DOSAGE OF HYDROXYCHLOROQUINE (PLAQUENIL)

ONLINE SURVEY BY PATIENT ORGANISATION NVLE

Z. Osman, W. Zacouris-Verweij, S. Otteren behalf of Lupus APS committee. Lupus APS committee, NVLE patient association, Utrecht, Netherlands

Background: Hydroxychloroquine (HCQ) has been proven effective in several immune mediated diseases. Long-term use of HCQ is very common in patients with systemic autoimmune disease. The greatest advantage of HCQ is that it may reduce the risk of flares and thereby allow glucocorticoid dose reduction. The risk/benefit ratio of HCQ is excellent but HCQ is also known for its potentially severe and fortunately rare side effect: retinal toxicity. In The Netherlands, there are no standard guidelines regarding the dosing of HCQ and ophthalmologic screening of HCQ-induced complications. The American Academy of Ophthalmology (AAO) has recently published their revised recommendations on screening and dosing of HCQ. Risk of retinal toxicity is mainly determined by the two most important risk factors: daily dose of HCQ (mg/kg/day) and duration of HCQ therapy (years). The AAO recommends a maximum daily HCQ dosage of <5.0 mg/kg real weight, to reduce the risk of toxicity.

Objectives: To raise more attention for the revised recommendation of the AAO, our patient organisation started an online survey asking patients with (systemic) autoimmune diseases which dose of HCQ (mg) they take on a daily basis.

Methods: Patients in the Netherlands were given the opportunity to complete the online survey at the website of the NVLE (Dutch patient association for people with Lupus Erythematosus, Anti-Phospholipid Syndrome, Systemic Sclerosis and Mixed Connective Tissue Disease) from July 26th – November 18th, 2017. The promotion of the survey took place solely through Social Media with a link to the survey. A total of 24 questions had to be filled in to complete the survey. Each individual was asked to write down their real weight (kg) for calculating the daily HCQ dosage (mg/kg/day).

Results: A total of 705 individuals completed the online survey. The daily dosage (mg/kg/day) available from 645 patients. The majority were females (n=645) and diagnosed with (systemic) lupus erythematosus (n=519). The average dosage of HCQ was 4.50±1.68 mg/kg/day. The daily dosage of 5 mg/kg exceeded by 258 of the patients (40%). Eighty-one individuals (12.6%) used a daily dosage of >5 mg/kg for more than 10 years. The most reported HCQ-induced complications were gastrointestinal complaints (n=55), problems with vision (n=43), and nausea (n=32).

Conclusions: Patients (and prescribing physicians) should be informed about risk of toxicity, proper dose levels, and the importance of regular annual screening. Physicians prescribing HCQ must aim for a daily HCQ dosage of less than 5.0 mg/kg/day, especially for patients using HCQ for already more than 10 years. (Inter)national guidelines regarding the screening and dosing of HCQ should be provided by the authorities to secure patient safety and reduce the frequency of (severe) retinal complications.

REFERENCE:

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**DOES UNDERSTANDING SLE MATTER TO DISEASE ACTIVITY IN SLE PATIENTS?**

A.S. Meara, P. Hackenberger, J. Yedimenko, C. Rodman, S.P. Ardoin, E. Peters,
Division of Immunology and Rheumatology; College of Medicine; Internal Medicine, The Ohio State University; The Department of Medicine; Department of Psychology, The Ohio State University, Columbus, USA

**Background:** Systemic lupus erythematosus (SLE) is a heterogeneous disease with high morbidity and mortality with complex long-term treatments. These dynamic treatments can be daunting especially to the 25%–60% of SLE patients who have cognitive and neuropsychiatric deficits. Patients lacking understanding of their own baseline health status and treatment options cannot effectively collaborate in making informed choices with their physicians.

**Objectives:** This project aimed to identify SLE patients’ comprehension of their medication regimens and disease outcomes in relation to standard markers of disease activity (SLEDAI) and damage (SLICC DI).

**Methods:** Patients >18 years were recruited from The Ohio State University (OSU) Lupus Vasculitis Glomerulonephritis (LVG) clinic. An IRB-approved 25-item true/false disease questionnaire was administered to 75 SLE patients who provided informed consent. Individual question and composite scores for each patient were correlated with their SLEDAI and SLICC DI scores. To our knowledge, a disease comprehension questionnaire has never been used in lupus patients.

**Results:** 75 SLE patients completed the comprehension questionnaire. Lower comprehension was associated with greater disease activity (r = –0.14), while no correlation was found between composite score and disease damage (SLICC DI) (r = –0.03). Figures 1 plot the comprehension composite scores against the SLEDAI. P values were not significant, but tending to correlate with the r. Evaluation of individual questionnaire items demonstrated: approximately 80% of patients did not associate heart disease with lupus, over 25% of patients did not recognize the side effects of prednisone, and over 15% of patients did not know lupus affects bone health.

**Conclusions:** These preliminary results suggest that patients with more understanding of their SLE diagnosis, comorbidities, and treatments had less measured disease activity. The comprehension questionnaire and SLEDAI characterise patients in their present disease state, so this correlation likely reflects the evolution of patient understanding and the fluctuating nature of their disease. Additionally, higher disease activity scores represent more severe disease, which could be associated with greater neurocognitive deficits leading to poorer scores on the comprehension questionnaire. The lack of correlation between composite score and SLICC DI is likely attributed to the discrepancy between a metric evaluating current knowledge and a long-term indicator that may derive from decisions made when patients’ comprehension was different than current. These initial results are promising and may represent a cost-effective opportunity for physicians to evaluate and address their patients’ comprehension gaps in an effort to improve shared decision making. However, more data are needed to test the robustness of these trends.

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**BLOOD CONCENTRATIONS OF COMPLEMENT SPLIT PRODUCT IC3B AND SERUM C3 ASSOCIATE WITH SLE DISEASE ACTIVITY**

A.H. Kim, V. Strand, D. Sen, Q. Fu, N. Mathis, M. Schmidt, R. Bruchas, N. Staten, P. Olson, C. Stilling, J. Atkinson, Rheumatology, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, Saint Louis; Immunology and Rheumatology, Stanford University School of Medicine, Palo Alto; Epidemiology and Biostatistics, Saint Louis University, Kypha, Inc., Saint Louis, USA

**Background:** The complement system plays a central role in systemic lupus erythematosus (SLE). Since complement activation occurs during SLE flares, complement products are predicted to be consumed with concomitant generation of activation-derived products at a rate proportional to the degree of disease activity. However, interpretation of values may be confounded due to the unknown impact of increased acute phase production of C3 and C4, as well as in individuals with low C4 gene copy number who have persistently low serum C4.

**Objectives:** To examine correlations between blood levels of complement split product iC3b and serum component C3 with clinically meaningful changes in disease activity in patients with SLE.

**Methods:** 159 consecutive subjects with American College of Rheumatology or Systemic Lupus International Collaborating Clinics classified SLE were enrolled into CASTLE (Complement Activation Signatures in Systemic Lupus Erythematosus), a prospective observational study. Patients with 1–7 study visits were included in this longitudinal analysis. 48 healthy volunteers were enrolled to establish the normal reference range of iC3b/C3. Serum C3 and C4 were measured by nephelometry. Blood levels of iC3b were assessed by a lateral flow assay. SLE disease activity was monitored utilising the Systemic Lupus Erythematosus Disease Activity Index 2K Responder Index-50 instrument.

**Results:** iC3b/C3 ratio, double-stranded (ds)DNA antibodies (Abs), and super-physiologic prednisone dose (>7.5 mg/day) each independently correlated with SLE disease activity employing multilevel multiple logistic regression analysis. Only iC3b/C3 was significantly associated with clinically meaningful improvements in disease activity among subjects receiving supraphysiologic doses of prednisone (high disease activity). iC3b/C3 outperformed C3 and C4 levels in discriminating both active versus inactive SLE disease and major flares versus no disease activity (figure 1). Finally, iC3b/C3, dsDNA Abs, ESR, and supraphysiologic prednisone dose were independently associated with lupus nephritis, while none were associated with SLE rash.

**Conclusions:** Blood iC3b/C3 ratio correlates with SLE disease activity and clinically meaningful improvement in disease activity. Furthermore, it discriminates between active versus inactive SLE, and major flares compared to those patients without disease activity.

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