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Electrophysiological Nerve Conduction Study to Evaluate Peripheral Nerves in Early Detection of Diabetic Peripheral Neuropathy in Type 2 Diabetes

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Abstract: ***Introduction: Diabetic peripheral neuropathy is the most common long term complications of DM. Nerve conduction studies are the most sensitive indices of the severity of neuropathy. Vitamin D is required for nerve cell growth and cell development, neuronal survival and has important role in regulating nerve axonal regeneration .It can be utilized for prevention and therapy of diabetic neuropathy. Aim: To study the association between Vitamin D levels and Nerve conduction velocity in Type 2 Diabetes Mellitus patients. Methodology: Total number of 60 subjects (diabetic subjects and the healthy controls) were examined to assess the Diabetic neuropathy. Sensory Nerve conduction velocity test was done along with the estimation of Vitamin D levels and HbA1c levels in all the diabetic subjects (HbA1c≥6.5%) and the healthy controls. Results: The analysis showed that the NCV decreased in diabetic patients with a low Vitamin D levels in comparison to healthy subjects with normal Vitamin D levels. Conclusion: In diabetic subjects there is progressive neuronal involvement which is accelerated by low Vitamin D levels and poor glycaemic control leads to development of diabetic neuropathy. Therefore, NCS can be employed for the early detection of neuropathy in diabetic patients.***

Keywords: Nerve Conduction Velocity, Vitamin D, Diabetes Mellitus

1. Introduction

Diabetes mellitus (DM) is a group of common metabolic disorders that comprises of chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative insulin deficiencies. It is specific disorder characterised by the condition of hyperglycaemia, insulin resistance, and relative impairment in insulin secretion (Harris MI. et.al, 1989). DM is a debilitating advance disease condition that affects nearly millions of people around the globe. There is an increase in the prevelance of diabetes around the world day by day and Diabetes Mellitus is speedily gaining the status of a potential epidemic in India. The concern is that India would be having the highest population of diabetes by the year 2025 and it is all set to become the "Diabetic Capital" of world in the coming future. (Abeer et al 2018, King H. 1998 et.al). Diabetic peripheral neuropathy (DPN) is one of the most commonly reported long term diabetic complication, affecting around up to the level of 50 % of type 2 diabetic patients (T2DM) (Boulton et. al, 2003).

Its occurrence is explained by many multifactorial etiologies that mainly including: the upregulation of the polyol pathway, functional and structural microvascular disturbances, nervous and ganglionic hypoxias, increased oxidative stress, impairment in glycosylation of axonal and microvascular proteins and also some impaired trophic factors which are in need for these peripheral nerves and their ganglia [Zochodne DW 1999 et.al]. In the asymptomatic stages, it leads to the diabetic foot as the disease process progresses, which proves to be a highly morbid condition that arises from the infection and the ulceration of the foot that ultimately proceeds to amputation. Therefore, identification of neuropathy in diabetics is considered to be important. (Partanen J, 1995 et.al.)

Nerve conduction studies (NCS) are electro diagnostic tests which are used to evaluate the ability of the electrical conduction of the motor and the sensory nerves. The early insulin therapy is able to provide neuroprotective effects in patients with Type 2 diabetes in individuals with diminished insulin secretion according to the Diabetes Control and Complications Trial Research Group, (Partanen J,1995 et.al.) (The DCCT, 1993 et.al) Many studies show that the presence of DPN among patients with diabetes leads to reduced quality of life, mainly attributable to the morbidity and mortality associated with DPN [Benbow S.J 1998, et.al , Davies M ,2006 et.al, Van Acker K 2009 et.al,]

Aim

To study role of nerve conduction velocity in type 2 Diabetes mellitus patients to evaluate Diabetic Peripheral Neuropathy (DPN).

2. Material and Methods

The present study was conducted in Rajeev Gandhi Centre for Diabetes and Endocrinology and Department of Physiology on patients of Type 2 Diabetes Mellitus (T2DM) attending OPD Jawaharlal Nehru Medical college hospital, Aligarh Muslim University from 2015 to 2017 after approval from the Ethical Committee of J. N. Medical College.

Design of the study was a prospective, cross sectional study. Total 60 subjects were taken. Out of these 60 subjects 30 were selected as cases for further study who met the

inclusion and exclusion criteria and gave the valid consent after explaining the procedure to the subject prior to entering for further investigations.

Selected patients were tested for neuropathy assessment after an overnight fasting of 10-12 hours in fasting state. Blood samples were collected for estimation of HbA1C, plasma glucose, post prandial glucose estimation. The patients of 29-69 years of age with a history of diabetes for 5-25 years (ADA) attending the diabetic OPD were selected.

- **Group 1:** 30 Type II diabetes mellitus patients with poor glycaemic control, of both sexes, of age group 29-69 years.
- **Group 2:** 30 Non-diabetic healthy subjects, of both sexes, of age group 29-69 years as a control group.
- **Consent** was obtained from each participant and procedure was explained.

Inclusion criteria of T2DM patients for the present study were patients aged 29-69 years diagnosed with diabetes mellitus on the basis of revised American Diabetic Association Criteria, ie, FPG ≥ 126 mg/dl and 2 hours post prandial plasma glucose ≥ 200mg/dl.

Exclusion criteria of these patients were, presence of thyroid disease (hypo/ hyperthyroidism), previous history of any systemic conditions related to polyneuropathy (alcoholic neuropathy, drug induced neuropathy, renal failure, malnutrition), trauma in the course of nerve to be examined & any exogenous toxins, metals.

Control group for the present study included non – diabetic, non hypertensive healthy individuals with age, sex, BMI (Body Mass Index) matching with those of the diabetic group.

Nerve Conduction Velocity

Windows based Computerized EMG/NCV equipment NeuroStim4 (Medicaid systems, Chandigarh, 160002, India) in NCV lab in the Department of Physiology was used for electrophysiological analysis using surface electrodes to record the NCV. Underlying **principle** for NCV of the study is the application of depolarising square wave electrical impulses to the skin over a peripheral nerve, producing a propagated Nerve Action Potential (NAP) which is recorded at a distance point over the same nerve. Supramaximal stimuli of 0.1ms duration at a frequency 1 Hz, filter setting for sensory conduction was 20Hz-3KHz.

The SNCV was calculated by dividing the distance (mm) between the stimulation and recording sites by the latency (ms).

$$SNCV = Distance / Latency (m/s)$$

Nerve conduction velocities were measured with standard surface stimulating and recording techniques. Electrodes were coated with electroconductive gel and held in place with adhesive tape. Nerve conduction velocity (m/s) was measured in both upper and lower limbs bilaterally.

Nerves studied are Median nerve, Ulnar nerve -Upper limb and Sural nerve -Lower limb

Normal Standard Values of NCV of concerned Nerves- (*Mishra & Kalita 3rd Edition)*

Nerves	NCV values (m/s)
Median	56.2 ± 5.8
Ulnar	61.45 ± 5.73
Sural	50.9 ± 5.4

Diabetic neuropathy in our subjects was assessed by NCV and also by the Modified Neuropathy Disability Score (NDS).

Clinical Diagnosis of Diabetic Polyneuropathy

Modified Neuropathy Disability Score (NDS)

Test		Score (Right limb)	Score (Left limb)
Achilles tendon reflex	0-1-2		
Vibration perception test (tuning fork)	0-1		
Thermal sensation test	0-1		
Tactile sensation test (pin prick)	0-1		

Both upper and lower limb examined
Total Disability Score (Maximum score is 10 points).
A score of 3 or higher is defined as positive for PNP

Monofilament Test

Simple screening test for Evaluation for peripheral neuropathy was done using 10 g / 5.07 Semmes-Weinstein monofilament (Diabetic Foot Care India, Chennai Engineering Service, India). The filament was placed perpendicular to the skin and pressure was applied until the filament just buckles with a contact time of 2 sec. The sensation of pressure using the buckling 10-g monofilament should first be demonstrated to the patient on a proximal site (e.g., upper arm).The patient was prevented from seeing it where the examiner applied the filament. Monofilament was applied at six sites to the plantar surface of great toe and at the base of the first, third or fifth metatarsals, mid sole and at heel of both foot. Normal Response is recorded as 6/6 and inability to perceive the sensation at any one site was considered abnormal .

3. Statistical Analysis

Statistical evaluation of the results was performed using the statistical package IBM SPSS version 22.The data was summarized to test the difference in the mean ± Standard deviation or range values between the groups 1 and 2 by using the Student's (unpaired) 't' test; p values < 0.05 were taken as the level of significance. Pearson's correlation was used to correlate between the different parameters.

4. Results

The baseline characteristics (age, sex, BMI, B.P) of non-diabetic (group1) with patients of T2DM (group2) , showed no significant differences amongst themselves (Table 1) -

Table 1: Comparison between Baseline characteristics of Controls- Group 2 (n=30) v/s T2 Diabetic subjects- Group 1 (n=30)

Variable	Controls (n=30)	Diabetic subjects (n=30)	p value
Age (yrs)	48.87 ± 10.2	54.53 ± 8.21	0.021*
BMI (kg/m^{2})	24.79 ± 2.21	26.47± 3.33	0.026*
Systolic B.P (mmHg)	128.27 ± 5.7	126.13 ± 7.85	0.232
Diastolic B.P (mmHg)	78.20 ± 3.90	80.73 ± 4.50	0.024*
Fasting plasma glucose (mg/dl)	102.17 ± 5.0	148.97 ± 37.47	0.000*
Post prandial plasma glucose (mg/dl)	128.43 ± 6.7	220.2 ± 41.64	0.000*
HbA1c (%)	5.94 ± 0.2	8.39 ± 2.5	0.000*

Table 2: Sensory Nerve Conduction Velocity Study of 30 Patients – (Group 2) of T2DM

S. No.	Observation	No. of patients
1	No impact – normal bilateral SNCV	2
2	Decrease in SNCV of one (Sural) nerve	16
3	Decrease in bilateral SNCV of two (Sural & median) nerves	8
4	Decrease in bilateral SNCV of all three nerves	4
	Total	30

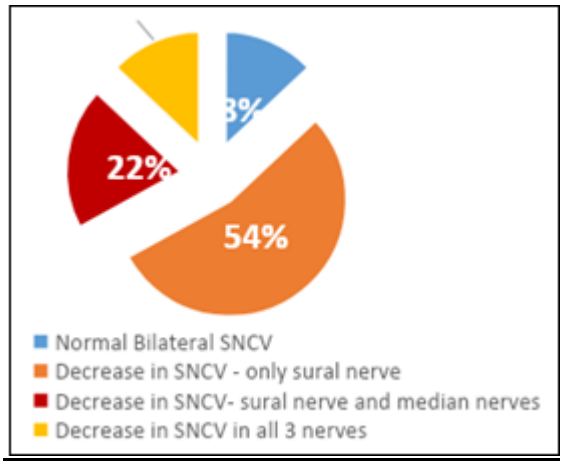

Figure 1

In SNCV test, among 30 patients of T2DM 8% normal SNCV of all nerves. In the rest 28 patients (92%) patients, decrease in SNCV was observed, 16 (54%) patients had decrease SNCV of only 1 nerve, namely the Sural nerve, 8 (22%) patients had decrease in SNCV of 2 nerves , mainly Sural and Median nerves . 4 (16%) patients had decrease in all the 3 nerves (median, ulnar, sural nerves) shown in table 2, fig 1.

Table 3: Comparison of SNCV in Non Diabetes and Type 2 Diabetes group

Nerves	Control (n = 30)	T2 Diabetes subjects (n = 30)	p – value
Rt: Median	50.02 ± 4.8	45.08 ± 6.9	0.002*
Rt: Ulnar	56.19 ± 4.98	45.10 ± 8.56	0.000*
Rt: Sural	51.30 ± 3.5	25.32 ± 12.31	0.000*
Lt: Median	50.87 ± 3.47	47.35 ± 8.9	0.04*
Lt: Ulnar	55.53 ± 3.49	49.71 ± 4.73	0.000*
Lt: Sural	51.10 ± 2.73	31.32 ± 11.65	0.000*

Variation in means of SNCV between non diabetic (controls) and diabetic group (group1 + group2) is significant in all the three nerves- (*p value <0.05 is significant)

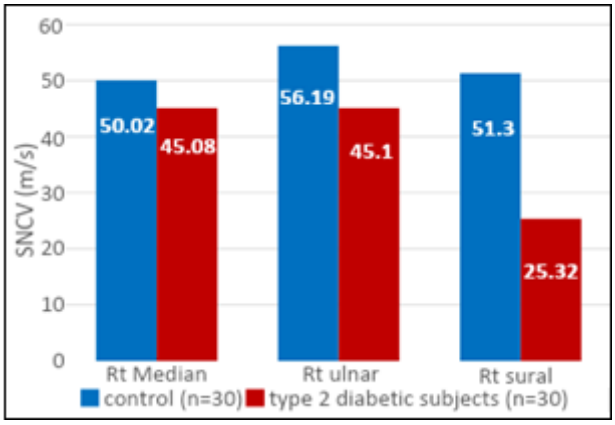

Figure 2: Shows the comparison of Mean SNCV across in control and Type 2 diabetes subjects

5. Discussion

Diabetic Neuropathy (DN) is a common complication of diabetes mellitus leading to severe morbidity. An intensive treatment of neuropathy at the sub clinical level decreases the risk of neuropathy [Dahl-Jorgensen K, et. al 1986]. One of the important methods for assessing nerve functions in DN is the Nerve conduction studies .In our study, we observed that the NCV progressively decreased from the controls (51.30 ±3.6) to the diabetics with poor glycaemic control (25.32± 12.31). These findings are in accordance with previous researchers [The DCCT Research Group et, al.1998]. Bansal et al in 2006 showed in their study that the slowing of NCV is due to the continuous damage occurring to the myelin sheaths and they are also of the opinion that the amplitude decreases with the rising HbA1c levels, thus resulting in the onset and progression of axonopathy [Abeer M et.al, 2019, Bansal V et, al. 2006]. Therefore, it is essential that the monitoring of diabetic patients with NCS in order to provide help in predicting the onset of DN. So we draw a conclusion, that the estimation of both NCV and the HbA1c levels in diabetics is helpful in identifying the risk category for DN, which is one of the main causes for severe morbidity among the diabetes. Also Clayton W, Elasy TA et al, 2009 showed that the accumulation of sugar products results in a decrease in the synthesis of nerve cell myoinositol, which inhibits Na+/K+ ATPase activity, that is required for normal neuron conduction .Thus, decrease in activity of Na+/K+ ATPase pump results in Na +/K+ retention, edema, myelin swelling, axoglial dysfunction and nerve degeneration; further leading to cause neuropathy.

Nerve conduction velocity test is considered a reliable for diagnosis of neuropathy so far. This procedure is sensitive, non invasive, easier to perform, more comfortable and produces results that are easier to measure [American Diabetic Association. *Diabetes Care* 1996]. In our study we observed that there is significant impact of duration of diabetes in onset and progression of peripheral neuropathy similar to Young RJ, et al.1990 in UK which showed that neuropathy was present in as many as 36% people with

duration of diabetes greater than 10 years as compared to 20% when duration of diabetes was 5 years. Therefore, it is essential that the monitoring of diabetic patients with NCS in order to provide help in predicting the onset of DN. So we draw a conclusion, that the estimation of both NCV and the HbA1c levels in diabetics is helpful in identifying the risk category for DN, which is one of the main causes for severe morbidity among the diabetes.

6. Conclusion

The present study showed that both, nerve conduction and glycated heamoglobin, are useful modality for detecting diabetic neuropathy. In diabetic subjects there is progressive neuronal involvement which is accelerated by poor glycaemic control leading to development of diabetic neuropathy.

7. Future Scope

Nerve conduction studies are one of the important methods for diagnosis and evaluation of diabetic sensorimotor polyneuropathy especially for the subclinical neuropathies. Routine Nerve Conduction Studies can be done regularly in diabetic subjects at least on yearly basis. Our study recognises that periodic screening should be carried out in diabetics to prevent long term complications of diabetes.

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