Modified collision study to isolate and study small fibre neuropathy in patients with Type 2 diabetes

Philo Hazeena, Sundar Shanmugam, Rithvik Ramesh, Shankar Venkatasubramanian

Department of Neurology, Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai, Tamil Nadu, India

ABSTRACT

Introduction: Diabetic distal symmetrical polyneuropathy (DSPN) can be categorized as small fibre, large fibre, and mixed neuropathy. Even though small fibre neuropathy is the most prevalent, unfortunately it is usually not recognized by routine electrophysiologic studies. In this study, we intend to examine the slow velocity small fibres responsible for small fibre DSPN, by isolating them using collision technique principle in patients with diabetes. **Methods:** This is an observational case-control study designed to compare nerve conduction values with application of collision technique in 60 patients with T2D and in 60 age and sex matched controls. **Results:** The collision study in patients with Type 2 Diabetes showed mean Latency of 10.5 ± 1.7 ms and mean Amplitude of 3.4 ± 2.3 mV on the right side and mean Latency of 10.5 ± 1.7 ms and the mean Amplitude of 3.5 ± 2.2 mV on the left side. There was a statistically significant difference (P value < 0.001) in the amplitute and latency of CNAPs of small fibres in median nerve innervated APBs of both arms between those with T2D and controls. **Discussion and Conclusion:** Collision study helps to examine the slower conducting fibres of the larger nerves. Our study suggests that the Collision Technique can be used to identify early peripheral neuropathy regardless of the diabetes status, thus making it more practically feasible and cost-effective.

Keywords: Collision study, distal symmetrical polyneuropathy, Type 2 diabetes

Introduction

In routine clinical practice, patients with peripheral neuropathy (PN) are regularly encountered and require symptomatic relief apart from an etiological enquiry. Amongst the numerous causes of PN, Type 2 Diabetes (T2D) is one of the most common causes of PN with epidemiological studies showing the occurrence of PN in up to 32% of those with T2D in India.[1] T2D and even impaired glucose tolerance can cause a spectrum of neuropathic manifestations, including distal symmetrical polyneuropathy (DSPN), acute treatment and non-treatment related neuropathies, autonomic neuropathy, mononeuropathy in addition to increased predilection for chronic inflammatory demyelinating polyneuropathy.[2] Amongst these, DSPN accounts for 50--75% of the neuropathies.[3] DSPN can be categorized as small fibre, large fibre, and mixed neuropathy. Even though small fibre neuropathy is the most prevalent, unfortunately it is usually not recognized by routine electrophysiologic studies which are limited to the study of large nerves.[4] This can lead to excessive investigation, which can cause a strain on resources and finances. In this study, we intend to examine the slow velocity small fibres responsible for small fibre DSPN, by isolating them using collision technique principle in routine electrophysiologic studies, in patients with T2D which would help provide a novel tool to identify this common neuropathy in clinical practice.

Address for correspondence: Dr. Philo Hazeena,
House No 44, Pantheon Apartments, Pantheon Road, Egmore,
Chennai - 600 008, Tamil Nadu, India.
E-mail: philohazeena@yahoo.co.in

Access this article online

Quick Response Code:

Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_1066_21

How to cite this article: Hazeena P, Shanmugam S, Ramesh R, Venkatasubramanian S. Modified collision study to isolate and study small fibre neuropathy in patients with Type 2 diabetes. J Family Med Prim Care 2022;11:265-8.

Material and Methods

This is an observational case-control study designed to compare nerve conduction values with application of collision technique in 60 patients with T2D and in 60 age and sex-matched controls. All patients were included after screening according to our inclusion and exclusion criteria. The study was conducted in the neurology outpatient and electrophysiology departments of Sri Ramachandra Institute of Higher Education and Research. The study protocol was approved by Institutional Ethics Committee (IEC no. CSP/17/MAY/57/139) and written informed consent was taken from all the participants. The patients were informed and clarified about the purpose of this study in the language understood by the patient, prior to enrolment. The study was conducted under the Declaration of Helsinki and the code of Good Clinical Practice.

The diagnosis of T2D was considered according to American Diabetes Association.[5] Patients with weakness and wasting of median nerve innervated muscle, prior asymmetrical sensory symptoms, sensory symptoms aggravated by certain postures, primary neck symptoms, and those with HbA1c greater than 8.5% were excluded. Control group included healthy volunteers without any comorbidities like T2D, systemic hypertension, thyroid dysfunction, or neurological disorders.

Neurophysiological tests

Nerve conduction recordings were performed using a 16-channel EMG machine. Surface disc electrodes were used to obtain the compound muscle action potentials (CMAP). CMAP recording was done by Belly-tendon recording with Ground kept in the palm. The low filter is set at 3 Hz, high filter 20 kHz, sweep 5ms, duration 0.1–0.2 ms, sensitivity 5 mV, rate non recurrent.

Collision technique was performed by recording an action potential from a selective muscle (Abductor pollicis brevis in our study) innervated by a nerve (Median nerve). The principle of the collision technique is based on the fact that a recorded action potential is a summation of the potentials carried by all the fibres of the nerve being tested, from the slowest to the fastest, and the aim is to attempt to allow for distinction amongst the separate components. This is done by application of two stimuli along the course of the nerve, first one distal (DS) and then proximal (PS), separated by a time delay called interstimulus interval (ISI). When DS and PS are applied simultaneously, that is, the interstimulus interval is zero there is no recorded action potential as both the compound nerve action potentials (CNAP) collide and cancel out. When the DS and PS are applied successively with a large time interval, that is, ISI is large, then the two CNAPs don't collide and the response from all the proximal nerve stimulation is recorded. Also, to consider is the fact that after stimulation the part of the nerve being stimulated will be in a refractory period, during which time the proximal impulses cannot pass through. So, when given sufficient time, the refractory period gets over and all the action potential from the PS arrives, crosses and gets recorded. So based on both these principles, as and when the ISI is decreased gradually, the recordings from the slow velocity small nerves decreases as the CNAPs from DS and PS start colliding as the faster CNAPS mediated via the larger nerves get through. But when the decreased further even the faster CNAPs don't get through. Conversely, when the ISI is increased upwards from Zero, at 20–30 ms, the large fast conducting fibre totally diminish and the small slow conducting fibres (small fibres) are elicited. In our study, the ISI was increased until the range of 100 ms, to obtain a stable small fibre CNAP, and then its latency and amplitude is measured.[6]

Statistical analysis

The data were compiled and proposed as the mean ± standard error of mean (SEM). The difference between cases and controls were analysed using one-way analysis of variance (ANOVA). Correlation analysis was used to find the correlation between the various parameters. Nerve conductance values between cases and controls were analyzed by paired *t*-test, Chi-square test, ANOVA test, and Pearson correlation as appropriate. A *P* value of < 0.05 was considered statistically significant. Analysis was done by software SPSS version 17.

Results

Sixty patients with T2D and 60 controls were included in this study. Out of 60 patients with T2D, there were 30 men with T2D and 30 women with T2D with a mean age of 51.86 ± 1.7 years. The mean age of control group was 50.8 ± 1.5 years.

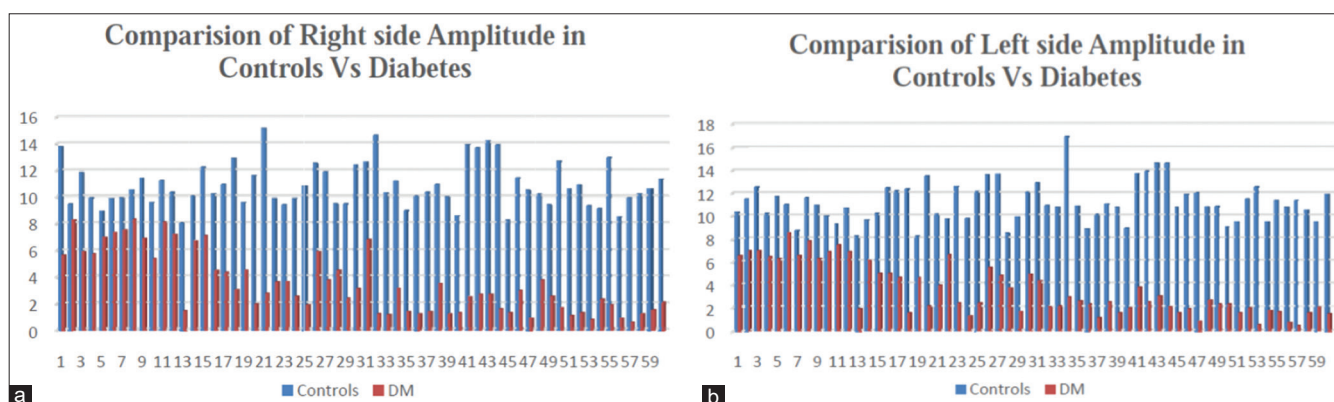### Comparison of nerve conduction values between those with T2D and controls

Nerve conduction with collision technique was applied to both APBs and data collected accordingly. The Collision study in patients with Type 2 Diabetes showed mean Latency of 10.5 ± 1.7 ms and mean Amplitude of 3.4 ± 2.3 mV on the right side and mean Latency of 10.5 ± 1.7 ms and the mean Amplitude of 3.5 ± 2.2 mV on the left side. The Collision study in the control group showed mean Latency of 6.84 ± 0.35 ms and the mean Amplitude of 10.86 ± 1.6 mV on the right side and mean Latency of 6.79 ± 0.4 ms and the mean Amplitude of 11.14 ± 1.7 mV on the left side. There was a statistically significant difference (*P* value < 0.001) in the amplitude and latency of CNAPs of small fibres in median nerve innervated APBs of both arms between those with T2D and controls [Figures 1a and b and 2a and b].

Comparison of nerve conduction values amongst patients with T2D

Those with T2D were further sub-grouped depending on the duration of the diabetes into four groups (less than 5 years, 5—10 years, 10–20 years, and more than 20 years) and the nerve conduction values were compared. Statistically significant prolongation of latencies and reduction of amplitude was observed as the duration of diabetes increased. To exclude the effect of age on the conduction values, the control group was subdivided into 4 groups (30–40 years, 40–50 years, 50–60 years,
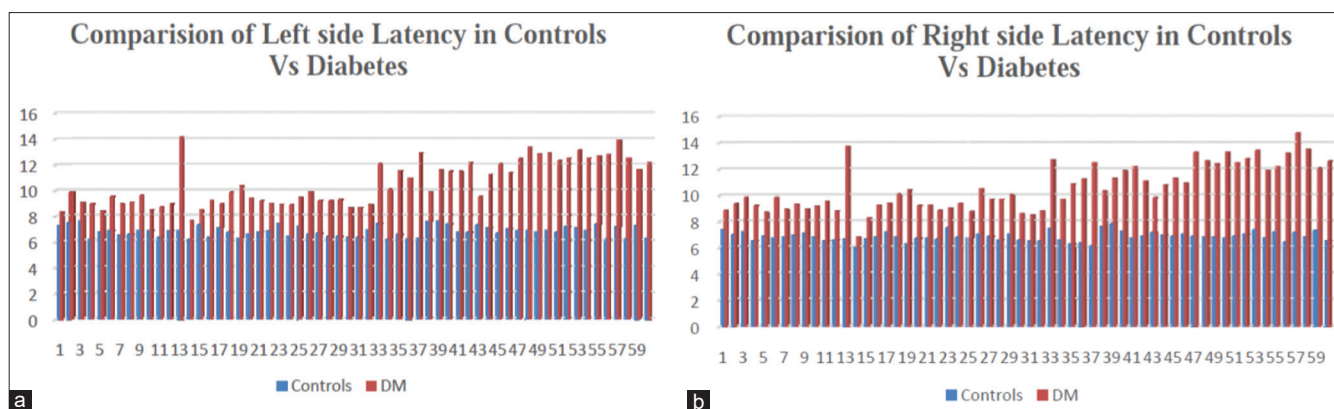
Figure 1: Right side latency (a) and amplitude (b) comparison between Diabetics and controls


Figure 2: Left side latency (a) and amplitude (b) comparison between Diabetics

and more than 60 years) and the nerve conduction values were compared. There was no statistically significant trend observed in the control group with progression of age. The amplitude and latency variation across increasing duration of diabetes (divided into 4 groups), and across different control age groups (divided into 4 groups) are represented in Figures 3 and 4. This shows a decreasing latency and increasing amplitude as the duration of DM increases, which is in contrast with the control groups which shows only age-related variation.

Discussion

Our study using the collision technique showed abnormal NCS values (prolonged latencies and decrease in amplitude) in patients with T2D when compared to healthy controls. We also observed that the prolongation of latencies and decrease in the amplitude increases with the duration of diabetes. On the other hand, the control group showed only age-related variation.

T2D leads to a spectrum of peripheral nerve involvement, of which the most common is small fibre neuropathy. This presents with burning or jabbing pain distally with associated sensory disturbances. Unfortunately, the effortless clinical diagnosis of this troublesome small fibre neuropathy is often not complimented by an electrophysiological abnormality in the conventional nerve conduction studies. This is because of
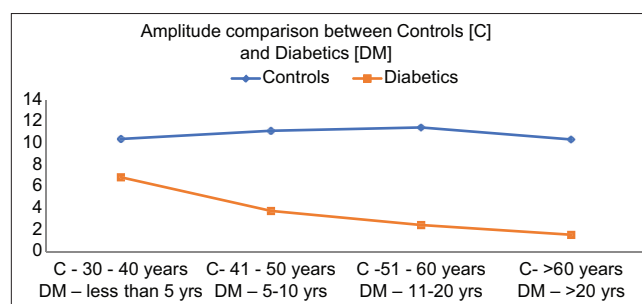
Figure 3: Amplitude comparison between controls and diabetics across age groups

the fact that these tests are intended to specifically study large fibres and the larger named peripheral nerves.[4] Until now, this practical difficulty was overcome by studying smaller sized nerves such as medial and lateral planar nerves.[7] Nonetheless, Collision study helps to examine the slower conducting fibres of the larger nerves. Collision technique has traditionally been used to prevent the spread of current to the nerve not being studied and to conduct neurophysiological tests in the presence of anomalous crossovers in the forearm between the median and the ulnar nerves.[8,9] Recently, they have been used to identify early involvement of small fibres in carpal tunnel syndrome.[10,11] However, the literature on using collision technique to evaluate small fibre neuropathy in T2D is sparse.

Latency comparison between Controls and Diabetics
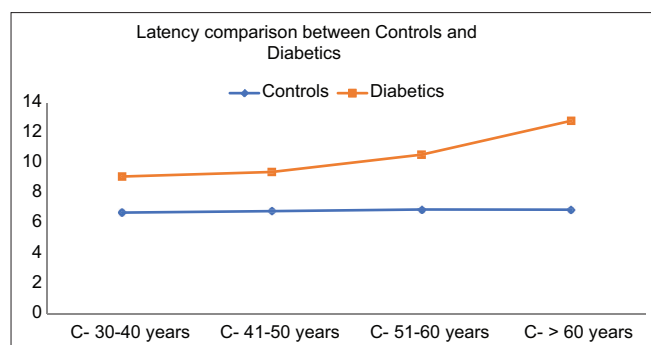
Figure 4: Latency comparison between controls and diabetics across age groups

Our study suggests that the Collision Technique can be used to identify early peripheral neuropathy regardless of the diabetes status, thus making it more practically feasible and cost effective. Moreover, the technique also offers an opportunity to study the progression of the small fibre neuropathy in diabetes thereby helping in monitoring these patients. Our study is a preliminary study that would pave way for more research in establishing the diagnosis of small fibre neuropathy in diverse clinical situations especially in diabetes. The limitations of this study include lack of follow-up data and absence of the dynamic glycemic status of patients with T2D within the group. In early peripheral neuropathy, lower limb involvement usually precedes upper-limb involvement and so to detect early neuropathy, lower-limbs have to ideally assessed. However, collision study in lower limbs require significantly stronger stimulus to generate sufficient amplitude in the recorded potentials, thereby making the procedure relatively painful. Further studies utilizing collision technology would be required to prove its utility in diagnosing early lower limb small fibre neuropathy.

Take home messages

1. Small fibre neuropathy is one of the more common manifestations of DM
2. Routine electrophysiological studies can be normal, in small fibre neuropathy.
3. Collision technique when applied to routine electrophysiology can show evidence of small fibre neuropathy and the abnormalities increases with prolonged duration of the disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Trivedi S, Pandit A, Ganguly G, Das SK. Epidemiology of peripheral neuropathy: An Indian perspective. Ann Indian Acad Neurol 2017;20:173-84.
2. Gibbons CH. Diabetes and metabolic disorders and the peripheral nervous system. Continuum (Minneap Minn) 2020;26:1161-83.
3. Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, *et al.* Diabetic neuropathy: A position statement by the American Diabetes Association. Diabetes Care 2017;40:136-54.
4. AANEM policy statement on electrodiagnosis for distal symmetric polyneuropathy. Muscle Nerve 2018;57:337-9.
5. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care 2019;42:S1-2.
6. Sander HW. Collision testing. Handb Clin Neurophysiol 2006;7:359-80.
7. Uluc K, Temucin CM, Ozdamar SE, Demirci M, Tan E. Near-nerve needle sensory and medial plantar nerve conduction studies in patients with small-fiber sensory neuropathy. Eur J Neurol 2008;15:928-32.
8. Kimura J. Collision technique. Physiologic block of nerve impulses in studies of motor nerve conduction velocity. Neurology 1976;26:680-2.
9. Koszewicz M, Szydlo M, Gosk J, Wieczorek M, Budrewicz S. Use of collision tests to identify physiological differences between the median and ulnar nerves. Muscle Nerve 2019;59:470-4.
10. Hakamada S, Kumagai T, Watanabe K, Koike Y, Hara K, Miyazaki S. The conduction velocities of slower and faster fibers for assessing CTS. J Neurol, Neurosurg Psychiatry 1982;45:851-3.
11. Sundar S, Gonzalez-Cueto JA, Gilbert CS. Conduction velocity distribution estimation using the collision technique—Theory and simulation study. Biomed Signal Process Control 2008;3:94-101.