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Correlating Nerve Conduction Velocity and Duration of Type 2 Diabetes Mellitus: A Study Done On North Indian Population, In a Tertiary Care Hospital.

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Abstract

Background: Peripheral neuropathy is a common condition in diabetics which is associated with considerable morbidity and diminished quality of life. It is also associated with multiple risk factors. Nerve conduction velocity is a reliable indicator of peripheral nerve functions and helps in diagnosis and prognosis of peripheral neuropathy. The aim of this research was to find out the relationship between nerve conduction velocity of both motor and sensory nerves and duration since diagnosis of illness in patients of type 2 diabetes mellitus.

Material and methods: In this observational cross sectional study ,nerve conduction velocity testing (for bilateral Sural, Peroneal & Median nerves) was done on 48 patients of type 2 diabetes mellitus, which were later divided into two comparable groups on the basis of presence or absence of diabetic peripheral neuropathy. Correlation analysis was done between duration since diagnosis of diabetes and nerve conduction velocity of bilateral Sural, Peroneal & Median (both sensory and motor) nerves in these patients.

Results: Significant negative correlation was found between duration since diagnosis of diabetes and following –

Left Median motor nerve conduction velocity : r= -0.3831 **, p = 0.0072**

Left Sural nerve conduction velocity : r = -0.3030 **, p = 0.0363**

Conclusion: Peripheral nerve functions and nerve conduction velocity worsen with duration in patients of type 2 diabetes mellitus.

Keywords-duration since diagnosis of type 2 diabetes mellitus, Nerve conduction velocity (NCV),type 2 diabetes mellitus(T2DM) .

Introduction

Peripheral neuropathy is the most common neuropathy observed in diabetics [1,2]. Typical diabetic peripheral neuropathy (DPN) has been defined as a 'symmetrical, length-dependent sensorimotor polyneuropathy due to metabolic and microvascular changes resultant of chronic

exposure to hyperglycaemia and cardiovascular risk covariates. Abnormal nerve conduction test appear to be the first objective quantitative indication of the condition'[3.] Painful DPN has been reported to be considerably high with symptoms persistent inspite of multiple drugs used for its treatment and also causes limitation of daily activities [4]. DPN also increases the risk of amputations [5] and foot ulcers [6] in diabetics. Thus, identification of risk factors for neuropathy might provide a means to identify patients at high risk for lower-limb complications, as well as lead to timely interventions or treatments.

There are various factors that independently associated with DPN in diabetics.[7,8].According to a health survey done in the American population independent associations were found between the symptoms of peripheral neuropathy in diabetics and hyperglycemia ,longer duration of diabetes and hypertension[7].Duration of diabetes along with various other factors like age, glycated hemoglobin levels, history of insulin treatment use and male gender independently increased risk of prevalence of neuropathy in diabetics [8].

Pathogenesis of DPN involves both vascular factors and various metabolic interactions [9]. Nerve fibres in diabetics without DPN are more as compared to those with DPN , this also causes loss of sensations in such patients [9]. Microvascular defects in the endoneurial vessels, have also been demonstrated on nerve biopsy [10].

At metabolic level the pathogenesis of DPN is an excesssive oxidative stress due to hyperglycaemia [11] , diversion of the abundant glucose to polyol pathway causing increase levels of sorbitol and fructose [12,13] and ultimately accumulation of sorbitol inside the nerve cells resulting in osmotic stress/imbalance [14] and possibly effecting metabolism of inositol and Na^+/K^+ -ATPase as well [15].

In this neuropathic condition involvement of lower limbs preceeds that of upper limbs and sensory loss follows the typical 'glove and stocking' pattern.[16]. Motor deficits are usually uncommon in early stages of DPN [16].

For the diagnosis and assessment of this condition electrophysiological testing is a noninvasive method, quick to detect slight changes and a reliable measure of diabetic neuropathy [17].This test is quantitative and a longitudinal follow up is possible [17]. Nerve conduction studies (NCS) have been suggested as an early and reliable indicator of Peripheral neuropathy [3,18].NCS provide an objective and quantitative assessment of the typical diabetic peripheral neuropathy and have been included in the minimal criteria, given by Tesfaye et al for diagnosis of this neuropathy [3].

Nerve conduction velocities (NCV) have shown less variability than amplitudes in NCS [18] therefore, we chose NCV as a parameter to interprete and analyse the result of nerve conduction study and hence peripheral nerve functions.

Although duration of diabetes has been found to be associated with DPN [7, 8, 19] studies depicting a direct correlation between these two variables in diabetics are few. Such studies that include patients of exclusively type 2 diabetes mellitus from the Indian population are further scarce. Therefore, this study was conducted with the aim of exploring a direct relationship between duration of diabetes and DPN in T2DM patients, belonging to north India.

Material and Methods

This observational cross sectional type of study , was carried out in the department of Physiology in collaboration with departments of Biochemistry and Medicine of Lady Hardinge Medical College (LHMC) and associated hospitals which situated in New Delhi, India. Study period was between November 2014 to March 2016.

The study protocol was carried out as per declaration of Helsinki. Institutional ethics committee for human

research provided us ethical clearance for this study and informed & written consent was taken from all study participants.

Detailed history taking and examination was done for all study participants. We included 48 eligible T2DM patients which consisted of two groups –Group I consisting of 24 T2DM patients with DPN and Group II consisting of 24 T2DM patients without DPN. Minimal criteria, given by Tesfaye et al[20]was followed for determining presence or absence of DPN.

Nerve conduction velocity (NCV) of bilateral Sural, Peroneal & Median (both sensory & motor) nerves was done on all patients. The minimum values of nerve conduction velocity used for diagnosing peripheral neuropathy in our study were as follows; Median motor nerve-54.44 m/sec, Median sensory nerve -36.05m/sec, Peroneal nerve -42.14m/sec [21] and Sural nerve -30.5m/sec [22].

Inclusion criteria consisted of new or already diagnosed cases of T2DM in the age group of 40- 60 years, as per ADA guidelines [23].Our study group consisted of only north Indian population. Patients of type 1 diabetes mellitus, Pre diabetics (as per ADA criteria [23] were excluded from our study.

Duration since the diagnosis of T2DM by physician was recorded (in years) for all patients.

SCHWARZER TOPAS EMG/NCV/EP neurophysiological measuring system (provided by NATUS, Europe) was used for NCV measurement .Subjects were asked to lie in supine position for peroneal and median nerve testing and in prone position for sural nerve testing [21] and each nerve was tested in following way:

- Sural nerve: Active electrode was placed between lateral malleolus and tendoachilles. Distal to active electrode, reference electrode was placed. Nerve stimulation was given at the junction of middle and lower third of lower leg , around 10-16 cm proximal to active electrode [21].
- Median sensory nerve: Active electrode was placed at 1st interphalangeal joint. Reference electrode was placed 3 cm distal to active electrode. Nerve stimulation was given at the wrist [21].
- Median motor nerve: Active electrode was placed at abductor pollicis brevis muscle and reference electrode was placed 3cm distal to active electrode at 1st metacarpophalangeal joint. Nerve was stimulated at two points -first being 3cm proximal to distal wrist crease and second point being at elbow, near volar crease[21].
- Peroneal nerve: Active electrode was placed over extensor digitorum brevis muscle and reference electrode was placed at the base of little toe. Nerve was stimulated at two points – first stimulation point was at ankle 2cm distal to fibular neck and second stimulation point was in lateral part of popliteal space [21].

Statistical Analysis: Statistical evaluation of data was done using Graph Pad Prism software version 6. Mean and Standard error of mean (Mean ± SEM) / median of the variables were calculated. After testing for normal Gaussian distribution, intergroup comparison was done using Unpaired t-test, Mann Whitney U test and Chi square test as per requirement. Correlation was assessed using the Spearman's / Pearson's correlation coefficient, as per data distribution.

Results

Out of the 48 diabetics in our study 42 were receiving Metformin and 21 were additionally receiving Methylcobalamin. 6 of the study patients were newly diagnosed and were yet to be started on any treatment. Duration since diagnosis of the disease showed a ranged from 0 to 10 years with a median value of 2.00 years ,25

% percentile at 0.625 years and 75 % percentile at 5.00 years.

Table 1: Characterstics of the study population in the two groups

Groups	I (n=24)	II(n=24)	p value
Age(yrs) Mean± SEM	50.00 ± 1.07	47.88 ± 0.92	0.1392®
BMI (kg/m^2) Median	25.00	23.50	0.0623@
25% percentile	24.25	23.00	
75 %percentile	26.00	25.75	
SEX distribution	M = 16 F = 8	M = 12 F = 12	0.2416#

® Unpaired t-test, @ Mann Whitney U test, #Chi square test, M -Male, F-Female

Table 1 illustrates anthropometric characteristics of study population. The two study groups had no significant differences with respect to age, sex distribution and BMI, thus they were comparable for study.

Table2: Showing significant correlation of years since diagnosis of T2DM with motor and sensory NCV.

Parameters	Correlation with years since diagnosisofT2DM (n=48)
Left Median Motor nerve conduction velocity	**r = -0.3831@ p = 0.0072*** **
Left Sural nerve conduction velocity	**r = -0.3030# p = 0.0363***

@ -Spearman's Correlation Coefficient, # -Pearson's Correlation Coefficient

Table 2 shows a significant negative correlation between duration since diagnosis of T2DM (X-axis) and NCV (Y-axis) of Left median motor and left sural nerve for 48 diabetic patients.

Correlation between duration of T2DM since diagnosed in years and NCV of various other nerves (for the 48 study patients) was as follows-

Right sural nerve#: r = -0.2049, p = 0.1624, left median sensory nerve @: r = 0.01121, p = 0.9397, left Peroneal nerve#: r = -0.1986, p = 0.1761, right Median motor nerve@: r = -0.2561, p = 0.0789, right median sensory nerve @: r = 0.05726, p = 0.6991, right peroneal nerve#: r = -0.1831, p = 0.2129.

@ - Spearman's Correlation Coefficient, # -Pearson's Correlation Coefficient.

Hence, the result of correlation analysis between NCV of all other nerves and duration since diagnosis of T2DM came out to be non significant

Discussion

In our study, NCV of a motor nerve (left median) and a sensory nerve (left sural) showed separate significant negative correlations with duration since diagnosis of T2DM .This means that as the duration of illness increased in these patient, NCV of the above mentioned nerves decreased and falling measurements of NCV of these nerves were significantly correlated to time lapsed since the disease was diagnosed in these patients.

Since, NCV is a reliable indicator of peripheral nerve functions [3,18], our study suggests that peripheral nerve functions decline with passage of time in T2DM.The preceeding statement seems to be true both for motor as well as sensory peripheral nerves as per results of our study.

Our results are supported by a similar study done by Boulton et al where, on a follow up assessment they observed a significant decrease in motor NCV of median nerve in diabetics[24] .However their study population consisted of both IDDM and NIDDM patients.

Decreasing peripheral nerve functions ultimately result in neuropathy , therefore our study also puts forwards for consideration that duration of type 2 diabetes is a risk

factor for DPN .In other words, longer the patient suffers from T2DM more are the chances of development and progression DPN in him /her as previously suggested by several authors.[7,8,19,25].

Duration of diabetes has been found to be independently related to symptoms of sensory neuropathy in non- insulin dependent diabetics[7].Longer duration of diabetes has also been found to be positively associated with neuropathy by other studies as well[8,19,25].Thus our work corroborates well with the available literature.

There were various confounding factors in our study which could have effected the outcome. Many patients were receiving Metformin which effects peripheral nerve functions by causing vitamin B12 deficiency[26]**.** Methylcobalamin was also included in treatment regime of some patients and that might have effected peripheral nerves [27, 28].Our sample size was also small.

Therefore, it is recommended to carry out such a study on large population and minimizing the above mentioned confounding factors.

Conclusion

Duration of T2DM is a risk factor for worsening of peripheral nerve functions and NCV.

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