Lupus
2022, Vol. 31(6) 767–768

DOI: 10.1177/09612033221093506
journals.sagepub.com/home/lup
SAGE

Comparison of hydroxychloroquine titers measured in frozen/thawed serum and whole blood obtained from lupus patients

Date received: 19 December 2021; accepted: 23 March 2022

Sir,

To the Editor: Nonadherence to therapy in systemic lupus erythematosus (SLE) has a major impact on disease progression and relapses, not to mention unnecessary therapeutic escalation. While unmasking nonadherence, through pill counts, refilling data, and electronic monitoring devices, remains challenging in many chronic diseases, measurements of whole blood (WB) hydroxychloroquine (HCQ) titers offer a specific option in SLE. Since HCQ is prescribed in virtually all SLE patients and has a long half-life, WB HCQ titers are only marginally influenced by the so-called white coat compliance effect corresponding to a short improvement of adherence the few days preceding an appointment. Severely nonadherent patients are therefore readily identified by a WB HCQ titer <200 ng/mL.[1] In the same paper, the authors highlighted that a WB HCQ concentration of 1000 ng/mL had a 96% negative predictive value for disease exacerbation, suggesting a cut-off of 1000 ng/mL as a therapeutic target to achieve.[1]

In expert centers, serum samples from SLE patients are stored in biobanks at regular intervals and kept frozen for years to allow further studies. This is especially relevant for disease manifestations, such as lupus nephritis, whose outcome is mostly determined after a long follow-up. Longitudinal measurements of HCQ titers in stored samples are valuable tools to address the contribution of chronic nonadherence to poor outcome. In this respect, the first step is to determine a frozen/thawed serum versus WB HCQ titer ratio. Two recent studies compared HCQ titers measured in serum and WB [2, 3] and found a conversion ratio of 0.53 [2] and 0.54,[3] which means that serum HCQ levels are half of those measured in WB.

We collected serum and WB from 50 consecutive HCQ-treated adult SLE patients, fulfilling the 2019 EULAR/ACR classification criteria. The study was approved by the ethics committee of UCLouvain and supported by *Cap48, Belgium*. Serum was frozen at −20° for a few hours and then thawed. In the same high-performance liquid chromatography run, HCQ titers were measured in frozen/thawed serum and WB.

HCQ was undetectable in frozen/thawed and WB in two patients. Mean (SD) HCQ levels measured in the remaining 48 patients were 428 (296) and 844 (598) ng/mL in frozen/thawed and WB, respectively. Of note, these titers are lower than the aforementioned standard therapeutic goal. Correlation between frozen/thawed and WB HCQ titers is illustrated in the (Figure 1). The mean ratio of frozen/thawed to WB levels was 0.51, very similar to the fresh serum to WB ratio measured by the two other groups, 0.53 [2] and 0.54[3].

There are some limitations to our work as we did not look at different lengths of time. Moreover, the samples studied did not allow to compare frozen/thawed and WB levels at higher concentrations of HCQ.

In conclusion, our data indicate that frozen/thawed HCQ levels are half of those measured in WB samples. By extrapolation, one should consider that lupus patients with frozen/thawed HCQ levels <100 ng/mL are severely nonadherent. This result raises the possibility to

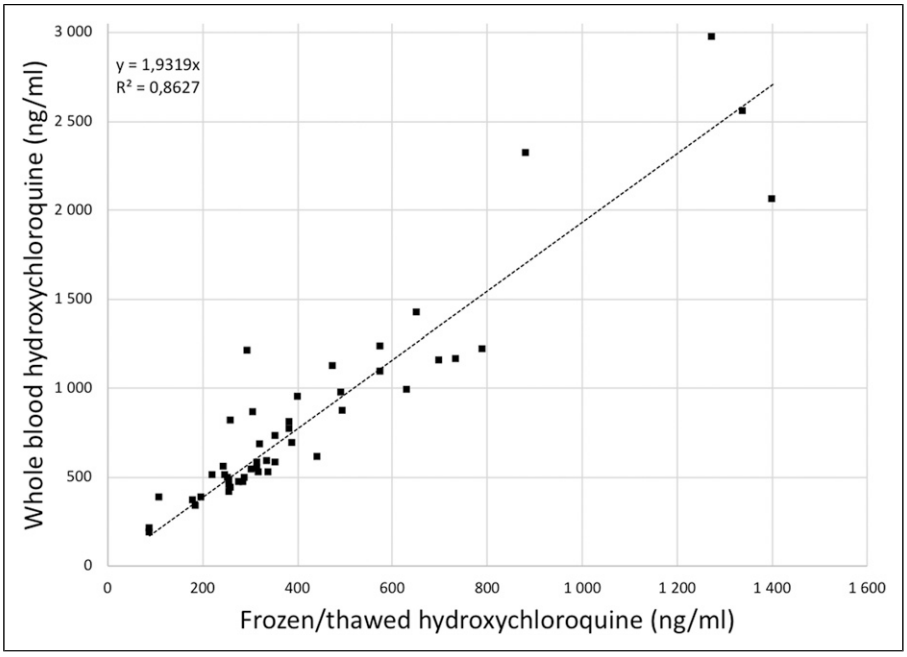

Figure 1. Correlation between frozen/thawed serum and whole blood hydroxychloroquine titers in lupus patients.

retrospectively use serum bank samples to assess chronic nonadherence.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study received financial support from *Cap48 Belgium*.

ORCID iD

Charlotte Anne Baert https://orcid.org/0000-0002-1388-3207

References

1. Costedoat-Chalumeau N, Amoura Z, Hulot JS et al. Low blood concentration of hydroxychloroquine is a marker for and predictor of disease exacerbations in patients with systemic lupus erythematosus. *Arthritis Rheum* 2006; 54: 3284.
2. Blanchet B, Jallouli M, Allard M et al. Hydroxychloroquine levels in patients with systemic lupus erythematosus: whole blood is preferable but serum levels also detect non-adherence. *Arthritis Res Ther* 2020; 22: 223.
3. Carlsson H, Hjorton K, Abujrais S et al. Measurement of hydroxychloroquine in blood from SLE patients using LC-HRMS: evaluation of whole blood, plasma, and serum as sample matrices, *Arthritis Res Ther*, 2020; 22: 125.

Charlotte Anne Baert[1*]
Séverine Nieuwland[1]
Tatiana Sokolova[1]
Farah Tamirou[1]
Frédéric Houssiau[1]

[1]*Service de Rhumatologie, Cliniques Universitaires Saint-Luc et Pôle de pathologies rhumatismales Inflammatoires et systémiques, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Bruxelles, Belgium*

Corresponding author:
Dr Charlotte Anne Baert, Service de Rhumatologie, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Bruxelles, Belgium. Email: charlotte.baert@uclouvain.be