www.ijpbs.net

INTERNATIONAL JOURNAL OF PHARMA AND BIO SCIENCES

Internationally indexed journal

Indexed in Chemical Abstract Services (USA), Index coppernicus, Ulrichs Directory of Periodicals, Google scholar, CABI ,DOAJ , PSOAR, EBSCO , Open J gate , Proquest , SCOPUS , EMBASE ,etc.

Rapid and Easy Publishing

The "International Journal of Pharma and Bio Sciences" (IJPBS) is an international journal in English published quarterly. The aim of IJPBS is to publish peer reviewed research and review articles rapidly without delay in the developing field of pharmaceutical and biological sciences

Pharmaceutical Sciences

- Pharmaceutics
- Novel drug delivery system
- Nanotechnology
- Pharmacology
- Pharmacognosy
- Analytical chemistry
- Pharmacy practice
- Pharmacogenomics
- Polymer sciences
- Biomaterial sciences
- Medicinal chemistry
- Natural chemistry
- Biotechnology
- Pharmacoinformatics
- Biopharmaceutics

Biological Sciences

- Biochemistry
- Biotechnology
- Bioinformatics
- Cell biology
- Microbiology
- Molecular biology
- Neurobiology
- Cytology
- Pathology
- Immunobiology

Indexed in Elsevier Bibliographic Database

(Scopus and EMBASE)

SCImago Journal Rank 0.288

Impact factor 5.121*

ISSN 6299 -0975

Chemical Abstracts Service (www.cas.org)

A division of the American Chemical Society

CODEN IJPBJ2

Google Scholar BETA

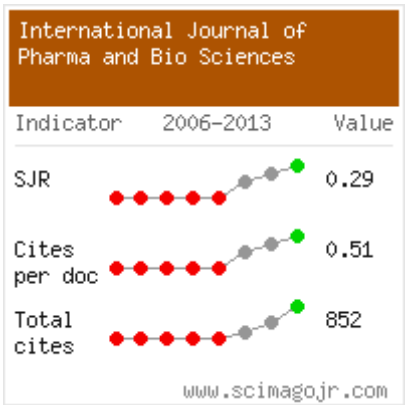
Elsevier Bibliographic databases (Scopus & Embase)

SNIP value – 0.77

SJR - 0.288

IPP - 0.479

SNIP – Source normalised impact per paper
SJR – SCImago Journal rank
IPP –Impact per publication
Source –www.journalmetrics.com
(Powered by scopus (ELSEVIER)



ProQuest

LUND UNIVERSITY

JSU JACKSONVILLE STATE UNIVERSITY

Jacksonville State University
Houston Cole Library
USA (Alabama)

UNIVERSITY OF OXFORD

Oxford, United Kingdom

INDEX COPERNICUS INTERNATIONAL

And indexed/catalogued in many more university

*Instruction to Authors visit **www.ijpbs.net**

For any Queries, visit "contact" of www.ijpbs.net

Int J Pharm Bio Sci 2015 Oct; 6(4): (B) 26 - 31

Research Article **Neurobiology**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

AN EVALUATION OF VIBRATION PERCEPTION THRESHOLD (VPT) TESTING AS AN EARLY PREDICTIVE DIAGNOSTIC MARKER OF NEUROPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS.

DR. RAMAKRISHNA MR[1], DR. TRUPTI RR[2], DR. ANTIN SS[1], DR. RAGHUKANTH REDDY[1] AND DR. ANANDKUMAR H[3*]

[1]Department of General Medicine, Navodaya Medical College Hospital & Research Centre, Raichur-584 103, karnataka
[2]Department of Physiology, Navodaya Medical College, Raichur-584 103, karnataka
[3]Department of Microbiology, Navodaya Medical College Hospital & Research Centre, Raichur-584 103, karnataka

ABSTRACT

Diabetes mellitus is a systemic metabolic disorder associated with serious life threatening complications, diabetic neuropathy is most common among them. Evaluation is often difficult because of variation in the patient's interpretation of the symptoms, as well as the inherent subjectivity of sensory examination. The early recognition and appropriate management of neuropathy in patients with DM is important as asymptomatic patient are at increased risk of developing diabetic foot with slight injury. In present study we have assessed the impairment of vibration perception threshold (VPT) using biothesiometer. Out of 50 diabetic cases, 33 (66%) were female and 17 (34%) were male patients. Among them, 39 (78%) had abnormal VPT, of which 27 (54%) showed sever grade of neuropathy, 8 (16%) had moderate and 4 (8%) had mild grade of VPT. Out of 22 cases, 20 patients with diabetes for more than 5 years had severe sensory loss. The association between long duration of diabetes mellitus and neuropathy was statistically significant (p>0.001). We can conclude based on the study results that all diabetic cases irrespective of clinical symptoms of neuropathy should be assessed by VPT for early diagnosis & future therapy to prevent progression of disease.

KEY WORDS: Type 2 DM, diabetic neuropathy, vibration perception threshold test

DR. ANANDKUMAR H
Department of Microbiology, Navodaya Medical College Hospital & Research Centre, Raichur-584 103, karnataka

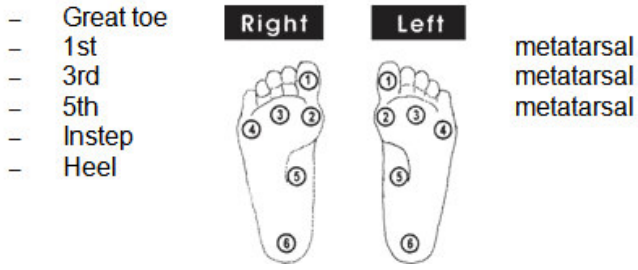
INTRODUCTION

Type 2 diabetes mellitus (DM) is a systemic metabolic disorder associated with serious life threatening complications, diabetic neuropathy is most common among them[1]. Neurological abnormalities affecting the distal lower extremities are known to appear in early stages of type 2 DM[2]. It has been clearly shown for decades that diabetic neuropathy is a direct consequence of abnormal glucose turnover, chronic hyperglycemia in type2DM leads to a fourfold increase in the neuronal glucose levels which cannot be neutralized by the anaerobic and glycolytic burst as happens in the muscle cells[3]. Glucose neurotoxicity develops due to accumulation of free radicals in neurons[4]. The reported incidence of neurologic involvement varies from25 to 90 percent of adult diabetic patients[5-10]. The severity of the symptoms associated with diabetic neuropathy may vary from a mild, unnoticed to a distressing chronic invalidism. The most common neurologic disturbance in diabetes is involvement of the peripheral nerves. The early symptoms of peripheral nerve involvement are usually sensory. Evaluation is often difficult because of variation in the patient's interpretation of the symptoms, as well as the inherent subjectivity of sensory examination[11]. Diabetes affects both large and small myelinated fibres& unmyelinated nerve fibres as well[12,13]. The early recognition and appropriate management of neuropathy in patients with DM is important for a number of reasons; 1) Non diabetic neuropathies may be present in patient with diabetes, 2) number of treatment options exist for symptomatic diabetic neuropathy, 3) Up to 50% of diabetic neuropathy may be asymptomatic but patient are at increased risk of developing diabetic foot even with slight injury, 4)autonomic neuropathy may involve every system in the body and 5)autonomic neuropathy causes substantial morbidity and increase mortality if cardiovascular autonomic neuropathy is present[18,19].

MATERIALS AND METHODS

The prospective cross section study was conducted at the Navodaya Medical College Hospital and Research Center based on patients coming to out-patient department from November 2014 to May 2015. A total of 50 patients with known type 2 DM were included in the study after getting institutional ethical clearance and consent from the subjects.In present study we have assessed the impairment of vibration perception threshold(VPT) that enables evaluation of affection of large myelinated (Aα & Aβ) fibres. Biothesiometer was used in our study, which is a simple handheld device that gives a semi quantitative assessment of vibration perception threshold (VPT). First probe was applied to patient's hand to explain the feel of vibration clearly. Then patient is asked to concentrate on feet & tell as soon as he starts feeling the vibration and value is noted.With the patient lying supine, the stylus of the instrument is placed over the dorsal hallux and the amplitude is increased until the patient can detect the vibration; the resulting number is known as the VPT. This process should initially be demonstrated on the proximal site, and then the mean of three readings was taken over each hallux.

In our study we have taken average of 6 specific points in both feet



Quantification of vibratory sense was detected in 50 diabetic patients. During recording the voltage was increased gradually from 0 to 50 volts as soon as the patient feels the vibration sense the reading is noted down. Based upon the value the severity of sensory loss in this patients is graded as follows:

Normal	<15
Mild	(16-20)
Moderate	(21-25)
Severe	(>25)

RESULTS

Out of 50 diabetic cases, 33 (66%) were female and 17 (34%) were male patients. Among them, 39 (78%) had abnormal VPT, of which 27 (54%) showed sever grade of neuropathy, 8 (16%) had moderate and 4 (8%) had mild grade of VPT. Whereas 11 (22%) of diabetic patients showed normal VPT.

Table 1
Distribution of patients based on severity of diabetes mellitus

	MALE	FEMALE	TOTAL
NORMAL (<15)	7	4	11
MILD (16-20)	4	0	4
MODERATE (21-25)	5	3	8
SEVERE(>25)	17	10	27
TOTAL NO OF PATIENTS	33	17	50

Table 2
Association between severity of sensory loss (VPT) and duration of diabetes mellitus in known case of diabetic patients

(a)

		GRADINGOF SEVERITY				
		<15	16-20	21-25	>25	**Total**
DURATION OF DM (YRS)	<1	2	1	0	1	4
	1 to 5	8	3	7	6	24
	>5	1	0	1	20	22
Total		11	4	8	27	50

(b)

Chi-Square Tests

	Value	Df	P
Pearson Chi-Square	24.641	6	.0001 <0.001 Highly significant

In the above table2 (a) the grading of severity has been compared with that of duration of diabetes, it shows that the severity of loss increases with increasing duration of diabetes. Out of 22 cases, 20 patients with diabetes for more than 5 years had severe sensory loss. On applying Pearson chi-square tests to above table1 (a) the results show us that the duration of diabetes had a significant role in the development of peripheral neuropathy (p<0.001).

Table 3
Association between severity of sensory loss (VPT) and age in diabetic patients

(a)

		GRADINGOF SEVERITY				
		<15	16-20	21-25	>25	**Total**
AGE GROUP (YRS)	31-40	2	1	2	2	7
	41-50	5	0	2	3	10
	51-60	4	2	3	17	26
	>60	0	1	1	5	7
Total		11	4	8	27	50

(b)

Chi-Square Tests

	Value	Df	P
Pearson Chi-Square	11.303	9	.255 >0.05 Not significant

In our study, 17(62.9%)of 27 patients having severe sensory loss belonged to age group 51-60 and 5(18.5%) patients had greater than 60 years of age as depicted in table-3a. The pearson chi square tests (table3b) shows no statistical significance (p>0.05) of association between age of the patient and severity of sensory loss based on VTP, but this is too early to comment as the sample size is small.

Table 4
Association of severity of diabetes mellitus and sex

(a)

		GRADINGOF SEVERITY				
		<15	16-20	21-25	>25	**Total**
Sex	Male	7	4	5	17	33
	Female	4	0	3	10	17
Total		11	4	8	27	50

(b)

Chi-Square Tests

	Value	Df	P
Pearson Chi-Square	2.243	3	.524 >0.05 Not significant

Out of 27 patients 17 were males with sever sensory loss and 10 patients were females. The pearson chi square tests showed no significant (p>0.05)) association between sex of the patient and severity of sensory loss based on VTP, this may be due to lack of large sample size.

DISCUSSION

Diabetic neuropathy is one of the most common complication in patients who have long standing DM, some patients with severe involvement of sensory loss may not have any signs and symptoms. There are various test to assess the severity of sensory loss in diabetic patients, among them biothesimetry is one of the test to assess peripheral neuropathy which is used in

the present study. Previous studies showed that in mild to moderate diabetic neuropathy, the biothesiometer VPT serves excellent reliability and serves as an appropriate screening tool[14]. VPT testing in diabetic neuropathy had done by many authors[12,15,16]. But very few reports have been documented in our country. Therefore this study is done to assess if VPT testing can be applied in our country for early diagnosis of diabetic peripheral neuropathy. The use of biothesiometer has served a satisfactory tool for quantifying vibratory sense[16]. More over one study showed, very recently biothesiometry /QST study is being used for diagnosis of neuropathy especially of small & large fibre, which increases the sensitivity of detecting neuropathy from 30-90% or more[17]. In present study the result shows diverse values of VPT testing. Most of the clinical neuropathic patients showed abnormal VPT either graded normal, mild, moderate & sever. Among the diabetic neuropathic patients, 4 had mild sensory loss and 11 were normal with no sensory loss. The reason for different grades of neuropathy is due to variable duration of illness. Even more important is every subclinical case of neuropathy in diabetes should be assessed by VPT testing to find out the probability of developing neuropathy. Van Deusen RW *etal,* stated that in mild to moderate diabetic neuropathy the biothesiometer VPT serves excellent reliability and serves as an appropriate screening tool[17]. Therefore, it may be advocated that therapy should be instituted in these subclinical cases of neuropathy on the basis of VPT abnormality to prevent disease progression along with glycemic control.

CONCLUSION

It cannot be over stated that the complications of the diabetic foot are common, complex, and costly, mandating aggressive and proactive preventive assessments by physicians. All patients with diabetes must have their feet evaluated at least at yearly intervals for the presence of the predisposing factors for ulceration and amputation (neuropathy, vascular disease and deformities). If abnormalities are present, more frequent evaluation of the diabetic foot is recommended depending on risk category. It is through systematic examination and risk assessment, patient education, and timely referral that we may further reduce the unnecessarily high prevalence of lower-extremity morbidity among this population. Though there are other methods to identify loss of protective sensation (LOPS) in the diabetic foot like 10-g monofilament test, pinprick sensation test and Ankle reflex test, VPT test being semi-quantitative method, it helps to predict and grade the risk of diabetic neuropathy. From our study, we can conclude that all diabetic cases irrespective of clinical symptoms of neuropathy should be assessed by VPT for early diagnosis & future therapy to prevent progression of disease.

ACKNOWLEDGEMENT

We thank Dr. Anant Takalkar, Professor of Community medicine, Navodaya Medical College, Raichur, Karnataka for providing relevant statistical analysis for our study.

Conflict of interest

Conflict of interest declared none

REFERENCES

1. Vincent AM, Callaghan BC, Smith AL, Feldman EL. Diabetic neuropathy: cellular mechanisms as therapeutic targets. *Nat Rev Neurol,* 7: 573-583, (2011).
2. Basić-Kes V, Zavoreo I, Rotim K, Bornstein N, Rundek T, *et al*. Recommendations for diabetic polyneuropathy treatment. *Acta Clin Croat,*50: 289-302 (2011).
3. Tomlinson DR, Gardiner NJ Glucose neurotoxicity. *Nat Rev Neurosci,* 9: 36-45, (2008).

4. Golbidi S, Badran M, Laher I. Diabetes and alpha lipoic Acid. *Front Pharmacol*, 2: 69, (2011).
5. Duncan, GG. Diseases of Metabolism. 4th Ed., Philadelphia,W. B. Saunders Company, pp. 870-73, (1959).
6. Bonkalo, A. Relation between neuritis and clinical background in diabetes mellitus. Arch. Int. Med., 85:944-54, (2005).
7. Broch OJ and Klovsted O. Polyneuritis in diabetes mellitus. *Acta Med. Scandinav*, 127: 514-42, (1947).
8. Bailey AA. Neurologic complications associated with diabetes. Diabetes, 4:32-36, (1955).
9. Goodman J I, Baumoel S, Frankel L, Marcus LJ and Wassermann S: The Diabetic Neuropathies. (American Lecture Series Publication No. 151) Springfield, 111, Charles C Thomas, p. 138, (1953).
10. Markman P, Allen EA and Jackson, WPU. Analysis of the retinal, cardiovascular, and neurological disorders in diabetics attending an outpatient clinic. South African M. J., 33: 682-89, (1959).
11. Feldman EL, Stevens MJ, Thomas PK. A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy. Diabetes Care,17: 1281–1289, (1994)
12. Shy ME, Frohman EM, So YT. Therapeutics andTechnology Assessment Subcommittee of the American Academy of Neurology. Quantitative sensory testing: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology, 60: 898–904,(2003) .
13. Skillman TG, Johnson EW, Hamwi GJ, Driskill HF. Motor nerve conduction velocity in diabetesmellitus. Diabetes, 10: 46–51, (1961).
14. Van Deusen RW, Sanchez MM, Derr JA. Vibration perception threshold testing in patients with diabetic neuropathy: ceiling effects and reliability. Diabet Med,18: 469–475, (2001).
15. Jamal GA, Hansen S, Weir AI, Ballantyne JP.QST added more accuracy, sensitivity & specificity in diagnosing diabetic neuropathy. The neurophysiologic investigation of small fibre neuropathies. Muscle Nerve,10: 537–545, (1987).
16. Sorensen, Lea BHSc, Molyneaux, Lynda RN, Yue Dennis K. The Level of Small Nerve Fiber Dysfunction Does not Predict Pain in Diabetic Neuropathy: A Study Using Quantitative Sensory Testing. Clin J Pain,22: 261–265, (2006).
17. Perkins BA, Olaleye D, Zinman B. Simple screening test for peripheral neuropathy in the diabetes clinic. Diabetes Care,24: 250–256, (2001).
18. Vinik AI, Maser RE, Mitchell BD, Freeman R: Diabetic autonomic neuropathy (Technical Review). *Diabetes Care* 26:1553–1579,2003
19. Boulton AJM, Malik RA, Arezzo JC, Sosenko JM: Diabetic somatic neuropathies(Technical Review). *Diabetes Care,* 27: 1458–1486, (2004).
20. Thomas PK: Classification, differential diagnosis and staging of diabetic peripheral neuropathy. *Diabetes,* 46 (2):S54– S57, (1997).
21. Pryce TD. Motor involvement is proximal and asymmetric in location & sensory affection is mainly distal & symmetrical nature. Brain, 6: 416–431, (1893).
22. Coppini DV, Young PJ, Weng C, Macleod AF, Sönksen PH. Outcome on diabetic foot complications in relation to clinical examination and quantitative sensory testing: a case-control study. Diabet Med,15: 765–771, (1998).
23. Manivannan M, Periyasamy R, Narayanamurthy VB. Vibration perception threshold and the law of mobility in diabetic mellitus patients. PrimCare Diabetes, 3: 17–21, (2009).