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Exam room, chair side evaluation of retinal edema: Improving accuracy and precision for identification of subclinical diabetic macular edema

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Abstract

BACKGROUND: Early detection of diabetic macular edema (DME) is important for improving patient outcomes. Currently, the gold standards are slit lamp stereo biomicroscopy examination and fluorescein angiography (FA). Detecting DME with a slit lamp is subjective and can be difficult in the early stages of the disease. FA is invasive and involves discomfort and risk to the patient. A new diagnostic test, the Heidelberg Retina Tomograph (HRT) Retina Module (Heidelberg Engineering, Heidelberg, Germany), is noninvasive, objective, and sensitive to early changes in the retina. It is purported to locate and quantify retinal edema such as DME, independent of retina thickening. Presented are a series of case reports comparing retinal photography, FA, HRT, and ocular coherence tomography (Stratus OCT; Carl Zeiss Meditec, Jena, Germany) results on patients with DME. The purpose is to determine the clinical utility of the HRT for discerning DME compared with clinical stereo biomicroscopy impression and FA.

CASE REPORTS: In this representative case series, the author's first stereo biomicroscopy impression, macular photographs, retinal fluorescein angiographs, Stratus OCT images, and HRT Retina Module images from 5 type 2 diabetic patients (3 insulin and 2 non–insulin dependent) with retinopathy are presented. All patients are men, with a mean age of 56.4 (range, 51 to 62). Subjects had diabetes mellitus type 2 for an average of 14.4 years (range, 10 to 22) and were experiencing fluctuations or loss in vision. In all cases, DME was clearly identifiable on FA although sometimes questionable by stereo biomicroscopy. Nonstereo retinal photos and OCT examinations were inconclusive or unremarkable in 4 of 5 cases. The HRT Edema surrogate "e" index and map results showed areas of DME that were very similar to those of the FA images.

CONCLUSIONS: In this case series, the HRT Retina Module provided useful clinical information on DME patients including the quantification and extent of both subclinical and clinically significant DME. Although more rigorous study is warranted, such immediate feedback from a noninvasive, safe, diagnostic tool is invaluable in clinical practice, particularly with the advent of prophylactic nutritional genistein-based multivitamin supplements such as Bausch & Lomb Ocuvite DF (Rochester, New York).
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Diabetic macular edema (DME) is a frequent complication of diabetes, developing in at least 14% to 25% of patients with diabetes, depending on age of onset and use of insulin.[1] It is the leading cause of decreased vision from diabetic retinopathy (DR).[2] Minor, early DME often goes undetected and gradually worsens, with the underlying retinopathy progressing to minor blood vessel leakage and, finally, to the more severe and difficult-to-treat condition of proliferative diabetic retinopathy (PDR) with retinal thickening and intraretinal cystoid spaces.

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Even successful treatment of DR generally results in some vision loss. Unfortunately, patients can reach the stage of irreversible visual loss from DR with relatively few symptoms, making it no surprise that DR is the leading cause of blindness in the working-age population in developed countries such as the United States.[3]

Early detection of DR and DME can substantially reduce the risk of visual impairment and blindness caused by diabetes.[4] A referral can be made to the patient's primary care physician or endocrinologist, who will likely recommend changes in diet and exercise, medications, or both, that can result in better control of the diabetes and that may delay the onset or slow the progression of DR.[5,6] For example, the recent addition of an oral genistein-based multivitamin to address both prophylaxis and treatment of DME and diabetic ocular health can further assist optometrists in addressing the unmet needs of diabetic patients. This is especially true for those with subclinical or mild DME, in which traditional laser therapy (focal or diffuse) may be medically inappropriate. Bausch & Lomb (Rochester, New York) introduced Ocuvite DF in June 2007. This is a genistein-based diabetic eye vitamin supplement with anti-edema properties. The components of this supplement (soy-based genistein, alpha lipoic acid, vitamins C, E, B1, B3, and B6) have been found in scientific studies to reduce vascular dysfunction, oxidative stress, and age-related glycosylation (AGE) end products.[7]

In addition to being indicative of DR, in some cases macular edema may also be indicative of a branch vein occlusion or, less commonly, advanced hypertension, which could benefit from earlier referral to the primary care physician as well.[8] If needed, improving the hemoglobin A1c (HbA1c) and early laser treatment by a retinal specialist can be effective at stopping minor leakage from progressing to proliferative retinopathy. Clinical outcomes from laser photocoagulation are much better, and the risk of visual loss is less if patients are screened and treated early.[9,10]

The primary barrier to early diagnosis of DME is the paucity of diagnostic options. Dilated 7-field stereo photography is a time-consuming endeavor involving multiple pairs of images, photographic or digital. Standard ophthalmoscopic examination is subjective and has only moderate sensitivity and specificity for edema.[11] Fluorescein angiography (FA) has been able to show early edema or "preretinopathy" in 21% to 42% of diabetic adults who had results that were considered negative for retinopathy with other methods.[12,13] Compared with standard retinal photography, FA is better able to detect subtle DME as the fluorescein leaks from retinal capillaries.[14]

FA is not a test typically provided in an optometric setting. The lack of digital fluorescein angiography equipment as well as staff training in this diagnostic test necessitate referral elsewhere. There are also good reasons for clinicians to delay FA. FA is an invasive diagnostic test that carries a limited but real risk of an anaphylactic reaction to sodium fluorescein. In at least 7 reported cases, patients have died from anaphylactic shock after fluorescein administration. Serious or life-threatening reactions have been estimated to occur in 1:1,900 to 1:22,000 procedures,[15,16] and clinicians have been cautioned not to administer this diagnostic test unless they are equipped to handle acute anaphylaxis.[17] At the very least, FA causes discomfort and sometimes nausea or vomiting for patients undergoing the procedure.[18,19] Finally, in addition to the risks and discomfort, FA is a staff-intensive procedure for practices and a costly one for patients or their insurers. For all these reasons, an equally effective but safer and more convenient surrogate for FA would be quite valuable in clinical practice.

Evidence from recent clinical studies suggests objective information from retinal imaging devices can provide useful clinical information on DME.[20-29] Studies investigating edema detection with the Heidelberg Retinal Tomograph (HRT) Retina Module (Heidelberg Engineering, Heidelberg, Germany) have found good agreement with clinical assessment,[20-22] and some research suggests DME may be identified before clinical stereo biomicroscopy detection.[20-23]

In this case series, the author compares his stereo biomicroscopy impression with several types of images obtained for 5 consecutive type 2 diabetic patients with retinopathy during a 2-month period in 2005. For all 5 patients, standard retinal photographs and central retinal fluorescein angiographs were compared with 2 new types of noninvasive imaging devices, HRT and Stratus OCT (Carl Zeiss Meditec, Jena, Germany), that have shown potential as possible surrogates for FA.

The Stratus OCT uses low coherence interferometry and utilizes the echo time delay of backscattered light from a super-luminescent diode to differentiate various retinal layers. Software algorithms are used to detect the boundaries of these retinal layers and then convert them into thickness measurements. Information from 6 radial B scans is averaged into a thickness map. A color-coded map of the retinal thickness is provided, and a normal eye will be displayed as blue centrally. Hotter orange and red colors indicate greater thickness. Sector averages are displayed with numerical values indicating average thickness of each sector, and colors within each sector indicate comparison with normative data. Map diameters are typically 1 mm, 3 mm, and 6 mm. The Stratus OCT has been shown to detect DME.[24,26-29]

The HRT utilizes confocal scanning laser ophthalmoscopy to analyze the optic nerve and nerve fiber layer. The Retina Module for the HRT evaluates retinal fluid (hydration) in the macula but not cross-sectional tissue structure. This module provides edema maps that are purported to locate and quantify DME, independent of retina thickening. (The newest version of this software, not available at the time of this study, however, also provides retinal thickening measurements, 3-dimensional surface topography, and combined edema and retinal thickness maps.)

The HRT device utilizes a fast 24-msec confocal laser scan. Three images, each derived from 64 such scans, provide data redundancy for the software algorithm to process and result in a single image largely free of ocular movement artifacts. The Heidelberg TruTrack technology further utilizes 10 anatomic retinal landmarks for exact