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Comparative analysis of electrophysiological parameters of sural nerve in normal and type-2 diabetic subjects

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ABSTRACT

The study was designed to evaluate sural nerve conduction of type-2 diabetes mellitus (T2DM) patients that were asymptomatic for neuropathy and compare their findings with age and sex matched healthy individuals. Using a standard technique, sural nerve conduction study was conducted on 100 T2DM patients with no clinical features suggestive of neuropathy and 100 healthy volunteers, matched for age and sex, serving as control. Sural nerve latency, Amplitude and Conduction Velocity (CV) were measured using Nihoen Kohden EMG Machine. On comparison of the sural nerve conduction parameters, sural nerve distal latencies were significantly lower in the control group while the sural nerve conduction velocities and amplitudes were significantly higher in the T2DM group. The study showed significant difference between the sural nerve conduction parameters in T2DM patients without clinical features suggestive of peripheral neuropathy when compared with apparently healthy individuals.

KEY WORDS: ***Sural nerve; Diabetic neuropathy; Electrophysiology***

INTRODUCTION

Nerve conduction studies are an invaluable aid to evaluate and quantify the functional status of peripheral nerves. This evaluation includes measurement of sensory and motor conduction, amplitudes, velocities and latencies of peripheral nerves and these electrophysiological tests correlate with nerve biopsy results and they serve as a surrogate for histological determination in longitudinal studies.[1,2]

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate.[3] Similarly, the frequency of complications of diabetes is on the increase.[4] T2DM, with their complications, often has adverse impact on quality of life of the patients. Complications of diabetes include diabetic neuropathy (DN), retinopathy and nephropathy. Out of the complications of T2DM, DN is the most common diabetes complication occurring in about 60–70% of diabetic patients.[4,5] DN accounts for more than 60% of non-traumatic lower-limb amputations.[6]

The most common type of DN is distal symmetric polyneuropathy. It commonly affects the longest axons in the extremities first and progresses proximally in a stocking-glove pattern.[5]

A large number of the nerve dysfunctions start from the sensory nerves of the lower extremities.[5] Consequently, measurement of sensory nerve function in the lower limb nerves by electrical stimulation is mandatory and diagnostically rewarding.[7,8]

As far as the NC parameters are concerned, the sensory nerve conduction velocity as well as the sensory latency of the nerve provides the highest diagnostic sensitivity.[8]

Sural nerve is one of the most frequently affected nerves in DN. Like in many other conditions that manifest as or are complicated by polyneuropathy, sural nerve, which is a distal sensory nerve in the lower limbs, reliably exhibits nerve conduction changes in DPN.[9-13] Furthermore, it is highly correlated to the morphological severity of DPN as assessed by biopsy.[1,2]

Though, the number of people living with DM and DN in developing countries is regrettably on the increase, there is scarcity of electrodiagnostic facilities for NCS assessment necessitating reliance on less specific and less sensitive screening tools like the United Kingdom screening test (UKST) for diagnosis.[14,15] NCS are more sensitive than clinical examinations as the later does not offer quantitative results. Besides, the NCS are the least variable and non-invasive means of evaluating neuropathy.[16]

The study was designed to evaluate sural nerve conduction of T2DM patients that were asymptomatic for neuropathy and compare their findings with age and sex matched healthy individuals.

METHODOLOGY

The data was collected over a six-month period at the neuro-diagnostic laboratory of the Aminu Kano Teaching Hospital (AKTH), Bayero University, Kano, Nigeria. One hundred T2DM patients without features suggestive of DN and 100 age and sex matched controls were recruited in the study. The cases were already but recently diagnosed T2DM that were on treatment and were recruited from the diabetic clinics of the AKTH, Murtala Muhammad Specialist Hospital (MMSH) and other peripheral hospitals. Diagnosis of DM was made by consultant endocrinologists and senior residents in the endocrine and metabolic units in all cases. All participants with symptoms of neuropathy, chronic musculoskeletal disorders, thyroid disorder, leprosy, any other chronic systemic disease, alcoholics, smokers and pregnancy were excluded from the study. A basic neurological examination was performed to assess muscle power, stretch reflexes and sensation.

The NCS was performed with the patients and controls lying comfortably in the supine position. A standardized technique was used to obtain and record action potentials for sensory function of sural nerve.[17,18] The protocol adopted in the current study was like that elsewhere, with minor alteration.[19] The setting for a 4-channel electromyography machine (Digital Nihon Kohden machine [NM- 420S, H636, Japan]) used in the study was as follows: low cut was set at 5–10 Hz, high cut was set at 2–3 KHz, the amplification was set between 20,000 and 100,000 times, the electrode impedance was kept below 5 kΩ and the sweep speed for sensory nerve conduction was maintained at 1–2 ms/division and a stimulus duration of 50 µs to 1000 µs and current 0–50 mA were required for effective nerve stimulation.

Data was collected for latency measured from the onset of action potential, conduction velocity, and amplitude and sensory nerve action potential (SNAP) were measured from positive peak to the base.

All the studies were performed with surface recordings and stimulations.

The nerve was stimulated with bipolar surface electrode cathode located in the midcalf, 10-18 cm proximal to the active recording electrode.

The active recording electrode was placed just below the lateral malleolus. A ground electrode was placed between the stimulating and recording electrodes. Sensory nerve conduction was measured antidromically. The sensory nerve conduction velocity (SNCV) was measured by stimulating at a single site.

Analysis

All the data generated were collated, checked and analyzed using GraphPad Prism (version 6, GraphPad Software, Inc. CA 92037 USA). Quantitative variables were described using mean with standard deviation and median with range in case of parametric and non-parametric data respectively. Student t-test or Mann-Whitney test was used for the comparison of nerve conduction parameters between T2DM and control. P value of < 0.05 was considered significant.

Informed consent was obtained from every participant and ethical approval was obtained from the ethical review committee of the AKTH Kano.

RESULTS

A total of 100 T2DM patients, who were matched with 100 of the healthy volunteers by age and sex, comprised 58% males and 42% females were recruited in the study. Their mean age was 49 yrs ± 19 years. The mean duration of T2DM was 2.32 ± 0.83 years.

The median values of sural nerve velocities with their 95% confidence interval were 35.8 m/s (34.3-39.1) and 53.9 m/s (53.4-54.8) in the T2DM and control groups respectively (P<0.0001).

The mean values of the sural nerve distal latencies with their 95% confidence interval were 4.4 ms (4.2-4.5) and 3.2 ms (3.0-3.3) in the T2DM and control groups respectively (P<0.0001).

The mean values of sural nerve distal amplitudes with their 95% confidence interval were 7.1 µv (6.9-8.2µv) and 9.3 µv (8.9-9.9 µv) in the T2DM and control groups respectively (P < 0.0001) (**Figure 1** and **Table 1**).

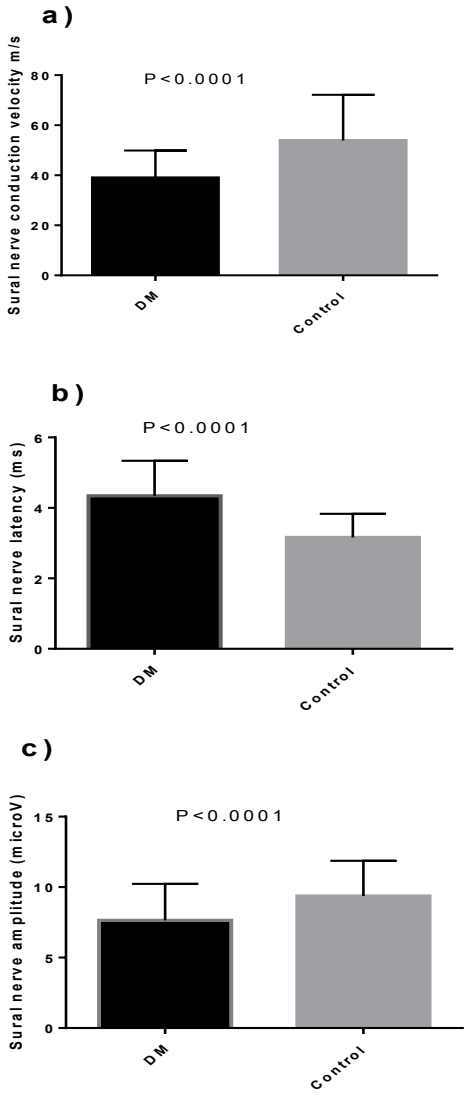

Figure 1. Comparison of Sural nerve conduction parameters in DM patients and matched control

Table 1: Comparison of sural nerve conduction parameters in diabetic subjects and age and sex- matched control

Body composition	Median	95% CI of Median	P value
Velocity			
DM	35.8	34.3-39.1	<0.0001
Control	53.9	53.4-54.8	
Latency (distal)*			
DM	4.4	4.2-4.5	<0.0001
Control	3.2	3.0-3.3	
Amplitude			
DM	7.1	7.1-8.2	<0.0001
Control	9.3	8.9-9.9	

**mean

DISCUSSION

The present study showed significant difference of sural nerve conduction parameters in T2DM patients without subjective features suggestive of peripheral neuropathy when compared with apparently healthy individuals. Our results are in keeping with reports from previous studies.[20,21] Sensory fibers in the lower extremities are generally first affected in patients with polyneuropathy, therefore, the value of sensory nerve conduction studies in the lower extremities is highly valuable in the diagnosis of polyneuropathy.[20,22]

Sural nerve conduction studies are used to evaluate the most distal peripheral nerves of lower extremities and it was suggested that subclinical or early peripheral neuropathy could be recognized with this method.[20,21] Killian and Foreman, in their evaluation of sural nerve conduction in normal subjects and those with peripheral neuropathy from various etiologies of peripheral neuropathy including diabetes, alcohol, arteritis, drugs, autoimmune disorders and unknown etiology showed that 77% showed abnormalities of sural sensory conduction. In the same study, it was also revealed that approximately 50% of the patients had abnormalities of motor nerves of the lower extremities.[20,23]

The mechanisms underlying disturbance of nerve conduction in diabetes include metabolic, vascular, autoimmune, and neuro-hormonal growth factor deficiency. Nonetheless, the prevailing theory suggests persistent hyperglycemia as the primary factor of the metabolic hypothesis.[24,25] Uncontrolled hyperglycemia increases polyol pathway activity with accumulation of sorbitol and fructose in nerves, damaging them through a yet unknown mechanism. This is accompanied by decreased myo-inositol uptake and inhibition of the Na^+/K^+-adenosine triphosphate with attendant retention of Na^+, edema, myelin swelling, axo-glial disjunction, and nerve degeneration.[26]

Given the fact that, the conduction velocity, distal latency and amplitudes of sural nerves in the diabetics were all significantly different from their age and sex matched healthy counterparts, there is suggestion that diabetes may cause DN by way of axonopathy and myelinopathy. This observation also reflect the findings in a clinico-pathological study in which both mechanisms were reported even though axonopathy was the predominant pathology overall and a third of nerves demonstrated demyelination.[27,28] Historically, the latter has been ascribed to axonal degeneration as the primary ischemic event with subsequent demyelination. In the studies, segmental demyelination and re-myelination was observed in 23% of sural nerve biopsies due to primary axonal degeneration.[27,28]

In conformity with reports of previous workers on sural nerve studies among diabetics,[29-31] the current study suggests that impairment of nerve conduction may be present in T2DM even in the absence of symptoms referable to neuropathy. Although slowing of median NCVs and prolonged distal latencies, which often

occurs early in the course of the disorder, are rife in T2DM, the relevance of these abnormalities to the future development of either subclinical manifestations or clinically apparent diabetic neuropathy is still largely uncertain.[26]

To the best of our knowledge, the current study is the first from Nigeria to comparatively assess nerve conduction status in T2DM using an electromyography machine rather than a questionnaire-based screening instrument. The results of the present study have a strong implication for early diagnosis and treatment of T2DM patients. It is our hope that the findings in this study will contribute to the knowledge in the area of neuropathy in T2DM with the view to emphasizing early screening, detection and apt therapeutic intervention for diabetic neuropathy.

CONCLUSION

The present study has shown that there is significant impairment of sural nerve conduction parameters in subclinical T2DM compared with apparently healthy individuals.

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