 mo (yes)	No	No	No	None
27	40	LLP	200	15 mo (yes)	Yes, fever ≤37.2°C	No	No	None
28	38	LLP	200	32 mo (yes)	No	No	No	None
29	18	DLE	200	10 mo (yes)	No	No	No	None
30	67	LLP and RA	200	36 mo (yes)	No	No	No	None

AGA, Androgenetic alopecia; *DLE*, discoid lupus erythematosus; *FFA*, frontal fibrosing alopecia; *HCQ*, hydroxychloroquine; *LPP*, lichen planopilaris; *RA*, rheumatoid arthritis.
*In the last 2 months.

Table II. Questions asked in the telephone survey and rheumatologic patients' answers

Patient, No.	Age, y	Rheumatologic diagnosis	HCQ dose, (mg/d)	Duration (ongoing?)	History of respiratory symptoms or fever*	Exposure to people with respiratory symptoms or fever*	Exposure to established COVID-19 cases	HCQ-related toxicity
1	37	SLE	200 × 2	18 mo (yes)	No	No	No	None
2	55	SA	200 × 2	24 mo (yes)	No	No	No	None
3	54	SA	200 × 2	24 mo (yes)	No	No	No	None
4	59	SA	200 × 2	20 mo (yes)	No	No	No	None
5	31	UCTD	200 × 2	36 mo (yes)	No	No	No	None
6	61	SLE	200 × 2	36 mo (yes)	No	No	No	None
7	31	SLE	200 × 2	30 mo (yes)	No	No	No	None
8	43	Myositis	200 × 2	8 mo (yes)	No	No	No	None
9	53	SLE	200 × 2	36	No	No	No	None
10	51	SLE	200 × 2	8 mo (yes)	No	No	No	None
11	64	Sjögren	200 × 2	170 mo (yes)	No	No	No	None
12	59	Sjögren	200 × 2	60 mo (yes)	No	No	No	None
13	34	UCTD	200 × 2	4 mo (yes)	No	No	No	None
14	33	UCTD	200 × 2	29 mo (yes)	No	No	No	None
15	47	SLE	200 × 2	12 mo (yes)	No	No	No	None
16	51	UCTD	200 × 2	60 mo (yes)	No	No	No	None
17	32	UCTD	200 × 2	24 mo (yes)	No	No	No	None
18	67	UCTD	200 × 2	16mo (yes)	No	No	No	None
19	36	SLE	200 × 2	19 mo (yes)	No	No	No	None
20	53	SLE	200 × 2	48 mo (yes)	No	No	No	None
21	52	SLE	200 × 2	240 mo (yes)	No	No	No	None
22	40	SA	200 × 2	34 mo (yes)	No	No	No	None
23	49	SS	200 × 2	144 mo (yes)	No	No	No	None
24	69	Sjögren	200 × 2	21 mo (yes)	No	No	No	None
25	45	SLE	200 × 2	36	No	No	No	None
26	42	SLE	200 × 2	78 mo (yes)	No	No	No	None
27	32	UCTD	200 × 2	38 mo (yes)	No	No	No	None
28	37	Sjögren	200 × 2	80 mo (yes)	No	No	No	None
29	42	UCTD	200 × 2	84 mo (yes)	No	No	No	None
30	48	UCTD	200 × 2	180 mo (yes)	No	No	No	None
31	33	UCTD	200 × 2	10 mo (yes)	No	No	No	None
32	53	SLE	200 × 2	140 mo (yes)	No	No	No	None
33	39	UCTD	200 × 2	2 mo (yes)	No	No	No	None
34	55	SLE	200 × 2	9 mo (yes)	No	No	No	None
35	37	UCTS	200 × 2	8 mo (yes)	No	No	No	None
36	38	SLE	200 × 2	18 mo (yes)	No	No	No	None

HCQ, Hydroxychloroquine; *SA*, seronegative arthritis; *SLE*, systemic lupus erythematosus; *SS*, systemic sclerosis; *UCTD*, undifferentiated connective tissue disease.
*In the last 2 months.

Table III. Survey's main results

Patients	No.	Mean age, y	Dose of HCQ	Mean duration, mo	History of respiratory symptoms or fever,* No. (%)	Exposure to people with respiratory symptoms or fever,* No. (%)	Exposure to established COVID-19 cases, No. (%)
Dermatologic	30	55.5	200 mg/d	14.2	1 (3.44)	1 (3.44)	0 (0)
Rheumatologic	36	46.16	200 mg 2×	50.1	0 (0)	0 (0)	0 (0)

HCQ, Hydroxychloroquine.
*In the last 2 months.

HCQ had not developed fever, sore throat, fatigue, cough, or dyspnea in the previous 2 months. One patient had reported a temperature of 37.2° C for only 1 day, without any other associated symptoms.

Mostly, the treatment was well tolerated, without related adverse events; only 2 patients described a brief episode of visual impairment. These patients were suggested to have an examination of the ocular fundus, beyond the regular 6-month ophthalmic follow-up already performed.

HCQ has immunomodulatory properties and an attractive adverse effect profile.[2] It could contribute to the suppression of the cytokine release syndrome responsible for the progression of COVID-19 to severe clinical forms through several mechanisms, including (1) reduction of T-cell activation and differentiation, (2) decreased production of cytokines by T cells and B cells (eg, interleukin 1 and 6 and tumor necrosis factor), and (3) attenuation of proinflammatory signaling pathways activation.

Interestingly, HCQ and chloroquine inhibit receptor binding and membrane fusion, 2 critical steps required for cell entry by coronaviruses.[3] However, HCQ offers advantages compared with chloroquine, including a better clinical safety profile, possible higher daily dose, and fewer pharmacologic interactions.[1,2,4] In our study, no patient already in treatment with HCQ developed symptoms suggestive for SARS-CoV-2 infection, although Italy is currently the third-most infected country in the world.

Limitations of our study are the low sample size and the absence of exposure to established cases of COVID-19 in the interviewed patients.

Further studies on larger samples are needed to assess the possible protective effect of HCQ on SARS-CoV-2 infection. We recommend extending this kind of survey to all patients actually in treatment with HCQ, possibly stratifying them according to residency, posology, other ongoing systemic treatments, comorbidities, and starting prospective observational study for a more extended period (4-6 months). The in vivo demonstration of prophylactic efficacy of HCQ could be a revolutionary result to prevent the transmission of the virus, until the development of a vaccine.

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