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COVID-19 in Individuals Treated With Long-Term Hydroxychloroquine: A Propensity Score-Matched Analysis of Cicatricial Alopecia Patients

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INTRODUCTION

Early in the COVID-19 pandemic, anti-malarial agent hydroxychloroquine (HCQ) was touted as a potentially effective COVID-19 treatment due to its purported anti-inflammatory and antiviral effects. However, subsequent studies not only called the therapeutic benefit of HCQ in hospitalized patients with mild[1] and severe[2] COVID-19 into question, but also its efficacy as *post*-exposure prophylaxis (PEP) in those with known exposures.[3] That said, considerable interest remains in HCQ as *pre*-exposure prophylaxis (PrEP), particularly in the outpatient setting. A recent meta-analysis of five randomized controlled clinical trials in which a total of 5,577 non-hospitalized (ambulatory) patients were treated with HCQ or placebo/standard-of-care for pre-exposure prophylaxis, post-exposure prophylaxis or outpatient therapy for COVID-19 found that HCQ was associated with a 24% reduction in COVID-19 infection, hospitalization or death (P=.025, RR, 0.76 [95% CI, 0.59 to 0.97]).[4] While these RCTs individually yielded estimates of effectiveness of HCQ that did not reach statistical significance, the authors postulated that early study termination was a likely contributor to the absence of statistical significance. While additional randomized controlled trials (RCTs) are planned,[5] we sought to investigate if HCQ confers protection against COVID-19 infection in ambulatory patients on chronic HCQ therapy *prior* to the onset of the COVID-19 pandemic. Thus, we performed a propensity score-weighted analysis of patients with cicatricial alopecia to identify any significant factors – including chronic HCQ use – impacting COVID-19 infection risk.

After obtaining IRB approval, we performed a retrospective chart review of patients with cicatricial alopecia who were evaluated at NYU Langone Health between 1/1/2019 and 5/1/2020 (visits in the final two months were conducted predominantly via telehealth). A total of 144 patient charts were reviewed for alopecia diagnoses, demographics, medication history and comorbidities (Table 1). Patients were contacted between 6/5/2020 and 7/1/2020 to determine whether they had developed COVID-19 infection (confirmed by PCR or antibody testing) during the initial wave of the COVID-19 pandemic in New York City, defined as 3/1/2020-5/15/2020.[6]

Propensity score-weighting was used to minimize bias from nonrandomized treatment assignment to HCQ (Supplemental Methods). Patients were weighted using estimated propensity scores that accounted for factors significantly associated with HCQ prescription including age, comorbid autoimmune disease, and alopecia diagnosis. The main outcome of interest was COVID-19 infection. The overall cohort was 85.4% female (mean age, 57 years). Forty-five patients (31.3%) were on chronic HCQ (mean length of therapy, 56.5 months [range, 3–240 months]) including 17 of the 45 patients (37.7%) seen after 3/1/2020 via telehealth encounters.

A propensity score-weighted multivariate logistic regression revealed that patients on HCQ had a *decreased* risk (OR 0.87, 95% CI [0.80, 0.96]) of COVID-19 diagnosis compared to patients not on HCQ (P=0.006) after adjusting for confounders identified by LASSO selection (Supplemental Methods). Unsurprisingly, predictors of increased risk of infection included maintaining residence in New York City from March-July 2020 (corresponding to the height of the COVID-19 pandemic in New York City; OR 1.21, 95% CI [1.01, 1.23], P=0.026). Interestingly, oral anti-androgen use was not significantly associated with infection risk (OR 0.94, 95% CI [0.88, 1.01], P=0.11) despite androgen-mediated SARS-CoV-2 vulnerability being cited as a potential explanation for higher rates of COVID-19-associated mortality among men (Supplemental Table 2).[7]

Despite using a rigorous propensity score-weighting approach

TABLE 1.

Characteristics of Study Participants (N=144)				
	COVID-19 Diagnosis			
	N (%)	No (N=132)	Yes (N=12)	*P*-value
Age, mean (SD)	57(13.0)	57.8 (13.4)	52.16 (13.8)	0.0284
Gender				0.0504
Male	21(14.6%)	16 (76.2%)	5 (23.8%)	--
Female	123(85.4%)	116 (94.3%)	7 (5.7%)	--
Alopecia Diagnosis*	144	--	--	0.8076
Lichen planopilaris	47 (32.6%)	41 (87.2%)	6 (12.8%)	--
Frontal fibrosing alopecia	56 (38.9%)	53 (94.6%)	3 (5.4%)	--
Discoid lupus erythematosus	22 (15.3%)	21 (95.4%)	1 (4.5%)	--
Other**	14 (9.7%)	12 (85.7%)	2 (14.3%)	--
Hypertension	36 (25.0%)	32 (88.8%)	4 (11.1%)	0.7805
Hyperlipidemia	28 (19.0%)	26 (92.8%)	2 (7.1%)	0.295
Diabetes	6 (4.2%)	6 (100.0%)	0 (0.0%)	0.0586
Obesity	7 (4.9%)	5 (71.4%)	2 (28.6%)	0.3101
Chronic kidney disease	1 (0.7%)	1 (1.0%)	0 (0.0%)	0.3395
Autoimmune disease	20 (13.9%)	19 (95.0%)	1 (5.0%)	0.1266
Oral anti-androgen use	47 (33.0%)	46 (97.8%)	1 (2.1%)	0.0158
Oral antibiotic use***	33 (23.0%)	29 (87.8%)	4 (12.1%)	0.5701
Tetracycline use	2 (1.4%)	2 (100.0%)	0 (0.0%)	0.1879
Oral immunosuppressant use	10 (6.9%)	10 (100.0%)	0 (0.0%)	0.0235
Hydroxychloroquine (HCQ) use	--	--	--	0.0655
HCQ dose	--	--	--	--
200 mg per day	25 (17.4%)	25 (100.0%)	0 (0.0%)	--
300 mg per day	3 (2.1%)	3 (100.0%)	0 (0.0%)	--
Alternating 200 mg and 400 mg every other day	4 (2.8%)	4 (100.0%)	0 (0.0%)	--
Other	13 (9.0%)	12 (88.8%)	1 (11.1%)	--
None	99 (68.8%)	88 (88.9%)	11 (11.1%)	--
Positive Household Contact	20 (13.9%)	16 (80.0%)	4 (20.0%)	0.2452
New York City Residence	64 (44.4%)	54 (84.4%)	10 (15.6%)	0.0111

N, Number; *SD*, Standard Deviation
P-value is based on propensity score weighted data
*Patients could be classified as having more than one alopecia diagnosis.
**Other alopecia diagnoses included central centrifugal cicatricial alopecia (CCCA), folliculitis decalvans, pseudopelade of Brocq and traction alopecia.
***Other than tetracyclines.

to adjust for baseline differences between patients on HCQ, it is possible that unmeasured confounders were not accounted for, resulting in residual treatment selection bias. Moreover, our cohort was predominantly female (85.4%), reflecting the gender predilection of cicatricial alopecia. Nonetheless, the strength of our study draws from our relatively *healthy* patient cohort. In contrast to other studies that have attempted to gauge susceptibility of patients on chronic HCQ to COVID-19 infection,[8] only a minority of our patient cohort (13.9%) demonstrated comorbid autoimmune disease. Thus, our study represents one of the first analyses of HCQ as potential PrEP for COVID-19 infection in patients that faithfully recapitulate a generally healthy population. While our sample size is limited, the evidence suggests HCQ may have some benefit, though further RCTs are warranted.

DISCLOSURES

Dr. Shapiro is an investigator for RegenLab. Dr. Lo Sicco is an investigator for RegenLab. The other authors have no conflicts of interest to disclose.

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