Usefulness of Monofilament Testing for Detecting Peripheral Neuropathy I

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ABSTRACT

Background. The monofilament test is a simple and inexpensive tool used for the detection of diabetic peripheral neuropathy in the community setting but it is unclear whether its use can be extended to patients with neuropathy that is not due to diabetes. Objective. We aimed to determine the sensitivity and specificity of the monofilament test in detecting peripheral neuropathy, diabetic or non-diabetic, using Nerve Conduction Studies (NCS) as the gold standard.

Methods. In a health assessment activity in Marinduque, patients were assessed by a neurologist as to whether or not they have neuropathy. Monofilament testing was done using the NHANES protocol with a 10-g Semmes Weinstein monofilament. Nerve Conduction Study was used as the gold standard.

Results. Fourteen patients were included in the study. A positive monofilament test was found to be significantly associated with a positive NCS result ($p<0.015$). The sensitivity of the monofilament test was 57.1%; the specificity was 100%. Positive predictive value was 1, negative predictive value was 0.7, pre-test probability was 83% and post-test probability was 96%.

Conclusion. Monofilament testing was found to be useful in detecting peripheral neuropathy in the community setting. If monofilament testing is positive, then peripheral neuropathy is ruled in. If the test is negative but the clinical suspicion is high, then NCS may be warranted. This cuts back the need for NCS to detect neuropathy in the community setting by more than half.

Key Words: monofilament, neuropathy, Semmes-Weinstein

Introduction

Monofilament testing is commonly used worldwide for the detection of diabetic peripheral neuropathy.[1-13] The American Diabetes Association recommends the use of a 10-g Semmes Weinstein monofilament in the test for the early identification of diabetic patients at risk for foot ulceration.[14] Monofilament tests are also recommended by the Consensus on the Diabetic Foot as an evaluation procedure for all diabetic patients.9 It is considered the best choice for clinical screening for diabetic peripheral neuropathy for multiple reasons including its portability, ease of administration, acceptability to patients and low cost.[15,16] It is unclear though if the use of the monofilament can be extended to patients with neuropathic changes that are not due to diabetes. [17]

In the recent years, several instruments have been utilized to detect peripheral neuropathy.[18] The ideal instrument should be readily available, easy to use and able to provide reproducible results with high sensitivity. Nerve conduction studies have been used as the gold standard, but these studies are time-consuming, expensive and impractical to operate in a primary care clinic. The monofilament test is simple and inexpensive; it would be easy to use it as a screening tool to identify patients with lack of protective sensation in the foot in a community that is being served mostly by primary health care workers.

The nervous system is one of the organ systems that are easily affected by environmental toxins. Chronic exposure to metals like lead, mercury and arsenic is known to cause peripheral neuropathies in susceptible individuals. In community health assessments conducted by the National Poison Management and Control Center, the determination of the burden of environmental toxicants on the health of the people is one of the primary objectives. Reliable but inexpensive assessment tools are needed to make robust conclusions about the health status of the communities. Whether the monofilament test can be used to detect neuropathies in these situations is not clear. The objective of the study was to determine the sensitivity and specificity of the monofilament test in detecting peripheral neuropathy in the primary care setting compared to NCS.

Methods

In a case finding activity for arsenic toxicity in Boac and Mogpog, Marinduque, Philippines from January 7-8, 2006, volunteer patients were screened by a group of physicians using the following criteria: those who lived in the area for a minimum of six months duration plus any one of the following conditions: dermatologic manifestations of chronic arsenicosis, skin cancer in unexposed areas, gangrene, distal paresthesias, or any two of the following: chronic cough for the last 2 months, non-pitting edema of the hands and feet, and hepatomegaly. Among patients who fit the above

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criteria, baseline demographic data, presence/ absence of diabetes and presence of neuropathic symptoms (including pricking/ burning sensation, numbness) were collected. All the patients underwent a comprehensive medical and neurological evaluation. Only one neurologist performed the examination on all patients. Based on the neurologic evaluation, a clinical assessment was then made on whether or not the patient had possible peripheral neuropathy.

Monofilament testing was then done on the patients using the NHANES Lower Extremity Disease Procedure for Peripheral Neuropathy.[19] Only one neurologist performed the monofilament testing on all the patients.

Participants were asked to lie supine on the exam table during the monofilament testing. While patients were unable to observe their feet, a standard monofilament (5.07/ 10-gram Semmes-Weinstein nylon monofilament) was used to apply slight pressure on three sites of the participant's feet: 1) plantar first metatarsal head, 2) plantar fifth metatarsal head, and 3) dorsum between the first and second metatarsals. (Figure 1) The last site is divergent from the site recommended by the NHANES protocol which recommended testing of the plantar hallux as the third site. The dorsal surface of the foot was chosen to avoid the presence of callosities in the plantar area which may give false results for insensitive points. The dorsum between the first and second metatarsals site has been validated for monofilament testing by previous studies.[6, 12]

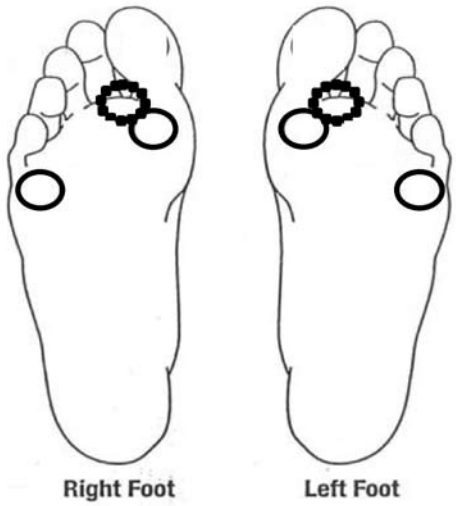

Figure 1. Areas in the feet stimulated for monofilament testing. Solid circles are in the plantar aspects of the feet while dashed circles are on the dorsum of the feet.

The monofilament was placed on the surface of the foot with a right angle to the skin; pressure was then increased until the filament buckled, indicating that a known amount of pressure had been applied. The sites were tested in a non-sequential order.

The following standard script (translated to Filipino) was used to explain the procedure to the patient:

"I want to test the sensation or sense of touch on the bottom of your feet. To do this test, I will use this small filament to apply pressure to different spots on your foot. It is not sharp and will not break the skin."

"As I apply the pressure I will be saying 'A, B' and I will be applying the pressure either as I am saying 'A' or as I am saying 'B'. I want you to tell me whether you felt the pressure when I said 'A' or when I said 'B'. Let me demonstrate on your arm."

"Do you understand?"

The sequence for application of stimulus was randomly generated beforehand and was different for each patient tested.

If the first response at any site was correct, the test was not repeated at that site. If the examinee cannot correctly identify the interval in which the stimulus was applied, the test was repeated at that site up to two times until a total of two similar responses were obtained. A site was defined as ***sensate*** if 1) the first response at a site by a participant was correct or 2) two out of three tests at a site yielded a correct response. A site was considered ***insensate*** if there were 1) two incorrect responses, 2) two "unable to determine" responses, or 3) 1 incorrect and 1 "unable to determine" response for a site. The presence of an insensate area in any of the three sites was considered a positive monofilament test for peripheral neuropathy.

The patients were then sent to another neurologist for NCS. Only one neurologist performed the NCS of all the patients in the study and he was blinded to the status of the subject on monofilament testing. A Cadwell Wedge machine was used for nerve conduction studies in all patients. Motor conduction velocities, distal motor latencies and distal compound muscle action potential amplitudes of the median, ulnar, peroneal and tibial nerves were studied. Additionally, sensory parameters, such as conduction velocities and amplitudes of the sensory nerve action potentials of the median, ulnar, radial and sural nerves were measured according to standard procedures. In this study, NCS were used as a gold standard to calculate the sensitivity and specificity of the monofilament test.

Sensitivity, specificity, positive predictive value, negative predictive value positive likelihood ratio and negative likelihood ratio were determined. This was computed using the SPSS software v13.0.

Results

There were 25 patients who were included in the two-day case finding for arsenic toxicity. Only 14 underwent NCS and hence were included in this study. The mean age was 64.9 $\pm$ 16.7, with ages ranging from 28 to 94 years. Most (71.4%) were over 60 years old. Females comprised 57.1% of the study population. Only one patient had been previously diagnosed with diabetes. Neuropathic symptoms were present in 64.3% of the patients. (Table 1)

Table 1. Baseline Characteristics of Study Patients

Characteristics	N=14
Age: mean ± SD	64.9 + 16.7
range	28-94
<60	28.6% (N=4)
≥60	71.4% (N=10)
Sex: male	42.9% (N=6)
Female	57.1% (N=8)
History of diabetes:	7.1% (N=1)
Presence of neuropathic symptoms:	64.3% (N=9)

On neurologic evaluation, most of the patients (85.7%) had abnormal sensory examination findings. These findings included decreased sensation to light touch, pain and vibration sense. Abnormal motor examination was found in only one patient who was unable to walk on heels and toes. Decreased deep tendon reflexes were present in 42.9% of patients. Of the 14 patients, six were diagnosed as to having possible peripheral neuropathy.

When compared to NCS results, the sensitivity of the clinical assessment in this study was 85.7% (95% confidence interval: 42.0% to 99.2%), and the specificity was 100% (95% confidence interval: 56.1% to 100%).

On monofilament testing, 28.6% (N=4) patients tested positive for peripheral neuropathy, while 50% (N=7) tested positive on NCS. All of those patients who were positive on monofilament testing also tested positive on NCS. However 42.9% (3 out of 7) of those who tested positive on NCS were negative on monofilament testing. (Table 2)

Table 2. Monofilament testing vs. NCS

Monofilament Testing	Nerve Conduction Study	
	Positive	Negative
Abnormal	4	0
Normal	3	7

The sensitivity of the monofilament testing in this study was 57.1% (95% confidence interval: 20.2%-88.2%) and the specificity was 100% (95% confidence interval: 56.1% to 100%). The positive predictive value was 1 (95% confidence interval 0.4-1.0) meaning 100% of the patients who test positive on monofilament testing truly have peripheral neuropathy, and the negative predictive value was 0.7 (95% confidence interval: 0.2-1.0) meaning 70% of the patients who test negative on monofilament testing truly do not have peripheral neuropathy. (Table 3)

Table 3. Sensitivity and Specificity of Monofilament Testing

	Monofilament Testing	
	Value	95% Confidence Interval
Sensitivity	57.1%	20.2%-88.2%
Specificity	100%	56.1%-100%
Positive Predictive Value	1	0.4-1.0
Negative Predictive Value	0.7	0.2-1.0
Pre-test Probability	83%	
Post-test Probability	96%	

The pre-test probability of detecting a peripheral neuropathy by history and neurological examination was estimated to be 83% and the post-test probability was 96%.

If we combine the clinical assessment and the monofilament test results (peripheral neuropathy is considered positive if either clinical assessment or monofilament testing is positive) and compare it with the NCS, sensitivity would increase to 100% (95% confidence interval: 56.1% to 100%) while specificity would remain 100% (95% confidence interval: 56.1% to 100%).

Discussion

In testing for peripheral neuropathy, many clinicians prefer using electrodiagnostic techniques. Although neurophysiologic examination is sensitive, specific, and reproducible regarding the presence and severity of peripheral nerve involvement,[22] it is not suitable for making a quick preliminary diagnosis in the primary care setting. Hence there is a need for an easier, less expensive and reliable way to detect the presence of peripheral neuropathy.

The monofilament was developed by von Frey in the late 1800s, using horse hairs of different diameters and lengths to test pressure sensation of the skin. Semmes and Weinstein revived this technique in the late 1950s to study peripheral neuropathy in brain-injured veterans, using a nylon filament embedded in a plastic handle. The Semmes-Weinstein monofilament assesses the threshold for light touch pressure in a semi-quantitative fashion. This instrument exploits the unique physical properties of a buckling column to produce a reproducible quantifiable force despite the force applied to the handle.[15]

Ever since the use of monofilaments in detecting diabetic peripheral neuropathy was reported in 1995, it has been widely used as a reliable means of testing for the absence of protective sensation, and has been recommended as a screening tool for diabetic neuropathy in addition to vibration testing.[10, 23] It is unclear however, if the use of the monofilament can be extended to identify neuropathic changes due to other etiologies. Previous studies have been done using the monofilament in the detection of foot lesion in older adults in both non-diabetic and diabetic populations. The results were suggestive that the use of the monofilament may be extended to the detection of other ulcer-producing conditions and lesions in other areas, such as the early detection of pressure ulcers.[17]

This study population was composed of 14 patients, only one of whom was a diagnosed diabetic. The 10-g Semmes-Weinstein monofilament testing was found to be very specific (100%) for peripheral neuropathy, while it was only moderately sensitive (57.1%). Previous studies on monofilament testing for diabetic neuropathy showed varying ranges of sensitivity and specificity. Several case-control studies report variable sensitivities and specificities up to 95% and 82%, respectively, but these studies used tests other than NCS as the gold standard.[24-27] A recent test comparing monofilament testing to NCS showed a

specificity of 96% and sensitivity of 77%,[10] much closer to the present study's findings.

The pre-test probability in this study is high most likely because a neurologist performed the history and neurologic examination. With a positive likelihood ratio of 5, the post-test probability increased further to 96%. These indicate that the monofilament testing does improve the ability to detect a peripheral neuropathy. Thus, when combined with clinical assessment, the sensitivity of the monofilament test in this study rose to 100%. This is congruent to recent results of the use of monofilament combined with clinical examination which compared favorably with other noninvasive procedures for detection of neuropathy and vascular insufficiency causing foot ulceration.[9, 25] Naturally, an experienced clinician, especially if backed up by some form of neurological scoring system, would have a very high sensitivity and specificity and has in fact been called the true gold standard.[28] However, in the context of widespread community-based screening, such expertise is not readily accessible, and there is a need to have some form of semi-quantitative screening that can be used by the most inexperienced to the most highly specialized health professional.[12] This study therefore, supports the use of the monofilament test to detect peripheral neuropathy in the community setting.

The results of this study may be interpreted as follows: if one of the three sites on monofilament testing is insensate, then peripheral neuropathy is ruled in. If the test is negative but the clinical suspicion is high, then an NCS may be warranted. In this way the need for NCS in screening for peripheral neuropathy is cut back by more than half (since sensitivity is 57%).

The authors recognize that the conclusions in this study have limitations. The study population consisted of individuals with a variety of symptoms, hence the wide confidence interval in the sensitivity and specificity of the monofilament test. The subjects were not randomly picked from the community so this lends some bias to the true sensitivity and specificity of the test. Also it would be interesting to investigate if the monofilament test can improve the probability of detecting a peripheral neuropathy when the pre-test probability is lower.

Conclusion

Monofilament testing may be extended beyond its current use in screening for diabetic neuropathy to include other types of peripheral neuropathy. The 10-g Semmes-Weinstein monofilament is probably the tool that can be most easily applied in detecting peripheral neuropathy in the community setting where an experienced neurologist is not accessible and where factors such as cost, ease of application, and portability are taken into consideration. While it is true that the monofilament is not the most sensitive tool to detect all patients with peripheral neuropathy, it does help to lessen the need for nerve conduction studies. Thus, it still represents a useful tool for clinical practice especially in the primary care provided its limitations are taken into consideration.

Due to the limitations of this study, it is recommended that future research be directed to checking the feasibility and usefulness of monofilament testing in detecting peripheral neuropathy in a larger non-biased population group. Also in future researches, the examiners who will be doing the monofilament test should be non-neurologists in the community. This is to check the applicability of the test in the community setting where it will be most beneficial. Prospective studies could also focus on determining the best sites on the foot to be tested in detecting all types of peripheral neuropathy since current protocols available are designed for detecting diabetic neuropathy only.

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