

Evaluating Hydroxychloroquine Toxicity With Multifocal Electretinography

Toxicity first affects small areas of the retina.

BY DONNELL J. CREEL, PhD

The antimalarial medications chloroquine and hydroxychloroquine are also prescribed to treat discoid or systemic lupus erythematosus, rheumatoid arthritis, dermatologic inflammation, and Sjögren syndrome, which together affect an estimated 7 million Americans. Chloroquine retinopathy presents as a characteristic “bull’s-eye” appearance of the macula, producing a ring scotoma in the field of vision. Figure 1 is an image of an ocular fundus using autofluorescence to designate an area of retinal damage.

To detect chloroquine toxicity, the American Academy of Ophthalmology recommends performing fundus examinations, 10-2 automated visual fields, and at least one objective test: multifocal electroretinography (mfERG), fundus autofluorescence imaging, or spectral-domain optical coherence tomography (SD-OCT).¹ By contrast, Amsler grid testing, color vision testing, fluorescein angiography, full-field ERG, and electro-oculogram are not considered to be helpful.¹⁻³ mfERG is a sensitive, objective, and reproducible test for detecting hydroxychloroquine toxicity.

Several drugs taken in high doses or for long periods of time can cause retinal degeneration with pigmentary changes. Culprits include thioridazine (Mellaril; Novartis, withdrawn from market worldwide 2005), chlorpromazine (Thorazine; GlaxoSmithKline, and generic formulations), Vigabatrin (aka gamma-vinyl-GABA: Sabril; Lundbeck, and generic formulations), and chloroquine and hydroxychloroquine (Plaquenil; Sanofi, and generic formulations).

The effects of toxic medications can be detected and quantified using ERG. Which type of ERG to apply

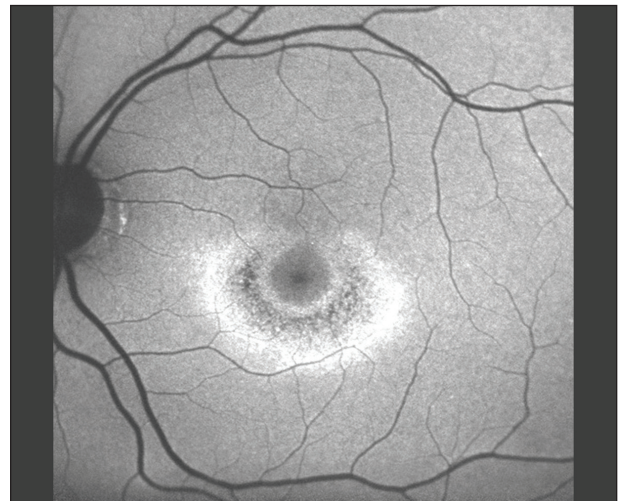


Figure 1. Fundus photograph using autofluorescence to better designate retinal damage in the macula. This example depicts late-stage severe toxic effects.

depends on the mechanism and site of retinal toxicity. Identifying retinal toxicity due to chloroquine or hydroxychloroquine is a pertinent application of mfERG.

SIGNS OF TOXICITY

Plaquenil toxicity first affects small areas of the retina between 5° and 15° from the fovea. Figures 2 and 3 show three patients at different stages of toxicity. Figure 2 bottom right shows a color display of normal mfERGs. The amplitude of the mathematically derived b-wave of the mfERG is displayed in a color scale. White represents

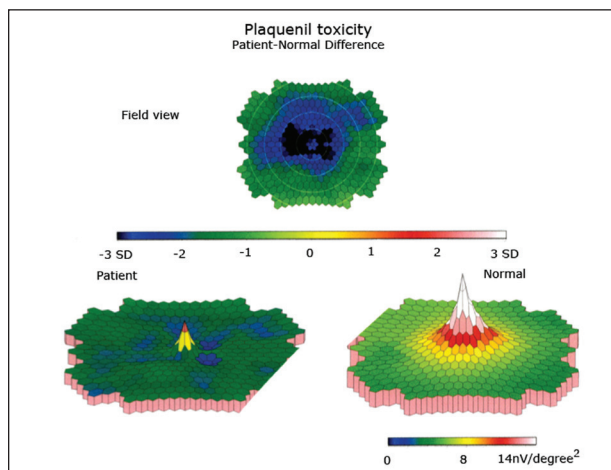


Figure 2. Color display of mfERGs indicating areas of significant macular damage from hydroxychloroquine toxicity. Bottom right is color display of normal mfERGs. The scale is the amplitude of the mathematically derived b-waves of the ERG displayed in color. Maximum amplitude is white. Area of no measurable b-wave is black.

maximum b-wave amplitude, and black indicates no measurable b-wave. Clinically, areas that map black usually represent blind spots to the patient, and dark blue reflects areas of blurry vision.

In Figure 2 to the left of the normal mfERGs, the color display shows areas of decreased mfERG amplitudes throughout the central macular area. The top color display shows an enhanced version of field loss created by subtracting the patient's mfERGs from the normal image. This patient was prescribed 2.5 times the maximum recommended dose of 400 mg/day. Toxicity was detected recording mfERGs within 4 months of initiating this dose. The patient recovered almost completely after the drug's cessation. If toxicity is detected early, some patients recover.

It should be noted that the recommended dosing of 6.5 mg/kg/day is based on ideal weight, not actual weight. For women, ideal weight is 100 lbs for 5 ft height, plus 5 lbs per extra inch of height. For men, ideal weight is 110 lbs for 5 ft height, plus 5 lbs per extra inch of height.

The American Academy of Ophthalmology guidelines recommend a baseline examination for patients starting these drugs to serve as a reference point; and to rule out maculopathy, an annual screening after 5 years of use unless there is suspicion of toxicity or presence of unusual risk factors. I recommend obtaining a screening mfERG within 4 to 6 months of starting medication for early detection of patients susceptible to toxicity, such as the patient illustrated in Figure 2. Consider

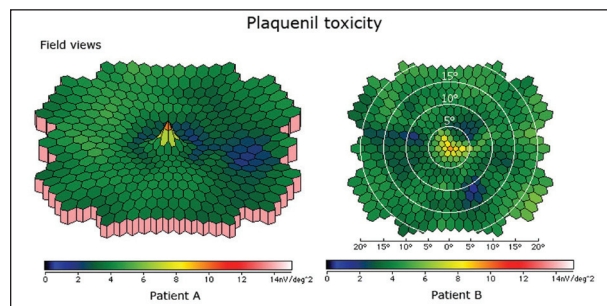


Figure 3. Color display of mfERGs of two patients, A and B, at different stages of toxicity. Patient A shows the more severe expression of damage ringing the foveal area. Patient B shows an earlier stage of toxicity with islands of retinal damage in areas 5° to 15° from the fovea.

that elderly patients can be more susceptible to toxicity, as can those with kidney or liver disease, and those with retinal disease.

Figure 3 shows two patients at different stages of toxicity. Patient A exemplifies the more severe expression of toxicity, displaying a conspicuous ring of depressed retinal function. Patient B shows a less severe stage of toxicity with small islands of retinal damage in the areas 5° to 15° from the fovea.

CONCLUSION

Chloroquine or hydroxychloroquine can cause retinal dysfunction detectable using mfERG before toxicity is clinically apparent.

Articles in the medical literature address how to record mfERGs.^{4,5} Scan the QR code in this article to view a video on EyetubeOD. ■

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