The Most Sensitive Test for Diagnosing Early Diabetic and Pre-Diabetic Neuropathy Comes to Your Office.

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Neuropathic pain is one of the most common reasons for a patient to seek medical attention. Often burning, tingling, numbness or pain in the feet can precede the diagnosis of diabetes or impaired glucose tolerance by years. It is perhaps in these early stages of neuropathy that our opportunity to intervene is at its greatest. Yet nerve conduction studies (NCS) and electromyography (EMG) can detect only half of all neuropathies related to impaired glucose tolerance. Over the past 10 years a new technique that involves a simple 3 mm punch biopsy has evolved which can detect over 87% of all neuropathies. This technique, called Epidermal Nerve Fiber Density. Testing (ENFD), is simple and can be performed in your office in just a few minutes ENFD testing provides objective evidence for end organ damage. In addition serial biopsies can track the effectiveness of therapy, be it exercise, diet, nutritional, or prescription meds. We believe skin biopsies for evaluation of ENFD should be incorporated into the evaluation of patients at risk for neuropathy.

The ability to quantify the number of small unmyelinated nerves in the epidermis has been a powerful research tool for over two decades. Initially available only at specialized centers, ENFD testing is now readily available through several commercial laboratories and covered by Medicare and the vast majority of commercial payors.

What Does the Test Entail?

ENFD testing involves taking a small 3 mm skin punch biopsy. This technique is easily learned, minimally invasive, and requires a superficial injection of lidocaine. No sutures are needed. The biopsy is only slightly uncomfortable and has a very low complication rate. The procedure takes less than 15 minutes to perform and leaves only a very small scar. Biopsies can be performed by a midlevel provider or advanced practice nurse.

The specimens are placed in fixative and shipped overnight to a commercial lab performing the test. During an elaborate and time-consuming processing procedure, specimens are cut and immunostained with PGP 9.5, a nonspecific axonal antibody [1]. Individual epidermal nerve fibers can be visualized and are manually counted. These values are compared to established normal values for epidermal nerve fiber count per mm available for several sites in legs and arm. Using this technique, the reported sensitivity and specificity is 88-92% [1]. The use of age- and gender-matched controls may improve specificity [2], but are not utilized by all labs. Abnormal ENFD has been set as less than the 5th percentile based on measurements in normal controls. This is a similar statistical mechanism used for determining normal values in NCS.

Because of the ease of obtaining skin biopsies these tests can be repeated serially to look for a change in response to a given therapy [3]. It can easily document progression or improvement. This modality has become widely accepted in clinical trials where changes in ENFD can be seen as early as 3-6 months, which is much sooner than one would expect to see changes on NCS.

Conclusions:

While skin biopsy for ENFD testing may not be necessary in every patient with suspected neuropathy, we believe there are a number of clinical situations in which it can be helpful. We believe that it can demonstrate early nerve damage in patients with impaired glucose tolerance or diabetes and is more sensitive than nerve conduction studies. This information can be used to motivate the patient with an objective sign of true end organ damage. It can also be used to follow the progression of a patient's therapy and is far more sensitive and specific than EMG/NCV. The biopsy procedure can be easily performed in an office and is reimbursed by Medicare and almost all commercial payors.

To find out more about how to incorporate skin biopsies into your practice you can contact www.CorinthianReferenceLab.com or call 855-CRL-LABS (855-275-5227).

References:

1. Lauria G, Hsieh ST, Johansson O, et al. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on the use of skin biopsy in the diagnosis of small fiber neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst. 2010;15:79-92.

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3. Epidermal reinnervation concomitant with symptomatic improvement in a sensory neuropathy. Muscle Nerve. 2003;27:507-9.

Disclosures:

Todd Levine and David Saperstein have a financial interest in Corinthian Reference Labs, an independent lab that performs epidermal nerve fiber density testing.