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COMPARISON OF SENSORY NERVE CONDUCTION BETWEEN OVERWEIGHT AND OBESE DIABETIC PERIPHERAL NEUROPATHY PATIENTS BASED ON ASIAN INDIAN BODY MASS INDEX STANDARDS

Physiology

Dr. S. Nirangjhana* MBBS., Postgraduate, Department of Physiology, PSG Institute of Medical Sciences & Research, Coimbatore-641004 *Corresponding Author

Dr. N. Shuba MD., Associate Professor of Physiology, PSG Institute of Medical Sciences & Research, Coimbatore-641004

ABSTRACT

Background: Obesity is a major component of metabolic syndrome that accentuates the inflammatory and oxidative stress in diabetic peripheral neuropathy (DPN). Based on the Asian Indian BMI standards, the prevalence of overweight is on the rise in India.
Aim: To compare the sensory nerve conduction parameters such as latency, amplitude and nerve conduction velocity in the median, ulnar and sural nerves between overweight and obese DPN patients.
Materials and methods: This cross-sectional study was conducted in the Department of Neurology with 80 type 2 DPN patients with Body mass index (BMI) > 23 Kg/m2. Sensory nerve conduction studies were performed. SPSS software was used for statistical analysis.
Results: Except for sural nerve, the nerve conduction studies in other nerves did not show a statistical significant difference between overweight and obesity.
Conclusion: Overweight affects sensory nerve conduction study in diabetic peripheral neuropathy similar to obesity.

KEYWORDS

Diabetic peripheral neuropathy, Overweight, BMI

INTRODUCTION

Type 2 diabetes mellitus is the predominant form of diabetes worldwide accounting for more than 90% of diabetic cases [1]. Among the microvascular complications of diabetes; diabetic neuropathy occurs in more than 50% of individuals with type 2 diabetes mellitus [2]. Diabetic neuropathy can manifest in the forms of polyneuropathy, mononeuropathy and/ or autonomic neuropathy. Out of these forms, distal symmetric polyneuropathy (DSPN) accounts for about 75% of the caseload in diabetic neuropathies [3]. A prevailing view for the pathogenesis of diabetic peripheral neuropathy is the inflammatory and oxidative stress that occurs as a result of metabolic syndrome [3]. Obesity is a major component of metabolic syndrome [4].

Based on the BMI classification criteria for Asian Indians, the prevalence of overweight and obesity (BMI ≥23 kg/m ^{2}) in India is on the rise [5]. For long it was known that obesity is a major risk factor for amplifying the severity of diabetic neuropathy. Now with the advent of newer guidelines for BMI classification [6] even diabetic patients with overweight (BMI 23-27.4 Kg/m^2) could be under risk for worsening severity of peripheral neuropathy on par with obesity.

Hence using nerve conduction study as a tool, we decided to compare the sensory nerve conduction study parameters such as latency, amplitude, and nerve conduction velocity in the median, ulnar and sural nerves between overweight and obese diabetic peripheral neuropathy patients (DPN) patients. Since the sensory component of the nerves is more affected in diabetic peripheral neuropathy [7], we have chosen sensory nerve conduction study. The null hypothesis employed here is that there is no difference in sensory nerve conduction between overweight and obese DPN patients. Sensory nerve conduction study parameters in DPN patients with both overweight and obesity were also correlated with BMI.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Neurology from December 2017 to December 2018 in 80 DPN outpatients after getting Institutional Ethics Clearance. The sample size was calculated with Open Epi software version 3.0 using the prevalence of overweight and obesity from ICMR-INDIAB study 2015 [8] and 95% confidence interval.

Inclusion criteria

- Age: 35-70 years
- BMI ≥ 23 Kg/m^2 (Subjects with BMI 23-27.4 Kg/m^2 were considered overweight and those with BMI > 27.5 Kg/m^2 were considered to be obese)
- Gender: Both males and females
- Subjects with a history of type 2 diabetic peripheral neuropathy for more than 1-year duration on treatment.

Exclusion criteria

- Subjects with hemolytic or aplastic anemias
- Subjects with vitamin B12 deficiency
- Subjects with thyroid disorders
- Subjects with inflammatory conditions such as connective tissue disease, CIDP (Chronic Inflammatory Demyelinating Polyneuropathy) or neuromuscular disease
- Subjects with signs of peripheral vascular disease
- Subjects with a history of cerebral infarction, cervical spondylosis or lumbar spondylosis.
- Subjects diagnosed with malignancies.
- Subjects with cardiac failure, hepatic failure or poor general conditions.

After getting informed and written consent, the data was collected. Recorders Medicare System (RMS) EMG EPM 2K version 1 was used to record the sensory nerve conduction parameters such as latency, amplitude and nerve conduction velocity (NCV). Onset latency (ms) was measured from the onset of stimulus artifact to the initial negative peak in antidromic conduction. Amplitude (μV) was measured from the baseline to the negative peak of the biphasic response obtained after supramaximal nerve stimulation and NCV (m/s) was measured by applying a stimulus at a single stimulus site. The formula utilised for calculating NCV was

$$\text{Conduction velocity} = \frac{\text{Distance between stimulating and recording electrodes (cm)}}{\text{Onset of latency (msec)}} \times 10$$

Fasting (FBS) and postprandial plasma glucose levels (PPBS) were estimated using hexokinase, UV, kinetic methods. Glycosylated hemoglobin (HbA1c) was assessed using high-pressure liquid chromatography (HPLC).

Serum cholesterol and triglycerides (TGL) were measured using enzymatic endpoint methods. Serum high-density lipoproteins (HDL) and low-density lipoproteins (LDL) levels were measured using direct enzymatic assays. Serum urea and creatinine were determined using enzymatic methods. Estimated glomerular filtration (eGFR) was calculated based on chronic kidney disease epidemiology collaboration (CKD – EPI) equation (2009).

The data collected were analyzed using SPSS IBM software version 24. Shapiro-Wilk test was used to test the normality of variables. Normally distributed data are presented as mean ± standard deviation (SD) and variables with skewed distribution are presented as median (interquartile range).

Independent t-test was used to compare the variables with normal distribution between DPN with overweight and those with obesity. Mann-Whitney U test was used to compare the variables with skewed

distribution. Pearson's correlation was used to correlate normally distributed nerve conduction study variables with BMI. Spearman's correlation was used to correlate skewed nerve conduction study variables with BMI. p-value < 0.05 (2-tailed) was considered to be statistically significant.

RESULTS

Table 1: Baseline characteristics and clinical profile between DPN with overweight and DPN with obesity

Variables	DPN with overweight n = 24	DPN with obesity n = 56	p-value
Age (years)	57.5 (45.75,67.75)	52 (44,61.5)	0.196
Body Mass Index (Kg/m^2)	26.65 ± 0.73	29.18 ± 1.20	0.000*
Duration of diabetes (years)	5 (4,7)	5 (4,7)	0.840
Fasting Blood Sugar (mg/dL)	122.5 (104.25,148.75)	122 (98.25,140)	0.564
Postprandial blood sugar (mg/dL)	193 (163.5,214)	189 (184.25,198)	0.785
HbA1c (%)	6.75 (6.5,7.875)	6.9 (6.8,7.4)	0.405
Total cholesterol (mg/dL)	186.33 ± 30.85	185.02 ± 26.26	0.846
High Density Lipoproteins (mg/dL)	30 (25.25,34.75)	29.5 (23.25,33.75)	0.639
Low Density Lipoproteins (mg/dL)	155.5 (120.5,171.75)	165 (146.25,179.5)	0.078
Triglycerides (mg/dL)	175 (159.25,180.75)	173 (154.75,184.75)	0.954
Serum urea (mg/dL)	21 (18,37)	25 (18,29)	0.850
Serum creatinine(mg/dL)	0.76 ± 0.19	0.67 ± 0.16	0.382
eGFR (ml/min)	97.55 ± 16.64	103.85 ± 14.85	0.098
Systolic Blood pressure (mmHg)	135 (128,143.5)	138 (126.5,146)	0.636
Diastolic Blood pressure (mmHg)	88 (82.5,92)	90 (82,92)	0.402

Data are presented as mean + SD and median (interquartile range). HbA1c- Glycosylated hemoglobin. eGFR- estimated Glomerular Filtration Rate. p-value< 0.05 (2-tailed) was considered to be statistically significant*

Out of 80 Diabetic peripheral neuropathy patients, 24 were overweight and 56 were obese. There was no statistically significant difference in age, duration of diabetes, FBS, PPBS, HbA1c, total cholesterol, HDL, LDL, TGL, serum urea, creatinine, eGFR, BP between DPN patients with overweight and those with obesity. Gender distribution was proportionally equal in both groups. Hence we can consider that these variables do not significantly affect the results of the study.

Table 2: Comparison of sensory nerve conduction study variables between DPN with overweight and DPN with obesity

Nerves	Nerve conduction study variables	DPN with overweight n = 24	DPN with obesity n = 56	p-value
Right median nerve	Latency (ms)	4.7 (3.62,5.17)	4.9 (4.12,5.2)	0.303
	Amplitude (μV)	14.9 (13.97,20.35)	14.85 (13.5,20.5)	0.589
	NCV (m/s)	49.05 (46.9,50.1)	48.85 (46.22,50.1)	0.916
Left median nerve	Latency (ms)	4.6 (3.72,5.2)	4.8 (3.62,5.37)	0.415
	Amplitude (μV)	15 (14.2,20.05)	14.8 (13.6,20.57)	0.992
	NCV(m/s)	46.9 (43.2,51.47)	43.35 (41.65,51.2)	0.291
Right ulnar nerve	Latency (ms)	4.42 ± 1.15	4.60 ± 1.10	0.951
	Amplitude (μV)	15 (14.2,20.12)	14.8 (13.5,20.5)	0.644
	NCV (m/s)	40.90 ± 9.39	38.96 ± 40.90	0.665
Left ulnar nerve	Latency (ms)	4.5 3.22,5.05)	4.5 (3.75,5.45)	0.326
	Amplitude (μV)	15.2 (14.2,20.75)	13.7 (13.12,19.52)	0.055
	NCV(m/s)	38.53 ± 6.46	38.27 ± 6.85	0.874
Right sural nerve	Latency (ms)	3 (2.52,4.15)	3.85 (2.95,4.2)	0.046*
	Amplitude (μV)	6.15 (4.2,7.37)	6.05 (4.22,8.42)	0.443
	NCV (m/s)	38.6 (30.5,49.1)	36.85 (30.7,49.17)	0.965
Left sural nerve	Latency (ms)	3.25 (2.5,4.2)	3.55 (2.5,4.55)	0.349
	Amplitude (μV)	5.5 (3.9,6.87)	4.1 (3.2,5.75)	0.009*
	NCV (m/s)	38.95 (27.35,48.2)	35.95 (29.57,49.12)	0.757

Data are presented as mean + SD and median (interquartile range). p-value < 0.05 (2-tailed) was considered to be statistically significant*

On comparing the sensory nerve conduction between DPN with overweight and DPN with obesity, there was no statistically significant difference in the latency, amplitude ,and NCV of median and ulnar nerves. Hence the null hypothesis of this study has not been disproved and the hypothesis stating that there is no difference in sensory nerve conduction between overweight and obese DPN patients still prevails in upper limb nerves.There was an increase in latency of the right sural nerve and a reduction in amplitude of the left sural nerve in DPN with obese when compared to DPN with overweight.

Table 4: Correlation between BMI and sensory nerve conduction variables in Diabetic peripheral neuropathy (n=80)

Nerves	Sensory nerve conduction variables	Correlation coefficient	p-value
Right median nerve	Latency (ms)	0.089	0.585
	Amplitude (μV)	-0.243	0.131
	NCV (m/s)	-0.009	0.958
Left median nerve	Latency (ms)	0.071	0.665
	Amplitude (μV)	-0.132	0.416
	NCV (m/s)	-0.018	0.913
Right ulnar nerve	Latency (ms)	0.061	0.710
	Amplitude (μV)	-0.052	0.748
	NCV (m/s)	-0.008	0.961
Left ulnar nerve	Latency (ms)	0.168	0.300
	Amplitude (μV)	-0.050	0.760
	NCV (m/s)	-0.036	0.827
Right sural nerve	Latency (ms)	0.335	0.035*
	Amplitude (μV)	-0.172	0.288
	NCV (m/s)	-0.053	0.744
Left sural nerve	Latency (ms)	0.024	0.882
	Amplitude (μV)	-0.251	0.118
	NCV (m/s)	-0.087	0.596

p-value< 0.05(2-tailed) was considered to be statistically significant

The correlation was not statistically significant except for the latency of the right sural nerve. But based on the correlation coefficient, with increasing BMI; latencies increase, amplitudes decrease, and nerve conduction velocities decrease in the median, ulnar and sural nerves.

DISCUSSION

In the present study, sensory nerve conduction study variables were affected in DPN with both overweight and obesity when compared to the normal reference values for sensory nerve conduction by Misra [9]. Latency was increased and amplitude, NCV was decreased in median, ulnar, sural nerves of both overweight and obese DPN patients. The main pathophysiology behind peripheral neuropathy is the relative loss of myelin fibers resulting in segmental demyelination. The involvement of the polyol pathway and non-enzymatic glycation of proteins that trigger oxidative and inflammatory stress damages the

neuronal cells [1] and this has been postulated as the pathogenesis for segmental demyelination [10].

A study by Ugoya S.O, et al had shown an association of obesity with diabetic peripheral neuropathy. It was observed that obesity, which is an index of insulin resistance predisposes to peripheral neuropathy [11].

In the present study except for the sural nerve, the sensory nerve conduction was affected in both overweight and obese DPN patients. Metabolic syndrome is a major contributor to oxidative stress of neurons and it comprises of obesity especially central obesity, insulin resistance, fasting hyperglycemia, hypertriglyceridemia, reduction in HDL, a rise in LDL and hypertension [4]. Out of these, obesity plays a pivotal role.

In the present study, latency of the right sural nerve and amplitude of the left sural nerve were affected more in obese DPN compared to DPN with overweight. A study by Kang J.H, Lee Y.S, et al in diabetic peripheral neuropathy subjects showed that sensory nerve conduction parameters of the sural nerve were affected in the lower limb when compared to NCV in upper limb nerves. Thus based on electrophysiological findings, nerves of the lower limb are more likely to be damaged diabetic sensorimotor polyneuropathy [12]. A study by Bril V, Ono Y, et al demonstrated by performing nerve biopsy study in diabetic subjects that sorbitol accumulation is more in the sural nerves [13].

Obesity is assessed by the Body Mass Index calculated by using the formula: weight in kg /(height in meters)^2. Based on the Asian Indian standards by WHO; people with BMI less than 18.5 kg/m^2 are regarded as underweight, BMI between 18.5 – 23 kg/m^2 are regarded as population with increasing but acceptable risk, BMI between 23 – 27.5 kg/m^2 as category with increased risk and BMI > 27.5 kg/m^2 as category with higher high risk [6]. The findings of the present study are in concordance with the Asian Indian BMI standards since sensory nerve conduction was affected above a BMI of 23 kg/m^2.

In the present study, with increasing BMI; the latency of sensory nerves increased, amplitude decreased, and nerve conduction velocity decreased. Slowing of NCV denotes ongoing myelin sheath damage and a reduction in amplitude suggests the degree of axonal degeneration [14].

This is supported by a study done by Brismar, et al which suggests that small-caliber non-myelinated fibers are affected first as a result of alteration in $Na^+ K^+$ channels at the nodes of Ranvier in obese subjects [15]. A study done by Yadav RL, Sharma D, et al revealed a reduction in the amplitudes of sensory nerves. This has been attributed to a decrease in the number of synchronously discharging neurons [16]. Similar results have been obtained in a study done by Giacinta, et al [17].

The limitation of the study is that the bias of selection and information could not be avoided as the study participants were selected from a single centre. Control group with BMI in normal range could not be recruited. Confounding factors were avoided to the best of abilities.

CONCLUSION

BMI > 23 Kg/m^2 is a risk factor that contributes to the increasing severity of diabetic peripheral neuropathy. The null hypothesis of this study has not been disproved and the hypothesis stating that there is no difference in sensory nerve conduction between overweight and obese DPN patients still prevails in upper limb nerves. Hence we can ascertain that overweight affects sensory nerve conduction study in diabetic peripheral neuropathy similar to obesity. We suggest that overweight must also to be addressed on par to obesity in the management of diabetic peripheral neuropathy

Conflict of interest

There was no conflict of interest in the present study

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