

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

Mendel, Arielle; Gordon, Caroline

DOI:
[10.1136/annrheumdis-2020-218164](https://doi.org/10.1136/annrheumdis-2020-218164)

License:
None: All rights reserved

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (Harvard):
Mendel, A & Gordon, C 2020, 'Hydroxychloroquine shortages among patients with systemic lupus erythematosus during the COVID-19 pandemic: experience of the Systemic Lupus International Collaborating Clinics', *Annals of the Rheumatic Diseases*. <https://doi.org/10.1136/annrheumdis-2020-218164>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

Mendel A, Bernatsky S, Askanase A, et al, Hydroxychloroquine shortages among patients with systemic lupus erythematosus during the COVID-19 pandemic: experience of the Systemic Lupus International Collaborating Clinics *Annals of the Rheumatic Diseases* Published Online First: 25 June 2020. doi: 10.1136/annrheumdis-2020-218164

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Download date: 11. May. 2021

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.

Arielle Mendel ¹, Sasha Bernatsky ^{1,2}, Anca Askanase,³
Sang-Cheol Bae ⁴, Ann Elaine Clarke,⁵
Nathalie Costedoat-Chalumeau ⁶, Dafna D Gladman ⁷,
Caroline Gordon,^{8,9} John Hanly,¹⁰ Søren Jacobsen,¹¹ Ken Kalunian,¹²
Anselm Mak ¹³, Marta Mosca,¹⁴ Bernardo A Pons-Estel,¹⁵
Guillermo Ruiz-Irastorza ¹⁶, Murray Urowitz ⁷, Évelyne Vinet^{1,2}

¹Division of Rheumatology, McGill University Health Centre, Montreal, Quebec, Canada

²Centre for Outcomes Research and Evaluation (CORE), Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada

³Division of Rheumatology, Columbia University Irving Medical Center, New York, New York, USA

⁴Division of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seongdong-gu, Republic of Korea

⁵Division of Rheumatology, University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada

⁶Centre de Référence Maladies Auto-immunes et Systémiques Rares, Service de Médecine Interne, Hôpital Cochin, Paris, France

⁷Lupus Program, Centre for Prognosis Studies in the Rheumatic Disease and Krembil Research Institute, Toronto Western Hospital, Toronto, Ontario, Canada

⁸Rheumatology Research Group, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK

⁹Rheumatology Department, City Hospital, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK

¹⁰Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada

¹¹Copenhagen Lupus and Vasculitis Clinic, Section 4242, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark

¹²Division of Rheumatology, University of California San Diego School of Medicine, La Jolla, California, USA

¹³Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

¹⁴Rheumatology Unit, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy

¹⁵Regional Center for Autoimmune and Rheumatic Diseases of Rosario, Sanatorio Parque, Rosario, Argentina

¹⁶Autoimmune Diseases Research Unit, Department of Internal Medicine, BioCruces Health Research Institute, Hospital Universitario Cruces, University of the Basque Country, Barakaldo, Spain

Correspondence to Dr Arielle Mendel, Rheumatology, McGill University Health Centre, Montreal, QC H3G1A4, Canada; arielle.mendel@mail.mcgill.ca

Handling editor Josef S Smolen

Contributors AM, SB, EV: conception or design of the study; data acquisition, analysis and interpretation; drafting the work; revising it critically for important intellectual content; final approval of the version published. AA, S-CB, AEC, NC-C, DDG, CG, JH, SJ, KK, AM, MM, BAP-E, GR-I, MU: data analysis and interpretation; revising the work critically for important intellectual content; final approval of the version published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests AEC reports consulting fees (less than \$10 000) from Bristol Myers Squibb, Exagen Diagnostics and AstraZenca, outside the submitted work.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The McGill University Research Ethics Board approved this survey.

Provenance and peer review Not commissioned; externally peer reviewed.



OPEN ACCESS

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Mendel A, Bernatsky S, Askanase A, *et al.* *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2020-218164

Received 30 May 2020

Revised 15 June 2020

Accepted 16 June 2020

Ann Rheum Dis 2020;**0**:1–2. doi:10.1136/annrheumdis-2020-218164

ORCID iDs

Arielle Mendel <http://orcid.org/0000-0001-9732-616X>

Sasha Bernatsky <http://orcid.org/0000-0002-9515-2802>

Sang-Cheol Bae <http://orcid.org/0000-0003-4658-1093>

Nathalie Costedoat-Chalumeau <http://orcid.org/0000-0002-1555-9021>

Dafna D Gladman <http://orcid.org/0000-0002-9074-0592>

Anselm Mak <http://orcid.org/0000-0002-4688-7829>

Guillermo Ruiz-Irastorza <http://orcid.org/0000-0001-7788-1043>

Murray Urowitz <http://orcid.org/0000-0001-7506-9166>

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.