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ROLE OF MEDIAL AND LATERAL PLANTAR SENSORY NERVE CONDUCTION STUDIES IN EARLY DETECTION OF DIABETIC NEUROPATHY

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Abstract:
Introduction:Diabetic neuropathy causes a wide spectrum of abnormalities from autonomic and cardiovascular dysfunction to diabetic foot with a prevalence of 10% in newly diagnosed diabetes, stressing the importance of early diagnosis. This study evaluates the utility of SNAPS of plantar nerves in patients with normal NCS for early detection of diabetic neuropathy.
Purpose of study: Evaluate the routine NCS and medial and lateral plantar nerve NCS in symptomatic diabetic patients and controls. To assess if medial and lateral plantar nerve NCS increases the sensitivity in detection of neuropathy in diabetic patients
Materials and Methods: 100 subjects were included in the study consisting of 50 (28 Male & 22 Female) Diabetic patients and 50 (25 Male & 25 Female) control group. NCS was performed for the evaluation of plantar nerves along with routine motor and sensory nerves on them, recruited from December 2017 to March 2018 in the Department of Neurology, SRIHER, Chennai.
Results: Among the 50 patients with Diabetes, we investigated 10 individuals each aged 31-40 years (mean 35.2±3.22), 41-50years (45.6±3.34), 51-60years (56.3±4.57), 61-70years (66.2±3.42) and 71-80 years (75.1±3.28) with the duration of diabetes for >25 years (29.3±3.46). 17 patients (34%) had normal NCS with prolonged SNAPS of plantar nerves, 23 patients (46%) had both. Abnormal NCS in Diabetes showed statistically significant prolongation of latency and reduction in amplitude and drop out in conduction velocity in all age groups and also as the duration of diabetes increased.
Conclusion: It may be possible to detect the neuropathy early in neurophysiological manner in diabetic PNPs by studying plantar sensory nerve conduction properties in addition to the nerve conduction parameters studied in a standard PNP protocol.
Keywords: Diabetic peripheral neuropathy, Medial and lateral plantar nerves, NCS

Introduction

India has one of the highest prevalence of Type II Diabetes Mellitus (T2DM) in the world. It is estimated that by the year 2030 there are will be nearly 80 million Indians with T2DM in the country. The disease constitutes a substantial burden for both the patient and health care system, mainly due to macro vascular and micro vascular complications. The prevalence of Diabetic Polyneuropathy (DPN) varies greatly in different studies, ranging from 8% to 59%. DPN significantly increases the risk of complications such as foot infections, deformities, gangrene, and amputations. The Diabetes Control and Complications Trial (DCCT) demonstrated that improved glycemic control can slow the progression of neuropathy. This study evaluates the utility of SNAPS of plantar nerves in patients with normal NCS for early detection of diabetic neuropathy. In 2000, India (31.7 million) topped the world with the highest number of people with DM and number raised to 69.2 million (8.7%) in 2015.[1] It is predicted that by 2030 DM may afflict up to 79.4 million individuals in India. [2] Studies in USA and UK reported that neuropathic pain syndromes have affected up to 70% population with DM and painful symptoms had occurred in 26% in patients without neuropathy and 60% of patients with severe neuropathy. [3] In India there had been a small number of trials to screen the current status for DPN, among them a study estimated an overall prevalence of neuropathy as 19.1% in south Indian Type 2 diabetic patients [4]. The DPN can be defined based on clinical features like numbness, signs like absent ankle reflexes and NCS as possible in patients with only Clinical features, as probable when combined with clinical signs and definitive when symptoms and signs are confirmed with NCS and also as sub clinical if only NCS abnormality is present without any signs or symptoms. [5] The hyperglycemia state in diabetes causes DNA damage, ER stress, mitochondrial dysfunction, apoptosis and loss of neurotrophic signaling. This cell damage can occur in neurons, glial cells and vascular endothelial cells, as well as triggering macrophage activation, all of which can lead to

nerve dysfunction and neuropathy. The relative importance of the pathways in this network will vary with cell type, disease profile and time. [6, 7, 8] Electrophysiological testing plays a major role in evaluation of patients with DSP using motor and sensory nerve conduction studies. Testing not only defines the fibers that are affected in DPN (motor and sensory), but also renders a gross estimate of the duration of the neuropathy, and gives an insight into the prognosis. Routine nerve conduction studies include evaluation of motor function of the median, ulnar, peroneal, and tibial nerves, and sensory function of median, ulnar, radial, and sural nerves. Velocities are in meters per second, motor amplitudes in millivolts, and sensory amplitudes in microvolts. These measurements of upper and lower limb motor and sensory nerve function show the presence, distribution, and severity of peripheral nerve disease. Nerve conduction studies (NCS) have always been considered the gold standard for the diagnosis of neuropathy. NCS correlate with clinical scores; nerve amplitude reflects the degree of nerve fiber loss. Usually in NCS abnormalities are detected in 45-60% of patients with type 2 diabetes. Severity of abnormality in NCS reflects a correlation with the glycemic levels and usually abnormal NCS increases with the duration of diabetes.[9] A study by Resni Kent al compared the aged population with diabetes and without diabetes and demonstrated walking speed,static and dynamic balance with coordination were reduced in diabetic population with electrophysiology tests [10]. studies showed bilateral NCS assessment of plantar nerves together increases the rate of diagnosis of diabetic distal sensory neuropathy compared to assessment of either of these nerves. [11]

Purpose of study

Evaluate the routine NCS and medial and lateral plantar nerve NCS in symptomatic diabetic patients and controls.

To assess if medial and lateral plantar nerve NCS increases the sensitivity in detection of neuropathy in diabetic patients.

Materials and Methods

50 Patients aged between 30-80 years with Diabetic Neuropathy Symptom score >2/4 (walking unsteadiness, neuropathic pain, paresthesia, numbness) and 50 healthy people without any neurological deficits or systemic illness were included in our study. Pregnant women, patients with other causes of neuropathy and patients not fitting the age limit were excluded. These 100 patients were evaluated in Department of Neurology, SRIHER from December 2017 to May 2018.

After recruiting the subjects, detailed history was taken regarding neuropathic symptoms, history of chronic drug usage, toxin exposure and about any symptoms suggestive of hypothyroidism and vitamin B12 deficiency. A detailed general and neurological examination was performed. After informed consent, NCS was performed for the evaluation of MNC, SNC and medial and lateral plantar nerve conduction in all 100 subjects. Nerve conduction study was done by using NIHON KOHDEN NEUROPACK S1 (NCS, EP & EMG) equipment. Routine investigations like Hemogram, urine routine examination, serum creatinine, chest X- ray, vasculitic profile, serum B_{12} and thyroid profile were done in whom electrophysiology is suggestive of neuropathy.

Motor nerve conduction studies (Distal latencies, CMAP amplitudes, CVs and F latencies) were done in bilateral median, ulnar nerves in upper limbs; bilateral peroneal and tibial nerves in lower limbs. Sensory nerve conduction studies (Distal latencies, SNAP amplitudes and CVs) were done in bilateral median, ulnar nerves in upper limbs; bilateral sural, peroneal, lateral plantar and medial plantar nerves in lower limbs. Surface electrodes were used for stimulating. Surface stimulation was performed at the medial and lateral part of foot. The amplitude of the SNAP was measured from peak to peak. The latency to the SNAP was measured to the negative peak. Skin temperature was controlled between 32°C-34°C. The machine settings were Sensitivity -10-20mV/Division, Sweep Speed -2mSec/Division, LFF-20Hz, HFF-3 KHz. The Instrumentation parameters were Intensity -50 and Above, Duration-0.2ms and above, Stimulation Rate-1Hz, Supra-maximal Stimulation.

Data entry and statistical analysis

Data was entered into Microsoft Excel sheet and analysed using IBM SPSS Statistics version 20.0. Descriptive statistics were expressed as Means and percentages. P-value of <0.05 will be considered statistically significant.

Results

Among the 100 subjects examined 50 subjects were healthy individuals and 50 subjects were Diabetic. Among the cases and healthy individuals 50% were females. Recruitment was done by considering equal distribution among ages. Among the healthy volunteers, there were 10 individuals aged 31-40 years (mean 35.4±3.27), 10 individuals aged 41-50 years (mean 46.2±3.19), 10 individuals aged 51-60 years (mean 56.1±3.51), 10 individuals aged 61-70 years (mean 66±3.33) and 10 individuals aged 71-80 years (mean 74.8±2.78). Among the 50 patients with Diabetes Mellitus, there were 10 individuals aged 31-40 years (mean 35.2±3.22), 10 individuals aged 41-50 years (mean 45.6±3.34), 10 individuals aged 51-60 years (mean 56.3±4.57), 10 individuals aged 61-70 years (mean 66.2±3.42) and 10

individuals aged 71-80 years (mean 75.1±3.28) with the duration of diabetes for >25 years (mean 29.3±3.46).

Table 1 shows Medial plantar nerve conduction in healthy individuals showed mean Latency of 2.88±0.41ms & 2.87±0.39ms (R & L), mean Amplitude of 14.56±4.86µV & 14.55±4.87 µV (R&L) and mean conduction velocity of 50.02±6.85m/s & 50.10±7.02m/s (R&L). Likewise Lateral plantar nerve conduction in healthy individuals showed mean Latency of 2.87±0.40ms &2.84±0.40ms(R&L), mean Amplitude of 14.55±4.38µV &14.5±4.78µV(R&L) and mean conduction velocity of 50.01±6.47m/s &50.2±6.75 m/s(R&L).

Compared to that in Table 2 shows mean latency, mean amplitude and mean conduction velocity of medial plantar nerve in diabetic patients were 4.2±1.17ms &4.29±1.14 ms(R&L) , 4.11±2.87µV &4.22±3.03µV (R&L) and 35.86±9.15 m/s & 35.61± 9.62 m/s(R&L) respectively. Mean latency, mean amplitude and mean conduction velocity of lateral plantar nerve in diabetic patients were 4.24±1.17ms & 4.42±1.18ms(R&L), 4.27±2.87 µV & 4.22±3.31µV (R&L) and 35.62±9.55m/s&35.48 ±9.48 m/s(R&L). In regard to the duration of diabetes showed following values,

In the 51-60 year group who had DM for 15-19 years, lateral plantar nerve conduction showed statistically significant prolongation of latencies, decreased amplitude and reduced conduction velocity on both sides but medial plantar nerve conduction showed statistically significance only in latency prolongation and reduction in amplitude but not in conduction velocity (p=0.0737) on both sides. In the age group of 71-80 years who had diabetes for > 25 yrs, statistically significant reduction in amplitude and delayed conduction velocity were present on both right & left medial and lateral plantar nerve conduction but latency prolongation (p=0.6804) was not statistically significant on both sides. In all other age groups namely 31-40years, 41-50 years, 61-70 yrs, (p=<0.0001) statistical significance was noted in all three parameters of latency prolongation, amplitude reduction and velocity reduction on both sides of medial and lateral plantar nerve conduction.

Table 1: NCS OF MEDIAL AND LATERAL NERVES IN CONTROLS

CONTROLS						
	MPN			LPN		
	AMP	LATENCY	CV	AMP	LATENCY	CV
RIGHT	14.56+/- 4.86mv	2.88+/- 0.41ms	50.02+/- 6.85ms	14.55+/- 4.38mv	2.87+/- 0.40ms	50.01+/- 6.47ms
LEFT	14.55+/- 4.87mv	2.87+/- 0.39ms	50.10+/- 7.02ms	14.5+/- 4.78mv	2.84+/- 0.40ms	50.2+/- 6.75ms

Table 2: NCS OF MEDIAL AND LATERAL PLANTAR NERVES IN DIABETIC PATIENTS

CASES						
	MPN			LPN		
	AMP	LATENCY	CV	AMP	LATENCY	CV
RIGHT	4.11+/- 2.87mv	4.2+/- 1.17ms	35.86+/- 9.15ms	4.27+/- 2.87mv	4.24+/- 1.17ms	35.62+/- 9.55ms
LEFT	4.22+/- 3.03mv	4.29+/- 1.14ms	35.61+/- 9.62ms	4.22+/- 3.31mv	4.42+/- 1.18ms	35.48+/- 9.48ms

Discussion

In Iyer KS study [12] recording sensory nerve action potentials (SNAP) from the medial and lateral plantar nerves was established using 30 healthy adults as subjects. Potentials were recorded with surface electrodes both antidromically and orthodromically. The mean latency and amplitude of the SNAP of the medial plantar nerve using antidromic stimulation were 2.5msec (+/- 0.32) and 16.3microV (+/- 6.5), respectively. Orthodromically, the latency was 2.5msec (+/- 0.35) and the amplitude 16.5microV (+/- 7.14). For the lateral plantar, antidromically the nerve latency was 2.5msec (+/- 0.35) and the amplitude 14.8microV (+/- 4.41). With the orthodromic procedure, the latency remained unchanged but the amplitude was 11.0microV (+/- 5.59). In the case of the lateral plantar nerve, the antidromic technique consistently resulted in higher amplitude responses. Our study was correlated with the antidromic stimulation method and we obtained similar results in terms of latency and amplitude. In Daniel Dumitru study [13] the mean latency of medial and lateral plantar nerves was 3.2±0.3 and 3.1±0.3 ms. The amplitude of the medial plantar and lateral plantar nerve were at a range of 10-30µV and 8-20µV, this study was not directly compared with our study, but they may provide insight into the present study.

Table 3: NEUROPATHY IN CASES VS CONTROLS

NCS	NORMAL (NEUROPATHY ABSENT)	ABNORMAL (NEUROPATHY PRESENT)
CASE	10 (20%)	40 (80%)
CONTROL	50 (100%)	0

Table 4: NCS WITH PLANTAR NERVES IN CASES

ABNORMAL NCS WITH PLANTAR NERVES INVOVED	23 (46%)
NORMAL NCS WITH PLANTAR NERVES INVOLVED	17 (34%)
BOTH NORMAL	10 (20%)
TOTAL	50

Table 5: COMPARISON STUDIES WITH PLANTAR NERVES NEUROPATHY

STUDY	No. OF PTS	percent
PRESENT STUDY	40	80%
NODERA ET AL 2002[14]	133	69%
K ULUC ET AL 2008[11]	30	60%
JAE YOUNG ET AL 2008[15]	15	48%

In current study total 18 nerves (8 motor, 10 sensory) are studied per individual and that could be reason behind high prevalence and adding medial plantar nerve and lateral plantar nerve increased the prevalence as expected. In our study the plantar nerves were involved in 17(34%) of subjects with a normal routine NCS of diabetics which was similar to 7 out of 15 (48%) study by Jae Yong et al.[15] Sensitivity of detection of neuropathy has increased from 23 (46%) to 40 (80%) by including plantar nerves in NCS as in Nodera et al. from 27% to 69% as showed in table 5.[14] In our study 17 (34%) of the subjects had an abnormal medial and lateral plantar nerve studies with a normal routine NCS represented in table 4. This shows that incorporating the study of these nerves to routine NCS would be helpful. Table 3 shows that assessment of medial plantar and lateral plantar NCS along with routine NCS in our study showed that neuropathy detection has increased from 23(46%) subjects to 40(80%). Hence sensitivity of detecting neuropathy in diabetics may increase by addition of plantar NCS to routine NCS. Nerve conduction study also shows that the prolongation of latencies and decrease in the amplitude and drop in conduction velocity increases, as the duration of diabetes in the patient increases was in agreement with Perkins et al review. [16] The reference values of plantar nerves SNAPs with more validated studies may be developed for the same purpose.

Conclusion

It may be possible to detect the neuropathy early by electrophysiology in diabetes by studying plantar sensory nerve conduction properties in addition to the nerve conduction parameters studied in a standard PNP protocol.

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