AMERICAN COLLEGE OF RHEUMATOLOGY

POSITION STATEMENT

SUBJECT: Screening for Hydroxychloroquine Retinopathy

PRESENTED BY: Committee on Rheumatologic Care

FOR DISTRIBUTION TO: Members of the American College of Rheumatology
Medical Societies
Centers for Medicare and Medicaid Services
Managed Care Organizations/Third-Party Carriers
Arthritis Foundation

POSITIONS

1. Patients treated with hydroxychloroquine should have access to periodic eye examinations both at baseline and over the duration of therapy to allow for early recognition of potential retinal toxicity.
2. Examinations should take advantage of technologies with the potential to detect retinopathy before patients recognize visual loss.
3. The timing and extent of surveillance monitoring should take into account individual risk factors for toxicity related to hydroxychloroquine use.

BACKGROUND:

Hydroxychloroquine (HCQ, brand name Plaquenil) is commonly used for the long-term management of a variety of chronic rheumatic diseases including systemic lupus erythematosus and rheumatoid arthritis. A range of potential toxicities related to HCQ use have been reported but in general the drug is well tolerated and serious toxicity is unusual (1).

One of the most important sites of potential HCQ toxicity is the retina. Early retinal toxicity, characterized by paracentral scotoma, usually goes unnoticed by patients. However, more advanced toxicity, characterized by foveal damage, is associated with paracentral and eventually central vision loss. Unfortunately, HCQ-related toxicity in the retina may not be reversible and may progress even after the drug has been discontinued.

Progression of retinal toxicity, including progression following the cessation of therapy, is associated with diffuse macular damage. However, detailed analysis in a limited number of patients indicates that “detection of retinopathy at an early or moderate stage...effectively limits postdrug progression and prevents major foveal damage” (2, 3). The purpose, therefore, of periodic eye exams in patients taking HCQ is to recognize toxicity, if it occurs, at the earliest possible stage. Toward this end, the American Academy of Ophthalmology (AAO) has published guidelines for retinal toxicity monitoring (4, 5).
Recent studies suggest that retinal toxicity may occur more frequently than previously recognized, further highlighting the need for regular screening. Initial studies using a variety of detection methods estimated the risk between 0.5-0.65% in long-term users (6-8) and found the incidence of retinopathy to be associated with the duration of therapy, increasing to 1.0% and then 2.1% after 10 and 15 years of therapy, respectively (8). In a more recent study of 2361 patients that made use of visual field testing or spectral-domain optical coherence tomography (SD-OCT), the prevalence of retinopathy was found to be much higher. Overall prevalence in this study was 7.5% and increased with dose and the duration of therapy (9).

Appropriate dosing of HCQ to avoid toxicity is an area of some uncertainty. Previous recommendations by the AAO to limit HCQ dosing to 6.5 mg/kg of ideal body weight have been revised to 5 mg/kg of actual body weight (5). Some authors recommend 6.5 mg/kg of actual body weight with a cap at 400 mg per day and further adjustments for renal insufficiency (10). To date, there are no data demonstrating that monitoring blood levels of HCQ is useful in dosing HCQ to prevent retinal toxicity.

In addition to dose and duration of therapy, other factors must be considered when prescribing HCQ and making recommendations about monitoring. Co-existing conditions such as macular degeneration, retinal dystrophy and cataracts may increase susceptibility to HCQ toxicity and/or complicate the interpretation of monitoring exams. Reduced kidney function and concurrent use of tamoxifen have also been identified as risk factors for retinopathy (9). Asian patients demonstrate an early pattern of retinal toxicity that is different from patients of European descent and thus monitoring exams in Asian patients should be adapted accordingly (5). Further research to identify other risk factors including genetic predispositions for HCQ-associated toxicity is underway.

Patients beginning therapy with HCQ should be informed of potential adverse drug reactions including retinal toxicity and that periodic monitoring and early recognition can limit the impact of macular toxicity. All individuals starting these drugs should have a complete baseline ophthalmologic examination within the first year of treatment including examination of the retina with a dilated exam and visual fields by an automated threshold central visual field test (Humphrey 10-2). If available, objective testing such as multifocal electroretinography (mfERG), SD-OCT, or fundus autofluorescence testing (FAF) is also recommended. Examination by Amsler grid is no longer recommended as it has been deemed too dependent on patient interpretation.

If the patient is considered low risk and baseline examination results are normal, the AAO has recommended that no further specialized ophthalmologic testing for HCQ toxicity is needed for 5 years. Some ophthalmologists and optometrists may elect to screen more often based on the patient’s risk factors. For patients who are considered high risk, based on the above risk factors or others that may be determined, annual eye examination is recommended without the 5 year gap. If any abnormality is detected by Humphrey 10-2 testing or retinal examination, follow up with the previously mentioned objective testing is imperative.

If toxicity is suspected or demonstrated, ideally the HCQ should be stopped. However, there are situations when this is not straightforward, e.g., when toxicity is early and the diagnosis of
maculopathy is tenuous, the treatment with HCQ has been very effective, and alternatives to HCQ are undesirable. Under such circumstances, the rheumatologist, ophthalmologist and patient must reach a collective decision to stop the drug or cautiously continue therapy with close monitoring, with the knowledge that some vision could be lost.

Appropriate standards for addressing potential retinopathy from HCQ in children and adolescents have not been sufficiently addressed in the literature. Retinal abnormalities or new interference with vision (including color vision) can be an indication of toxicity and should be discussed with the consulting ophthalmologist on an urgent basis. Use of HCQ in children younger than 7 years of age may be limited by difficulty in obtaining satisfactory evaluation of vision in this age group. For this reason, the pediatric age group should receive an annual examination, as a minimum standard of care, until definitive studies in children indicate that increasing this monitoring interval is appropriate.

Approved by the Board of Directors: 03/03, 05/06, 8/10, 8/11, 08/16

REFERENCES