Asian Journal of Medicine and Health

18(7): 9-15, 2020; Article no.AJMAH.58047
ISSN: 2456-8414

Accuracy of Monofilament in the Assessment of Diabetic Neuropathy

Vasudha Sanklapur[1*], S. Shruthi[1] and Nazir Attar[1]

[1]Department of General Medicine, Yenepoya Medical College, Mangalore, Karnataka, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author VS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SS and NA managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2020/v18i730219
Editor(s):
(1) Dr. Maria Manuel Azevedo, University of Porto, Portugal.
Reviewers:
(1) Wagih Gamal Eldin Abd Elghany Elbarrany, Um Al-Qura Uiversity, Saudi Arabia.
(2) Ahmed Chyad Abbas AL-Barqaawee, Altoosi University College, Iraq.
(3) Zainab Shakir Mahmood, College of Medicine, Iraq.
Complete Peer review History: http://www.sdiarticle4.com/review-history/58047

Short Research Article

Received 22 April 2020
Accepted 29 June 2020
Published 06 July 2020

ABSTRACT

Background: Diabetes Mellitus is one of the leading contributors of global burden of chronic diseases. Detection of diabetic end-organ damage, particularly during its early stages, is very crucial and significant. Peripheral neuropathy is a known vascular complication of chronic diabetes. Several modalities of detecting peripheral neuropathy clinically are available. The purpose of this study was to evaluate Semmes-Weinsten monofilament10gm in screening the diabetic peripheral neuropathy.

Aims and Objectives: To assess the accuracy of monofilament test in assessment of Diabetic neuropathy.

Materials and Methods: We analysed the data collected from 50 patients admitted in the medical wards or attending medical outxpatient department, diagnosed to have Diabetes, from august 2018 to august 2019. The results of three clinical tests, monofilament test, vibration (test) and ankle jerk (test), were performed. In the next phase nerve conduction velocity was examined in those with peripheral neuropathy. The results then compared with each other and with the gold standard nerve conduction velocity study.

**Corresponding author: E-mail: drvasudhas@live.in;*

Results: Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 and SPSS V.22 software was used to analyze the data. The sensitivity and specificity of monofilament test as in comparison with other clinical tests as well as the gold standard nerve conduction test was found to be 58% and 88% respectively. The sensitivity of achilles reflex was 30% and specificity being 80% in comparison with the nerve conduction velocity test. The sensitivity and specificity of vibration sense was 38% and 58% respectively. Hence the Simmes-Weinstein monofilament test was found to be more accurate test for clinical diagnosis of peripheral neuropathy in patients with diabetes.
Limitations: Study population was small.
Conclusion: This study showed that Semmes-Weinstein monofilament can be easily used as a simple and inexpensive device for screening for peripheral neuropathy.

Keywords: Diabetes; peripheral neuropathy; monofilament; clinical diagnosis.

1. INTRODUCTION

Involvement of the peripheral and autonomic nervous systems is probably the most common complication of diabetes. Clinical diabetic neuropathy is categorized into distinct syndromes according to the neurologic distribution, although many overlap syndromes occur.

Prevalence depends on the disease duration. Based upon several large studies, is that approximately 50 percent of patients with diabetes will eventually develop neuropathy [1,2,3].

1.1 Pathogenesis

Strong evidence of the association between vascular risk factors and neuropathy was shown in the EURODIAB study.

Other factors which were significantly associated with the incidence neuropathy were, glycosylated haemoglobin levels, increased triglyceride levels, body mass index, smoking, and the co-existence of hypertension [4].

1.1.1 Metabolic factors

Advanced Glycation End Products- Glycation of plasma and tissue proteins leads to the [5] formation of Advanced Glycation End Products (AGEs) which plays an important role in diabetic microvascular complications [6]. The excess circulating glucose combines with amino acids on circulating or tissue proteins. This process initially is reversible and later irreversible [7]. Serum AGE concentrations are increased in patients with diabetes. These have strong cross-linking activity with collagen, which may play a role in the development of diabetic microvascular complications.

Hexosamine- Excess glucose shunts glycolytic intermediates into the hexosamine pathway, producing uridine diphosphate-N-acetyl glucosamine. Increased flux through the hexosamine pathway results in cellular damage and enhanced oxidative stress [8].

Protein kinase C- High glucose is converted to diacylglycerol that activates protein kinase C. Protein kinase C activation produces vasoconstriction and nerve hypoxia [9].

Sorbitol- Glucose that enters cells is metabolized to Sorbitol via the enzyme aldose reductase. Sorbitol accumulates within the cells leading to depletion of NADPH, a rise in cell osmolality and a decrease in intracellular myoinositol, all of these combined interfere with cell metabolism and predispose cells to oxidative stress [10].

Oxidative stress- Hyperglycemia via metabolic pathways and reactions results is oxidative stress and the accumulation of reactive oxygen species. This leads to peripheral nerve damage and the signs and symptoms of diabetic neuropathy [11,12].

1.1.2 Nerve ischemia

Due to the presence of thickened endoneurial blood vessel walls and vascular occlusions [13].

There is clinical evidence that there is a reduction in endoneurial oxygen tension in the nerves of diabetic patients with advanced polyneuropathy [14].

1.1.3 Nerve fiber repair mechanisms

Neurotrophic peptides such as nerve growth factor, brain-derived neurotrophic factor, neurotrophin-3, the insulin-like growth factors, and vascular endothelial growth factor that

normally mediate nerve repair, regeneration, are deficient in diabetics [15].

Reduction of insulin in type 1 diabetes may compromise nerve viability and repair as well [16].

1.2 Classification

Symmetric polyneuropathy- Distal symmetric sensorimotor polyneuropathy is the most common type of diabetic neuropathy. It is characterized by a progressive loss of distal sensation correlating with loss of sensory axons, followed, in severe cases, by motor weakness and motor axonal loss. The stocking-glove sensory loss is typical in this disorder.

Autonomic neuropathy- It is a common complication of diabetes. It cancause postural hypotension, gastroparesis, and enteropathy with constipation or diarrhea.

Polyradiculopathies- Diabetes frequently injures the nerve roots at one or more thoracic or high lumbar levels with subsequent axonal degeneration and frequent contralateral, cephalad, or caudal extension.

Diabetic amyotrophy (lumbar polyradiculopathy)- clinical features include the acute, asymmetric, focal onset of pain followed by weakness involving the proximal leg, with associated autonomic failure. Progression occurs over months and partial recovery may occur.

Thoracic polyradiculopathy- patients present with severe abdominal pain, sometimes in a band-like pattern, and frequently have undergone extensive gastrointestinal diagnostic studies in attempts to identify the etiology of their pain [17].

Diabetic neuropathic cachexia- associated with unintended severe weight loss and depression.

Mononeuropathies — There are two types of mononeuropathy associated with diabetes: cranial and peripheral.

The most common cranial mononeuropathies occur in those nerves which supply the extraocular muscles.Affected patients present with unilateral pain, ptosis, and diplopia, with sparing of pupillary function [18].

Facial nerve mononeuropathy occurs more frequently in diabetic than in nondiabetic patients [19,20].

The most common peripheral mononeuropathy in diabetic patients is median nerve involvement at the wrist. Ulnar mononeuropathy at the elbow or the wrist can also occur [21].

Mononeuropathy multiplex — Multiple mononeuropathies in the same patient causes mononeuropathy. The other major cause that can lead to this syndrome is vasculitis.

The 2017 ADA position statement for the screening of Neuropathy [22]:

- All patients with diabetes at the time of diagnosis of type 2 diabetes and five years after the diagnosis of type 1 diabetes.
- Individuals with prediabetes (impaired fasting glucose and/or impaired glucose tolerance) who have symptoms of polyneuropathy.
- After initial screening, all patients with type 2 or type 1 diabetes who do not have polyneuropathy should be screened at least annually.

2. MATERIALS AND METHODS

Study was conducted from august 2018 to august 2019 in the department of General Medicine, Yenepoya medical college after obtaining the IEC approval with 50 patients with diabetes who were admitted or attending out patient department. Clinical examination was performed to assess the peripheral neuropathy including:

Achilles reflex testing was evaluated by striking the achilles tendon with patient's knee flexed at 900, normal response is a plantar flexion. Abnormal response were noted as decreased or absent reflexes.

Vibration test Vibration testing was performed using a 128-Hz tuning fork. Patient was first taught, by pacing the vibrating tuning fork o the forehead or sternum. The vibrating tuning fork applied to the bony prominence at the dorsum of the first toe and the patient was asked to report both start of vibration sense and cessation of it.

2.1 10 gm Semmes-Weinstein Monofilament Test

Monofilament testing was performed bilaterally using a 10 gm (size 5.07) monofilament. At first a

reference stimulus was applied to the forehead or the sternum. The test at 10 points of the feet were evaluated. Ten points in each foot, including: nine plantar sites (distal great toe, third toe, and fifth toe; first, third, and fifth metatarsal heads; medial foot, lateral foot, and heal) and one dorsal site were tested. The filament is placed perpendicular to the skin and pressure is applied until the filament just buckles with a contact time of 2 sec. Inability to perceive the sensation at any one site is considered abnormal.

Nerve conduction study was done in those patients with indication.

2.2 Statistical Analysis

Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 and SPSS V.22 software was used to analyze the data. Categorical data is represented in the form of frequency and percentage,continuous data is presented as the Mean ± SD. The sensitivity and specificity of monofilament test as in comparision with other clinical tests as well as the gold standard nerve conduction test. Results were expressed as sensitivity and specificity as in comparison to the gold standard test.

3. RESULTS

In our study a total of 50 patients were examined and tested for peripheral neuropathy using different clinical tests. Among the 50 patients, 34(68.00%) were male and 16 (32.00%) were females. The mean age of our study population was 55.10 ± 11.83 years (range 18-82 yr). The mean duration of diabetes mellitus was 5.57 ± 4.73 yrs. The mean random blood glucose was 260.14 ± 96.76(range 124.00 -586.00) .The mean HbA1c in the study population was 8.56 ± 1.75 gm %. The mean BMI in our study population was 22.73 ± 3.13.

The results showed that the majority of patients (76%) had HbA1c levels greater than 7%. It is shown that these patients have had a poor control over their diabetes. Examination revealed, 19 (38%) patients were healthy and without neuropathy and 31 individuals (62%) had neuropathy. Testing with 10gm Monofilament revealed peripheral sensory neuropathy in 29 (58%) of patients. Among the patients who underwent nerve conduction study 31(62%) had presence of neuropathy.

Table 1. Demographic variables

Demographic variables	Mean ± SD
Age	55.10 ± 11.83
Male	34(68.00%)
Female	16 (32.00%)
Random blood sugar	260.14 ± 96.76
HbA1c	8.56 ± 1.75
Duration of disease	5.57 ± 4.73
BMI	22.73 ± 3.13

The study showed that the sensitivity and specificity of vibration test was 38% and 58% respectively, achilles tendon reflex showed sensitivity and specificity of 30% and 80% respectively. The sensitivity and specificity of 10 gm Semmes-Weinstein was found to be 58% and 88% respectively. Nerve conduction velocity study was taken as gold standard test.

The area under the ROC curve was significantly greater for the monofilament test which was 0.48 compared with that for achilles tendon reflex (0.36) and for vibration test (0.34).

4. DISCUSSION

The clinical practice of bedside examinations such as ankle jerk response, vibration test using tuning fork and monofilament testing are not being rigorously followed. This has majorly contributed to the underdiagnoses of neuropathy and its related sequelae.

As neuropathy poses a threat to potential complications, early detection of diabetic polyneuropathy is important. Early detection, followed by therapeutic interventions, helps in decreasing the morbidity of diabetic polyneuropathy.

Table 2. Sensitivity and specificity of 10 gm monofilament test in comparison to ankle jerk, vibration test and nerve conduction study

Variable	Sensitivity %	Specificity %	AUC
Nerve conduction study	1(reference)	1(reference)	1
10 gm monofilament test	58	88	0.48
Achilles tendon reflex	30	80	0.36
Vibration sense	38	58	0.34

All patients with polyneuropathy (including asymptomatic) should receive foot care education. The patient should be instructed to carefully inspect his or her feet every day.

In this study, it was found that 31 patients (61%) had developed peripheral neuropathy. Associated with glycemic control, HbA1c (mean 8.56 ± 1) and random blood glucose (260.14 ± 96.76) levels in this study showed that most patients had poor blood glucose control. Monofilament test detected peripheral neuropathy in diabetic patients with 58% sensitivity and with a specificity of 88%, which was more than the other clinical tests with sensitivity of vibration test being 38% and that of achilles tendon reflex being 30%.

Shahram Baraz et al., compared the accuracy of monofilament testing at various points of feet in diabetic neuropathy 150 patients with diabetes mellitus. In his study it was concluded that monofilament can easily be used as a simple and inexpensive device for screening [23].

In a study by Carissa Paz C. Dioquino et al, they found that when they combined the clinical assessment and the monofilament test results and compared it with the NCS, sensitivity would increase to 100%, while specificity would remain 100%. The sensitivity of the monofilament testing in this study was 57.1% and the specificity was 100% [24].

In a cross-sectional study done at Diabetes Clinic, Ghulam Mohammad Mahar Medical College Hospital, by Javed Ahmed Phulpoto et at, monofilament test had a low sensitivity (62.8%) but a high specificity (92.9%) and accuracy (77.9%). This study concluded that simple bed side tests, like the monofilament test is useful for assessing peripheral diabetic neuropathy, even in those subjects in whom foot care practices are not followed [25].

Bruce A. Perkins et al, conducted a 4 year Prospective study examined the baseline monofilament examination score and other simple sensory screening tests (Superficial pain sensation, Vibration testing) by receiver operating characteristic curve analysis. The inferred that the area under the ROC curve was significantly greater for the monofilament examination compared with that for other simple sensory tests [26].

5. CONCLUSION

The use of monofilament solely or in combination with NCS or other reflex tests for neuropathy screening method is an easy and accessible method; and by early detection, it can prevent complications that include leg ulcers and amputation in patients with diabetes. The use of this test in our study showed that when factors such as cost and ease of use are concerned, then 10-g Semmes-Weinstein monofilament is effective for detection and screening peripheral neuropathy. The sensitivity and specificity of monofilament is found to be greater than the other clinical tests such asvibration sense and achilles tendon reflex in assessing peripheral neuropathy. Hence to be considered as a essential bed side clinical test in diabetics for early detection of peripheral neuropathy and prevention of complications.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: The rochester diabetic neuropathy study. [Internet]. Neurology. U.S. National Library of Medicine; 1993.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=8469345
[Cited 2020 May 12].
2. Dyck PJ, Litchy WJ, Lehman KA, Hokanson JL, Low PA, O'Brien PC. Variables influencing neuropathic endpoints: The rochester diabetic neuropathy study of healthy subjects. [Internet]. Neurology. U.S. National Library of Medicine; 1995.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=7783874
[Cited 2020 May 12].

3. Edwards JL, Vincent AM, Cheng HT, Feldman EL. Diabetic neuropathy: mechanisms to management. [Internet]. Pharmacology & therapeutics. U.S. National Library of Medicine; 2008.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=18616962
[Cited 2020 May 12].
4. Tesfaye S, Perkins, Bril V, Geleris J, Doremalen Nvan, Mehra MR, et al. Vascular risk factors and diabetic neuropathy: NEJM [Internet]. New England Journal of Medicine; 2005.
Available:https://www.nejm.org/doi/10.1056/NEJMoa032782?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub=www.ncbi.nlm.nih.gov
[Cited 2020 May 12].
5. JW, TSRB. Maillard reaction products in tissue proteins: New products and new perspectives [Internet]. amino acids. U.S. National Library of Medicine; 2003.
Available:https://pubmed.ncbi.nlm.nih.gov/14661090/
[Cited 2020 Jul 3].
6. Sugimoto K, Yasujima M, Yagihashi S. Role of advanced glycation end products in diabetic neuropathy. [Internet]. Current pharmaceutical design. U.S. National Library of Medicine; 2008.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=18473845
[Cited 2020 May 12].
7. Ahmed N, Thornalley PJ. Advanced glycation endproducts: what is their relevance to diabetic complications? [Internet]. Diabetes, Obesity & Metabolism. U.S. National Library of Medicine; 2007.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=17391149
[Cited 2020 May 12].
8. Brownlee M. Biochemistry and molecular cell biology of diabetic complications [Internet]. Nature News. Nature Publishing Group; 2001.
Available:https://www.nature.com/articles/414813a
[Cited 2020 May 12].
9. Evcimen ND, King GL. The role of protein kinase C activation and the vascular complications of diabetes [Internet]. Pharmacological Research. Academic Press; 2007.
Available:https://www.sciencedirect.com/science/article/abs/pii/S1043661807000904?via=ihub
[Cited 2020 May 12].
10. Oates PJ. Aldose reductase, still a compelling target for diabetic neuropathy. [Internet]. Current drug targets. U.S. National Library of Medicine; 2008.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=18220710
[Cited 2020 May 12].
11. Vincent AM, McLean LL, Backus C, Feldman EL. Short-term hyperglycemia produces oxidative damage and apoptosis in neurons. [Internet]. FASEB Journal: Official publication of the Federation of American Societies for Experimental Biology. U.S. National Library of Medicine; 2005.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=15677696
[Cited 2020 May 12].
12. Vincent MA, Russell, James WL, Phillip, Feldman, et al. Oxidative stress in the pathogenesis of diabetic neuropathy [Internet]. OUP academic. Oxford University Press; 2004.
Available:https://academic.oup.com/edrv/article/25/4/612/2355264
[Cited 2020 May 12].
13. Fagerberg SE. Diabetic neuropathy: A clinical and histological study on the significance of vascular affections. [Internet]. Acta medica Scandinavica. Supplementum. U.S. National Library of Medicine; 1959.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=13821282
[Cited 2020 May 12].
14. Newrick PG, Wilson AJ, Jakubowski J, Boulton AJ, Ward JD. Sural nerve oxygen tension in diabetes [Internet]. British Medical Journal (Clinical Research Ed.). U.S. National Library of Medicine; 1986.
Available:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1341910/
[Cited 2020 May 12].
15. Kennedy JM, Zochodne DW. Impaired peripheral nerve regeneration in diabetes mellitus [Internet]. Wiley Online Library. John Wiley & Sons, Ltd; 2005.
Available:https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1085-9489.2005.0010205.x
[Cited 2020 May 12].
16. Brussee V, Cunningham FA, Zochodne DW. Direct insulin signaling of neurons reverses diabetic neuropathy [Internet].

Diabetes. American Diabetes Association; 2004.
Available:https://diabetes.diabetesjournals.org/content/53/7/1824.long
[Cited 2020 May 12].

17. Kikta DG, Breuer AC, Wilbourn AJ. Thoracic root pain in diabetes: The spectrum of clinical and electromyographic findings. [Internet]. Annals of neurology. U.S. National Library of Medicine; 1982.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=7059131
[Cited 2020 May 12].
18. Brown MR, Dyck PJ, McClearn GE, Sima AA, Powell HC, Porte Jr. Central and peripheral nervous system complications. [Internet]. Diabetes. U.S. National Library of Medicine; 1982.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=6298038
[Cited 2020 May 12].
19. Pecket P, Schattner A. Concurrent bell's palsy and diabetes mellitus: A diabetic mononeuropathy? [Internet]. Journal of neurology, neurosurgery, and psychiatry. U.S. National Library of Medicine; 1982.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=7119834
[Cited 2020 May 12].
20. Adour K, Wingerd J, Doty HE. Prevalence of concurrent diabetes mellitus and idiopathic facial paralysis (Bell's palsy). [Internet]. Diabetes. U.S. National Library of Medicine; 1975.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=1126588
[Cited 2020 May 12].
21. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: The rochester diabetic neuropathy study. [Internet]. Neurology. U.S. National Library of Medicine; 1993.
Available:https://www.ncbi.nlm.nih.gov/pubmed?term=8469345
[Cited 2020 May 12].
22. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic neuropathy: A position statement by the american diabetes association [Internet]. Diabetes care. American Diabetes Association; 2017.
Available:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6977405/
[Cited 2020 May 11].
23. Baraz S, Zarea K, Shahbazian HB, Latifi SM. Comparison of the accuracy of monofilament testing at various points of feet in peripheral diabetic neuropathy screening [Internet]. Journal of Diabetes and Metabolic Disorders. BioMed Central; 2014.
Available:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3922886/
[Cited 2020 May 20].
24. Usefulness of Monofilament Testing for Detecting ... [Internet]; 2009.
Available:https://www.apamedcentral.org/Synapse/Data/PDFData/0012AMP/amp-43-3-4.pdf
[Cited 2020 May 20].
25. Abrar Shaikh JAPKMG. Role of bedside methods in evaluation of diabetic peripheral neuropathy. [Internet]; 2012.
Available:http://www.diabeticfootcareindia.com/files/Vibrometer-Pakistan.pdf
[Cited 2020 May 20].
26. Perkins BA, Orszag A, Ngo M, Ng E, New P, Bril V. Prediction of incident diabetic neuropathy using the monofilament examination: A 4-year prospective study [Internet]. Diabetes Care. American Diabetes Association; 2010.
Available:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2890357/
[Cited 2020 May 20].

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/58047