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Hydroxychloroquine shortages among patients with systemic lupus erythematosus during the COVID-19 pandemic: experience of the Systemic Lupus International Collaborating Clinics

Early scientific and public enthusiasm for hydroxychloroquine (HCQ) as a potential therapy for COVID-19 has prompted over 100 registered trials to date, although its efficacy remains to be demonstrated.¹ Unfortunately, accelerated demand for HCQ has the potential to diminish supplies for patients with systemic lupus erythematosus (SLE), which is worrisome due to the known risks of SLE flare after HCQ withdrawal.² We previously reported that rheumatologists in most Canadian provinces observed HCQ shortages early in the COVID-19 pandemic.³ However, data are lacking on the global experience with HCQ access during the pandemic, specifically in SLE.

On 4 May 2020, we distributed an electronic survey to the 42 Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) members affiliated with SLE referral centres (<https://sliccgroup.org>), with reminders after 1 and 3 weeks. Physicians were asked about experiences with HCQ shortages during the COVID-19 pandemic, and whether they had been contacted by patients and/or pharmacists regarding difficulties accessing HCQ. Physicians who answered 'yes' to the latter question were asked to estimate how many and what proportion of their patients with SLE were affected. We inquired about regional measures taken that exacerbated or helped mitigate HCQ shortages for patients with SLE (free text responses).

We received 31 responses (rate 74%) from 13 of 15 countries represented in SLICC, mostly from Europe (29%), the USA (26%) and Canada (23%). Over half (55%) reported either previous (39%) or current (16%) HCQ shortages among patients with SLE during the pandemic (see [table 1](#)). Two-thirds (65%) were contacted by patients and pharmacies regarding difficulties accessing HCQ. Seventeen provided estimates of the number and proportion of their patients affected, which corresponded to a

median of 40 (IQR 15–90) patients per physician representing 15% (IQR 5%–35%) of respective SLE populations. Seven physicians noted that shortages resolved within 2–8 weeks. Members from four countries (Sweden, Denmark, Singapore, South Korea) reported no HCQ access issues among their patients.

Physicians identified regional factors contributing to HCQ shortages, including diversion of HCQ to hospitals (n=3), for clinical trials (n=2) or off-label empiric prescribing for COVID-19 (n=1).

Twenty-three (74%) reported system-level measures taken during the pandemic to preserve HCQ access for patients with SLE, which included limiting prescribing capabilities to specific specialties (n=9) or diagnoses (n=10) and limiting dispensed supply (n=3). Some restrictions may have inadvertently delayed HCQ access for patients with SLE, who had to wait for physicians to update diagnostic codes in medical records, confirm diagnoses with pharmacies or apply for waivers. In some cases, patients had to register for pharmacy dispensing programmes or were subjected to general dispensing restrictions. In Canada, the USA and the UK, patient and physician organisations advocated to health authorities for the rapid resolution of HCQ shortages.

Currently, there is no substitution for antimalarials in SLE. HCQ reduces disease flares,² damage⁴ and mortality,⁵ with fewer adverse effects compared with glucocorticoids and immunosuppressants.⁶ Regardless of the ultimate efficacy of HCQ for COVID-19, preserving patients' access to critical medications remains paramount. We observed that HCQ prescription restrictions were a common short-term strategy, although our cross-sectional survey was not intended to evaluate which mitigation strategies were most effective. Furthermore, physician estimates from single tertiary centres do not represent a comprehensive account of HCQ shortages or mitigation strategies and may not reflect the experience of an entire region or country.

According to this survey, HCQ access issues for patients with SLE occurred in multiple countries and continents during the COVID-19 pandemic. Because SLE can flare as little as 2 weeks after HCQ cessation,² further study of outcomes among patients who lost access to HCQ during the pandemic is warranted.

Table 1 Experience of HCQ shortages among patients with SLE during the pandemic and regional mitigation strategies

Country* (n responses)	Canada (n=7)	USA (n=8)	France (n=1)	UK (n=4)	Spain (n=1)	Italy (n=1)	Sweden (n=1)	Denmark (n=1)	Argentina (n=1)	Australia (n=1)	Turkey (n=2)	Singapore (n=1)	South Korea (n=1)
HCQ access issues													
Concerned about HCQ shortages, n													
Current	1	2	1	0	0	0	0	0	0	1	0	0	0
Resolved	1	5	0	3	1	1	0	0	1	0	0	0	0
Physicians contacted by patients re: HCQ access issue, n	3	8	1	3	1	1	0	0	1	1	1	0	0
Estimated % of patients with SLE affected (range)	3%–5%	5%–40%	70%	0%–5%	NR	20%	–	–	30%	50%	0%–1%	–	–
Regional mitigation strategies													
Limiting authorised prescribers	+		+				+	+		+		+	
Limiting HCQ to specific diagnoses	+	+			+	+		+		+	+		
Limiting dispensed supply	+												
Physician/patient association advocacy	+	+		+									
Hospital or pharmacies reserved supply for patients with SLE		+											

*One respondent did not indicate country of origin and is not included in this table.
HCQ, hydroxychloroquine; NR, not reported; SLE, systemic lupus erythematosus.

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REFERENCES

- Mahévas M, Tran V-T, Roumier M, *et al.* Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data. *BMJ* 2020;369:m1844.
- Canadian Hydroxychloroquine Study Group. A randomized study of the effect of withdrawing hydroxychloroquine sulfate in systemic lupus erythematosus. *N Engl J Med* 1991;324:150–4.
- Mendel A, Bernatsky S, Thorne JC, *et al.* Hydroxychloroquine shortages during the COVID-19 pandemic. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217835. [Epub ahead of print: 20 May 2020].
- Bruce IN, O’Keeffe AG, Farewell V, *et al.* Factors associated with damage accrual in patients with systemic lupus erythematosus: results from the systemic lupus international collaborating clinics (SLICC) inception cohort. *Ann Rheum Dis* 2015;74:1706–13.
- Alarcón GS, McGwin G, Bertoli AM, *et al.* Effect of hydroxychloroquine on the survival of patients with systemic lupus erythematosus: data from LUMINA, a multiethnic US cohort (LUMINA L). *Ann Rheum Dis* 2007;66:1168–72.
- Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, *et al.* Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review. *Ann Rheum Dis* 2010;69:20–8.