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USEFULNESS OF ADDING BIOTHESIOMETRY TO CLINICAL ASSESSMENT PROTOCOLS IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY AFFECTING LOWER LIMBS

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ABSTRACT

Background

Diabetes Mellitus is a major health problem of which Diabetic Peripheral Neuropathy (DPN) is an important complication resulting in ulceration and amputation. There are a number of bedside tests and evaluation which has been suggested for early diagnosis of DPN. This study aims to evaluate the usefulness of Biothesiometry when combined along with Diabetic Neuropathy Symptom Score (DNS) and Diabetic Neuropathy Examination Score (DNE) as compared against Nerve Conduction Study (NCS). NCS is considered as the gold standard in diagnosis of DPN.

Methods

This is a cross-sectional study which was done in the Department of Physical Medicine & Rehabilitation, Government Medical College, Thiruvananthapuram, Kerala which is a tertiary level referral center. The study was done in a one-year period between January 2018 and January 2019 in patients with diabetes who satisfied the inclusion criteria. Patients were first evaluated with a Performa which included DNS and DNE scoring and compared with NCS parameters. Vibration Perception Threshold (VPT) was assessed with a Biothesiometer and the combined results were compared with Nerve Conduction Study (NCS). The values obtained were entered in excel sheet and statistically evaluated.

Results

127 patients with Diabetes were recruited into the study out of which 49 were males and 78 were females with a mean age of 57.2 +/- 9.9 years. When patients who were clinically positive for DPN on evaluation with DNS and DNE were compared with NCS parameters, it was shown that there was a sensitivity of 96.2 % and specificity of 38.1% and when VPT measurement using Biothesiometer was added to the clinical evaluation the sensitivity was 100% with a negative predictive value of 100% and specificity of 23.8%. This study has shown that all of the patients who tested negative were true negatives.

Conclusion

This study concluded that addition of Biothesiometry to the combination of DNS, DNE for the evaluation of DPN is as good as NCS evaluation. Hence this combination will be useful in rural settings, where accessibility to expensive Electrodiagnostic machine is limited.

KEYWORDS : diabetic polyneuropathy, nerve conduction study, Biothesiometry, Vibration Perception Threshold

INTRODUCTION

Diabetes Mellitus is one of the largest health care problem of this century which is predicted to affect 366 million people by 2030[1]. Diabetic Peripheral Neuropathy (DPN) is the major complication of DM with a prevalence of around 50% and is also one of the most common causes of nontraumatic amputations. DPN has been defined as "symmetrical length-dependent sensorimotor polyneuropathy attributable to metabolic and microvessel alterations as a result of chronic hyperglycemia exposure and cardiovascular risk covariates" by Toronto Consensus Panel on Diabetic Neuropathy[2]. The Toronto consensus criteria define probable neuropathy as a combination of symptoms and signs of neuropathy which include the presence of two or more of the following; neuropathic symptoms, decreased distal sensation, or unequivocally decreased or absent ankle reflexes. Confirmed neuropathy requires abnormality of nerve conduction study (NCS) and a symptom or symptoms or a sign or signs of neuropathy. If NCS is normal, a validated measure of small-fiber neuropathy (with class 1 evidence) is required[3].

The standard of Medical Care in Diabetes 2020 mentions that DPN should be annually assessed in T2DM patients using medical history and simple clinical tests namely

1. Small fiber function: Pinprick and temperature sensation.
2. Large fiber function: vibration perception and 10g monofilament
3. Protective sensation: 10g monofilament

and that these tests not only screen for the presence of dysfunction but also predict the future risk of complications[7].

The Diabetic Neuropathy Symptom (DNS) scoring and Diabetic Neuropathy Examination (DNE) scoring are simple clinical examination methods to detect DPN. Previous studies have shown good correlation between DNS, DNE scoring and Nerve Conduction studies[4]. Vibration Perception Threshold measurement using Biothesiometer is a simple method of detecting large fiber dysfunction. There are conflicting reports regarding the usefulness of VPT detection in DPN[5]. Multiple studies have shown the relation between loss of VPT and Progress of various Indicators of DPN. In a study it was shown that patient with increased VPT were more likely to develop foot ulcers[6]. The present study is aimed to check if there is any added benefit of assessing VPT measurement using Biothesiometer over clinical examination as compared with NCS parameters which is considered as the gold standard.

METHODOLOGY

This is a prospective cross-sectional study done in Department

of Physical Medicine & Rehabilitation, Government Medical College, Thiruvananthapuram, Kerala, India. Institutional Ethics Committee approval was obtained for the study. The data was collected in the one-year period from January 2018 to January 2019. The study subjects were selected from patients with diabetes attending the Outpatient department who satisfied the following criteria

Inclusion Criteria

1. Patients who have been diagnosed with Type II Diabetes.
2. Age above 40

Exclusion Criteria

1. Those who do not give consent for study
2. Bilateral lower limb amputees
3. Those who have
- family history of inherited neuropathy
- occupational or environmental history of heavy metal exposure
- history of lumbar or cervical radiculopathy
- patients using medications which could cause polyneuropathy
4. Seriously ill patients

The sample size was calculated as 110 patients. The formula used was

$$n = \frac{p \; x \; q \; x \; (z_{1-\alpha/2})^2}{d^2}$$

$$z_{1-\alpha/2} = 1.96$$

$$p = 50\ \%$$

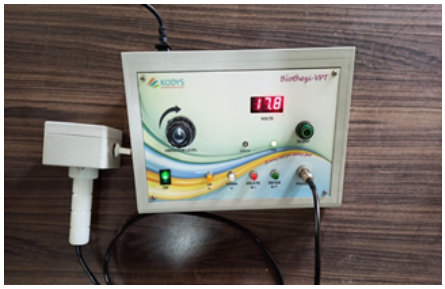
$$q = 100 - p$$

$$d - absolute\ precision$$

127 patients with diabetes were recruited, after taking informed written consent.

They were assessed using a clinical proforma which included DNS & DNE and VPT measurement using Biothesiometer (Kody's Biothesiometer). This was compared against parameters in Nerve Conduction Study Namely Sural nerve latency, Tibial Nerve amplitude, Tibial Nerve Latency and Tibial F Wave Latency. NCS was performed using Natus Electrodiagnostic machine. DNS values were considered as abnormal if the values were 1 or above and DNE was taken as abnormal if it was more than 3 and VPT was considered as abnormal if it was above 13 volts in any one of the areas tested. The Sural Nerve latency of >4.4 ms was taken as abnormal. Tibial Nerve Latency of >5.8 ms. CMAP amplitude of <8 mVolts and Tibial Nerve F wave latency of >55ms was considered as abnormal.

The results were compiled in MS Excel and a receiver-operator characteristic (ROC) curve analysis was done for statistical analysis.



Picture 1. Biothesiometer

Picture 2. Natus Electrodiagnostic Machine

RESULTS

The Out of the 127 patients with T2DM recruited mean age of the study cohort was 57.2 +/- 9 years and mean duration of T2DM in patients was 9 years. Out of the 127 patients 49 were males and 78 females. 14 patients were on Insulin, 68 patients were on Oral Hypoglycemic Drugs, 42 were on both Insulin and OHAs, and 3 patients on Alternative Medicine. In the study cohort 80 patients had uncontrolled glycemic status and 48 patients had controlled glycemic status.

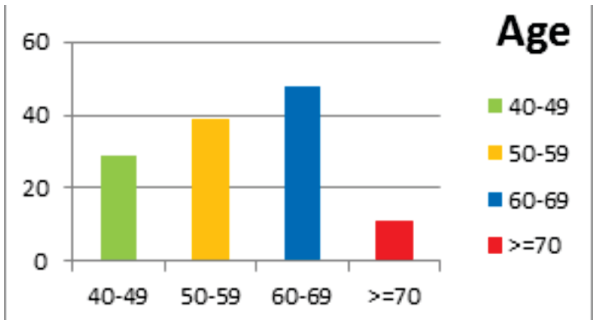


Fig1. Percentage Distribution Of The Subjects According To Age

101 patients who were symptomatic in DNS scoring were abnormal in NCS and 5 patients who did not have symptoms of DPN were found to have abnormal NCS. DNS when compared with NCS had a sensitivity of 95.3% and a specificity of 38.1% and a positive predictive value of 88.6% at 95% confidence Interval. However, 13 patients who were symptomatic in DNS scoring had normal values in NCS parameters

Chart 1. Comparison Of DNS To NCS

-	Positive DNS	Negative DNS
Abnormal	101	5
Normal	13	8

73 patients were positive for DPN in both DNE and NCS while 33 patients who were abnormal in NCS were found to be normal in DNE scoring. 7 patients who had abnormal DNE scoring were found to have normal values in NCS studies. DNE when compared with NCS had a sensitivity of 68.9%, specificity of 66.7%, positive predictive value of 91.3% and a negative predictive value of 29.8% at 95% confidence intervals.

Chart 2. Comparison Of DNE To NCS

NCS	Positive DNS	Negative DNS
Abnormal	73	33
Normal	7	14

Of the 127 patients who were assessed with Biothesiometer, 92 patients had abnormal values in both VPT and NCS parameters and 14 patients who had normal VPT measurements had abnormal values in NCS. The sensitivity was 86.8%, specificity was 28.6% with positive predictive value of 86% and negative predictive value of 38% at 95% confidence interval

Chart 3. Comparison Of VPT To NCS

NCS	Abnormal VPT	Normal VPT
Abnormal	92	14
Normal	15	6

Of the 115 patient who had abnormal results when DNS and DNE scoring was combined 102 showed abnormal parameters in NCS. When NCS is compared with combined DNS and DNE scoring a sensitivity of 96.2%, specificity of 38.1%, negative predictive value of 66.7% and a positive predictive value of 88.7% was obtained. When VPT measurement with Biothesiometry was added to the combined clinical assessment of DNS and DNE scoring all 106 patients who were positive in NCS were identified to have DPN by clinical methods, the sensitivity increased to 100%, specificity was 23.8%, negative predictive value of 100% and the positive predictive value was also 86.9% at a confidence interval of 95%. However, the total number of patients identified with the combination was 122 out of which 16 did not have NCS abnormality.

Chart 4. Comparison Of DNS & DNE/DNS, DNE & VPT To NCS

	Abnormal NCS	Normal NCS
DNS&DNE Abnormal	102	13
DNS&DNE Normal	4	8
DNS, DNE&VPT Abnormal	106	16
DNS, DNE&VPT Normal	0	5

DISCUSSION

This study was conducted to assess the usefulness of Biothesiometry when used along with clinical assessment methods of DNS and DNE as compared against NCS for the diagnosis of DPN. NCS is considered as the gold standard for assessment of Diabetic Peripheral Neuropathy.

The DNS scoring in our study have shown a sensitivity of 95.3% with a positive predictive value of 88.6%(CI-95%). In a study where DNS was compared with VPT[8] there was a sensitivity of 79% and specificity of 78%. DNE scoring in our study showed a sensitivity of 68.9%, specificity of 66.7% and a positive predictive value of 91.3% when compared with NCS. In a study done by Meijer et al they concluded that DNE is quiet sensitive in diagnosing DPN after comparing it with abnormal monofilament results, they got a sensitivity of 96% and specificity of 51% and while comparing with VPT measurement using Biothesiometer they got a sensitivity of 97% and specificity of 59%[11]. They also concluded that low specificity might burden prevention education programs. Hence the combination of different diagnostic tools, as advised in consensus reports will enhance specificity. In a study done by Young et al[9] when DNE was compared with VPT scoring it showed a sensitivity of 96% and specificity of 51%[9] but in our study the comparison was with NCS parameters which may be the reason for the reduced sensitivity and increased specificity. A strong relationship between DNS and DNE with Electrodiagnostic study has been shown in other studies[10]. In our study when both these were combined and compared to NCS parameters it was found to have a sensitivity of 96.2%, a specificity of 38.1%, a positive predictive value of 88.7% and a negative predictive value of 66.7% with odds ratio of 15.7 but when VPT value was also joined with these clinical assessment scoring the sensitivity increased to 100% and the negative predictive value was also 100% showing that those who were found free of DPN were true negatives and did not have neuropathy and there was also a positive predictive value of 86.9%, however the specificity had reduced to 23.8%.

So, all the patients who actually had Abnormal NCS parameters were identified with the combination of DNS, DNE and Biothesiometry (VPT), thus making it as good as doing NCS. Hence the combination of these three can be used in situations where NCS is not accessible or practical. Limitations of study- The study is not a true representation of the diabetic population as the cases were taken from a tertiary care center outpatient department.

CONCLUSION

This study has shown that a combination of DNS, DNE and VPT measurement can have similar sensitivity as NCS examination and can help in identifying subclinical cases. This is especially helpful in rural areas and situations where accessibility to costly Electrodiagnostic Machines is limited. DPN results in loss of protective sensation in the foot which lead to ulceration and amputation. This can be avoided with early diagnosis of DPN and instituting preventive measures like strict glycemic control and proper foot care practices. This combination of DNS, DNE and VPT is a good screening tool for DPN affecting lower limbs.

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