<https://doi.org/10.47660/CBR.2020.17237>

HYDROXYCHLOROQUINE BLOOD LEVELS IN STABLE LUPUS NEPHRITIS UNDER VERY LOW-DOSE HCQ REGIMEN (2-3 MG/KG/DAY): 12-MONTHS PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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BACKGROUND

The American Academy of Ophthalmology (2016-AAO), based on ocular toxicity risk, suggested that hydroxychloroquine (HCQ) daily dose should not exceed 5 mg/kg/day of real body weight. We have previously reported that the prescription of 2016-AAO dose was associated for most lupus patients with a 7-months low risk of flare pattern of HCQ blood levels. However, the minimum HCQ daily dose required to keep an adequate blood level is unknown. The aim of this study was to evaluate if a further reduction in the 2016-AAO dose would sustain 12-months HCQ blood levels in lupus nephritis (LN) patients with stable inactive disease. A rigorous and continuous clinical and laboratorial surveillance, particularly for disease flare was performed.

MATERIALS AND METHODS

A total of 81 LN patients under a prescribed full 2016-AAO dose of HCQ for ≥ 6 months and adequate baseline HCQ blood levels (≥ 613.5 ng/mL) were divided in two groups: one group prescribed reduced 2016-AAO-dose (2–3 mg/kg/day), $n = 36$; and the other group prescribed full 2016-AAO-dose (5 mg/kg/day), $n = 45$. All patients were evaluated at baseline, 3, 6 and 12 months. Hydroxychloroquine blood levels were determined by liquid chromatography-tandem mass spectrometry. Flare was defined as increase ≥ 3 in the SLE disease activity index 2000 and/or change or increase in therapy. Hydroxychloroquine blood cut-off level was divided in inadequate (< 613.5 ng/mL) and adequate (≥ 613.5 ng/mL).

RESULTS

Longitudinal evaluation revealed for the prescribed reduced 2016-AAO-dose group a significant decrease in HCQ blood levels from baseline to 3-months ($1,404.9 \pm 492.0$ vs. 731.6 ± 385.0 ng/mL, $p < 0.01$) and sustained levels at 6 ($p = 0.273$) and 12-months ($p = 0.091$) compared to 3 months. For the full 2016-AAO dose, a significant decrease occurred only from baseline to 12-months ($1,343.5 \pm 521.5$ vs. 991.6 ± 576.3 ng/mL, $p < 0.001$). Frequencies of patients with inadequate levels at 6 months was significantly higher in patients under reduced 2016-AAO than those under full 2016-AAO dose (56% vs. 23%, $p = 0.005$), as well as at 12-months (66% vs 32%, $p = 0.002$). 6-months and 12-months flare frequencies were comparable for reduced and full 2016-AAO dose groups ($p > 0.05$).

CONCLUSION

Our data demonstrated that a prescribed HCQ very low-dose regimen (2–3 mg/kg/day) does not sustain, for most patients, HCQ blood levels within the safe recommended cut-off for flare risk. The full 2016-AAO dose maintained HCQ levels way above this limit during the study.

ACKNOWLEDGEMENTS

We are grateful to all the research subjects for their gentle collaboration. We thank Elaine P. Leon, Margareth B.G. Vendramini and Nicole Fontoura from Laboratório de Investigação Médica 17 (LIM17), Paschoalina Romano, Valdemir M. Carvalho and Divisão

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de Laboratório Central (DLC) – Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil for their support.

FUNDING

This work was supported by grants from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) [#2015/03756-4 to SGP, NEA, CAS and EB; #2017/03983-6 for the LC-MS/MS system; #2017/14352-7 to TNP; and #2019/17272-0 to LVKK] and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) [#303422/2015-7 to CAS; #306879/2018-2 to EFB; and #305242/2019-9 to EB].

DISCLOSURE STATEMENT

The authors declared no potential conflicts of interest.