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RETINA FOCUS:

HOW DO YOU KNOW IF TREATMENT IS WORKING?

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Determining the effectiveness of treatment in a patient with suspected retinal pathology can be challenging. While visual acuity can serve as a benchmark, vision gains do not necessarily correlate with improvement in structure or global function. Despite the array of diagnostic modalities available to the eye care expert, very few of them deliver actionable information that is helpful in deciding if treatment is working, when to change course, or perhaps even when to cease treatment because risks outweigh the potential benefits.

The Need for Objective Metrics

In the busy clinical setting, clinicians need access to objective, quantitative information that will allow them to quickly determine whether the intervention they are using is having the intended effect. Because it measures electrical responses within the retina—cone cells in particular— flicker electroretinography (ERG) provides objective information about global retinal function. Flicker ERG tests have demonstrated the ability to detect retinal dysfunction in eyes with diabetic retinopathy (DR),[1,2] branch (BRVO) and central retinal vein occlusion (CRVO),[3,4] and uveitis,[5] among others. Flicker ERG also has prognostic value that is relevant for:

- staging diabetic retinopathy[6-8]
- predicting the development of ischemia secondary to CRVO[9]
- managing patients with uveitis[10,11]

Independently, each of the aforementioned applications of flicker ERG help build an impression about the health of the retina that is applicable to a variety of common pathologies seen by eye care experts. Armed with this knowledge, the clinician gains confidence in his or her treatment decision making process. Objective, quantifiable data is an invaluable asset when tracking progression and response to treatment in all types of cases, and especially so when results of other diagnostics and clinical tests are inconclusive.

Tracking Progression and Improvement

Yet, there is a more direct link between flicker ERG and its ability to affect treatment decisions. A multitude of research has shown that flicker ERG detects improvement in global retinal function after treatment, including in eyes with DR.[12] Other clinical variables, including visual acuity testing and OCT, are valuable in assessing patients' status, but they do

not provide conclusive evidence about the effect of treatment.

For instance, there is often a disconnect between reductions in macular thickness on OCT and visual acuity gains, and in some cases, patients may exhibit visual acuity gains despite prolonged edema on the macula. Additionally, progression on OCT images indicates structural loss that is irreversible – once cells are dead, they do not come back to life. On the other hand, flicker ERG can detect improvement in retinal function after injection of anti-VEGF,[12] information that is important for determining the next treatment interval, or, if there is no response, whether a switch to a different approach is warranted.

Predicting Progression and Outcomes

A similar paradigm exists in the treatment of CRVO. As noted earlier, flicker ERG can be used to detect and characterize ischemia and predict neovascularization with a greater degree of accuracy than angiography.[3,4,9,13] In addition, current analysis of angiographic findings are limited to the doctor's subjective interpretation; whereas results from electrophysiology tests are objective. Such quantitative metrics may spur a decision to initiate or increase the intensity of treatment to ward off ocular hypertension and potential irreversible vision loss.[14] Moreover, flicker ERG strongly correlates with VEGF concentration within the eye, thereby serving as an index for the efficacy of attempted VEGF blockade with intravitreal anti-VEGF agents.[15,16]

Uveitis is often considered a confusing clinical entity with many intersecting variables to consider. Use of the flicker ERG test can help determine the level of retinal dysfunction,[5,10] as well as predict which patients are likely to respond to anti-inflammatory therapy.[11,17] In fact, flicker ERG is considered to be a gold standard for monitoring the activity of a posterior uveitis entity, Birdshot Chorioretinopathy.[11,17]

Current methods of assessing activity in uveitis such as acuity, OCT, fields and assessment of clinical haze are variable across the uveitis spectrum. For example many choroidititides may not cause vitreous haze.

A drop in acuity may be the terminal event in the long course of a chronic inflammatory eye disease. Other methods of assessing activity and disease burden are urgently needed.

Because Diopsys increases patient access to electrodiagnostics, several uveitis entities can now be assessed for activity, and indeed treatment response, using flicker. The future for monitoring treatment now looks promising for these sight threatening conditions.

Fundamentally, a determination about whether a given treatment approach is working must consider several variables. Classic diagnostics and evaluations may be additive to the clinical impression; however, the process can be greatly facilitated by the availability of quantifiable, objective data about the function of the retina. As a measure of global retinal function, flicker ERG provides information that helps inform treatment decisions in a number of common pathologies.

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This article represents the experiences and opinions of William Ayliffe, FRCS, PHD. Physicians should make medical decisions based on the individual facts and history of each patient.