What You Should Know About Plaquenil (Hydroxychloroquine) Retinopathy

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Plaquenil (generic name hydroxychloroquine) is a drug developed in World War II as a prophylaxis and treatment for malaria that plagued allied soldiers in the Pacific theater.[1] It worked well in that role, but as an unexpected side benefit, soldiers with autoimmune diseases such as arthritis who took the drug noted improvement in their condition. From this observation, the hypothesis that it might be a treatment for these diseases developed. Subsequent clinical trials confirmed its efficacy and the drug has been a mainstay of rheumatologic therapy ever since. Unfortunately, in some patients retinopathy develops as a toxic side effect that is irreversible. For this reason, patients taking plaquenil in the United States are screened at intervals to detect the problem. In fairness, it should be noted that the expert committees of other countries, such as the United Kingdom and others, have decided not to screen patients as an official policy, deciding that the risk is too small to commit the scarce financial resources available in those nations to that purpose.

Risk Factors

The most important risk factor predisposing to development of plaquenil retinopathy is taking too high a dose.[2] Dosage should be adjusted to match lean body weight. It is common for patients to be prescribed 400 mg/d, but patients who are less than 5 feet 3 inches tall should not take this much, nor should patients weighing less than 135 pounds. Plaquenil is not distributed in the fat of the body, but only in the lean tissues, thus safe dosing is predicated on what has been termed ideal body weight, which is determined by height. Tables exist that provide conversions from height to ideal body weight.[3] If a patient is overweight, the ideal body weight, not the actual body weight, is used for appropriate dosing. If the patient is thin, the actual body weight should be used. Other risk factors are age (older confers more risk), cumulative dose over the years (higher confers more risk), pre-existing retinal disease (e.g. macular degeneration), and presence of renal or liver disease. It is possible to develop plaquenil retinopathy if dosing is appropriate, but it is much less common than if toxic dosing is undetected and allowed to continue.

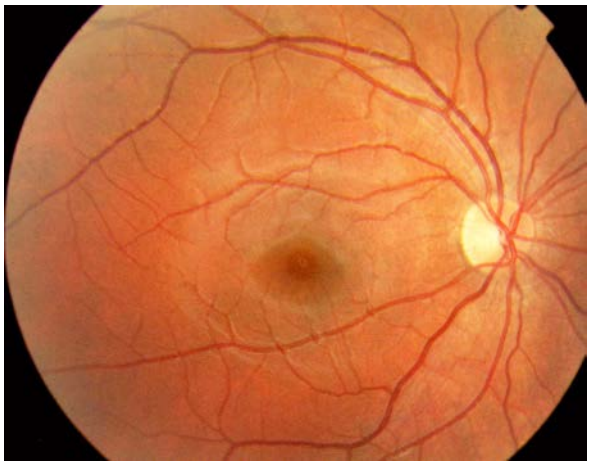
What Is Screening?

The single most important part of screening is a calculation by the eye doctor that the daily dosing is nontoxic. The daily dose should not exceed 6.5 mg/kg/d of plaquenil. If toxic dosing has been prescribed, the ophthalmologist will need to contact the prescribing internist to see if a reduction in dose to one less likely to cause retinopathy is possible. The eye doctor does not unilaterally change the plaquenil dose, but only begins a conversation on the subject with the patient and the internist. Dose reduction, or cessation if toxicity is discovered, arises from this team discussion with the internist and patient having the lead roles. After dose checking, the screening examination includes pupillary dilation and careful examination of the retina. Fig. 1 shows what a normal retina looks like, and fig. 2 a retina with plaquenil toxicity. Ancillary tests are necessary, as visible fundus changes are a late sign of toxicity.[4] At a minimum, a 10-2 visual field test is done to detect blind spots near the center of the visual field. If available, multifocal electroretinography, spectral domain optical coherence tomography, and fundus autofluorescence photography can be helpful, because they are somewhat more objective than visual field testing.

How Often Should Screening Be Done?

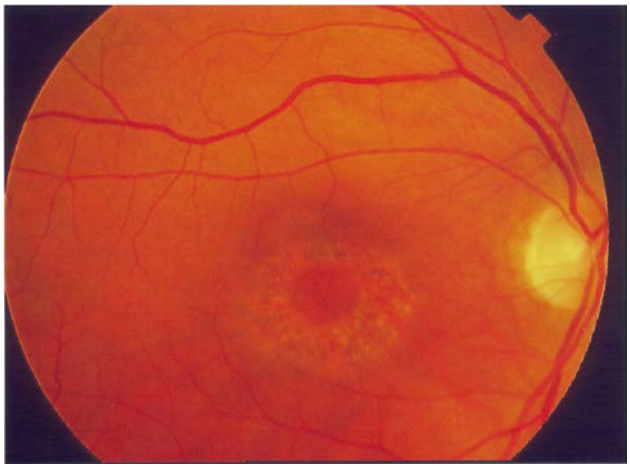
Before beginning plaquenil, a baseline examination should be done. Thereafter, it is appropriate to have a yearly examination.[2] The American Academy of Ophthalmology guidelines state that patients with no risk factors can defer a follow-up screening examination for 5 years, but this is an impractical recommendation as judged by practitioners, who do not abide by it.[5,6]

Fig. 1 Normal Fundus



Legend: Normal appearance of the macula

Fig. 2



Legend: Appearance of the macula in plaquenil retinopathy

Final Comments

Plaquenil retinopathy is irreversible in most cases. Therefore, preventing the condition through safe dosing is the first priority, and detection of the earliest sign of retinopathy through the use of screening with sensitive testing is the second. With attention to the details presented above, it should be extremely rare to develop the condition. If you have questions after reading this brochure, more in-depth research on your own is possible through the PubMed website of the National Library of Medicine, http://www.ncbi.nlm.nih.gov/entrez/query.fcgi. You can also submit a question online at the home page (click on Contact) of my website www.retinareference.com.

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