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Effect of Duration of Diabetes on Sural Nerve Conduction Parameters in Subjects with Type-II Diabetes Mellitus - A Cross sectional Comparative Study

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ABSTRACT

Background: Diabetes mellitus has become a rapidly rising global health-care problem in the recent decades. Amongst the wide spectrum of concurrent complications, Diabetic peripheral neuropathy (DPN) is quite common and distressing. The sensory symptoms may vary from numbness, hypo-aesthesia, allodynia to severe paresthesia. Long term consequences of these sensory disturbances are foot ulceration, imbalance, increased risk of fall and even amputations too. Since these symptoms interfere with the quality of life of diabetic individuals and also lead to increased socio-economic burden, immediate action to combat these is pre-requisite for health care development of any nation. Further, if timely diagnosed, these complications can largely be prevented. Nerve conduction study holds the gold standard tool to detect Diabetic neuropathy at its subclinical stage itself. Sural nerve is the commonest and most prevalent nerve involved, so it was considered for analysis. Duration of diabetes is an important factor which affects neurophysiology.
Thus, the aim of the present study is to study the effect of duration of diabetes on Sural nerve conduction parameters in subjects with type-II Diabetes Mellitus having varying duration of diabetes.
Method: Seventy-three Subjects with type-II Diabetes mellitus were divided into three groups according to the duration of disease. Group A:<5 years, B: 5-10 years, C: >10 years of diabetes. Bilateral Sural nerves were analysed using RMS EMG SALUS machine.
Result: Significant reduction of Sensory nerve action potential ($p<0.05$) was found as the duration of diabetes increased from Group A to C.
Conclusion: Long term Diabetes leads to Axonal degeneration in Sural nerves.

Keywords: Diabetic peripheral neuropathy, Nerve conduction study, Sural nerves, Diabetes mellitus, Duration of Diabetes, Axonal degeneration.

INTRODUCTION

Diabetes mellitus has become a rapidly rising global health-care problem in the recent decades. According to IDF (International Diabetes Federation), number of people with diabetes aged 20-79 years is predicted to rise to 629 million or to 693 million among 18-99 years by 2045.[1]

Amongst the wide spectrum of concurrent complications, Diabetic peripheral neuropathy (DPN) is quite common and distressing. [2]DPN has been defined by Toronto Consensus Panel on Diabetic Neuropathy as a "Symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and microvessel

alterations as result of chronic hyperglycemia exposure and cardiovascular risk variates."[3] Sensory symptoms may occur in the form of loss of pain sensation, "pins and needles" sensation, tingling, "electric-shock like" sensation, allodynia (painful sensation to inoffensive stimuli), or Hyperalgesia (increased sensitivity to painful stimuli).These symptoms may further progress to various disabilities such as foot ulcerations, increased risk of fall, gait disturbances, fall-related injury and even amputations as well. [3,4]

Hence, all the above complications eventually land up in poor quality of life and increased economic burden on nation and family. [5]

However, if timely diagnosed, all the above dreadful consequences can be treated and prevented as well. Nerve conduction study (NCS) holds the gold standard diagnostic tool to detect and evaluate peripheral neuropathy in it's subclinical stage itself. Several studies have shown the importance of Electrodiagnosis in DPN. [6-9]

Sural nerve has been found to be commonly affected nerve in DPN. Furthermore, Sural nerve biopsy studies show a high correlation between morphological pathology and Nerve conduction parameters. [10]

Duration of diabetes is another factor that can affect the neurophysiology in Diabetic individuals. Very few studies have been undertaken to study the correlation and effect of Duration of diabetes and Nerve conduction study parameters. [11-14]

Hence, the aim of the present study is to study the effect of duration of diabetes on Sural nerve conduction parameters in type-II Diabetes Mellitus. Nerve conduction velocity (NCV) and Sensory Nerve Action Potential (SNAP) amplitude of Bilateral Sural nerves were the parameters to be studied.

MATERIALS & METHODS

A total of 73 subjects diagnosed with type-II Diabetes mellitus (as per WHO) were recruited for the study from Neuro OPD. Subjects were divided into three groups based on Duration of Diabetes. Group A (n=24) <5 years duration of diabetes, Group B (n=24) 5-10 years and Group C (n=25) >10 years Duration of diabetes.

Study design: Cross-sectional Comparative

Sampling: Convenient Sampling technique

Inclusion criteria:

- Subjects diagnosed with type-II Diabetes mellitus (as per WHO Criteria),
- Both genders,
- Age range: 40-60 years,
- Willing and capable of providing consent.

Exclusion criteria:

- Subjects with type-I Diabetes,
- Chronic alcoholic,
- Chronic smoker,
- Drug induced neuropathy,
- Cerebrovascular stroke and peripheral neuropathy due to some other known cause,
- Peripheral artery disease or evidence of limb ischemia,
- Subjects who refuse to give consent,
- Skin lesion or swelling which could interfere with NCS
- Trauma in the course of the nerve to be examined.

METHOD

A basic clinical Neurological examination was done. Subjects were explained about the procedure and a written informed consent was obtained prior to data collection. Standard sanitization protocol was followed.

Procedure: B/L Sural nerve conduction study was carried out using RMS EMG SALUS machine (Figure1.) at room temperature (26+/-2 degree Celsius). Button electrodes were used. (Figure 2. Placement of electrodes) [15]

Figure 1. RMS EMG SALUS machine

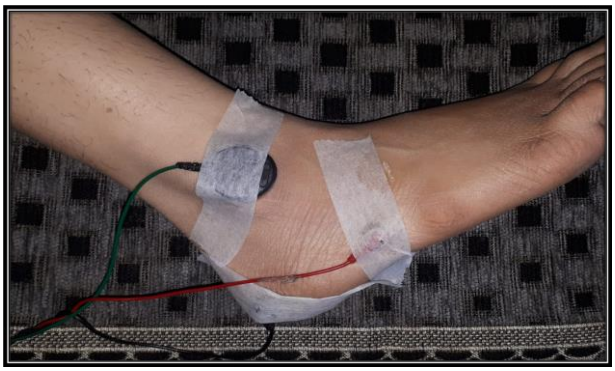


Figure 2 Placement of electrodes

Subjects were asked to assume side lying position. Knee of non testing lower limb was
flexed while the testing limb was kept straight supported by a pillow. Stimulation site was 10-16 cm proximal to the recording electrode, distal to the lower border of gastrocnemius at the junction of middle and lower third of leg (Figure 2). Sural nerve was stimulated antidromically. Intensity of current was increased gradually starting from 0 to highest level of 50 milli ampere (as per the requirement), until SNAP amplitude was consistent on the screen. Once the amplitude was elicited, live averaging was done to cancel out the artifact disturbances. Appropriate graph was then captured. Cursors were set to measure Distal latency (in ms), peak to peak (SNAP) amplitude (in micro Volt) and NCV (in m/s). All the above values were compared with the values obtained from Normal individuals as per Misra et al 2019. [15]

RESULT

A total of 73 subjects (males=59, females=14) participated in the study. Bilateral Sural nerves were studied. A total of 146 nerves were available for analysis. Statistical analysis was done using Microsoft excel 2007, Real statistics add-Ins. P value<0.05 was considered significant. Mean values for demographic data are as shown in Table1.

Table 1. Mean+/- SD values for Demographic data of all three groups and their p-values.

	Group A (n=24) Mean+/- SD	**Group B(n=24) Mean+/- SD**	**Group C(n=25) Mean+/- SD**	**P value**
Age (Inyears)	50.56+/- 5.26	52.91+/- 3.74	55.60+/- 3.27	0.267*
BMI (in m/kg^2)	24.93+/- 4.72	27.46+/- 4.95	25.16+/- 5.10	0.125*
Duration of Diabetes (in years)	2.64+/- 1.65	8.62+/- 1.49	16.45+/- 4.60	0.001**
Males	21	20	18	
Females	3	4	7	

***Non-significant**
****Significant**

Single factor ANOVA test was applied for Age and BMI for which p>0.05 for both parameters which signifies a non-significant difference and Kruskal Wallis test was applied for Duration of Diabetes (p<0.05, significant difference).
Table 2 shows the Mean+/- SD values for Bilateral Sural SNAP and NCV and their p-values in all three groups.

Table 2. Mean+/- SD for SNAP and NCV in Bilateral Sural nerves in Groups A, B and C and their p-values.

Parameter		Group A (n=24) Mean+/- SD	Group B(n=24) Mean+/- SD	Group C(n=25) Mean+/- SD	P value
SNAP (in micro volt)	Right	37.50+/-24.71	33.26+/-25.44	20.36+/-10.45	0.008**
	Left	48.87+/-40.29	35.55+/-19.59	23.65+/-22.1	0.001**
NCV (in m/s)	Right	28.26+/-9.17	28.18+/-7.57	27.60+/-6.25	0.950*
	Left	29.97+/-7.24	28.62+/-7.11	27.98+/-7.02	0.555*

***Non-significant**
****Significant**

Kruskal Wallis test was applied for SNAP amplitude comparison between groups. Single factor ANOVA test was done for NCV values comparison between groups. SNAP amplitude values were found to be significantly reduced as one moves from Group A to C, whereas NCV measurements did not show significant reduction from Group A to C.

Figure 3 and 4 shows the graphical presentations.

Figure 3 Comparison of Bilateral SNAP values (in micro volts) between Groups A, B and C

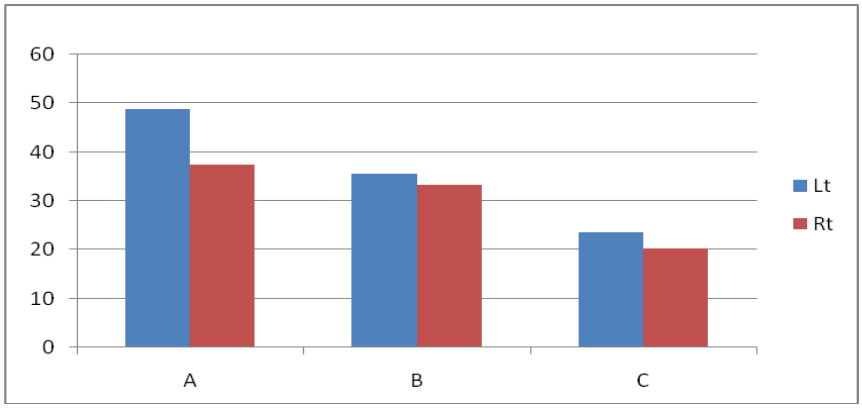
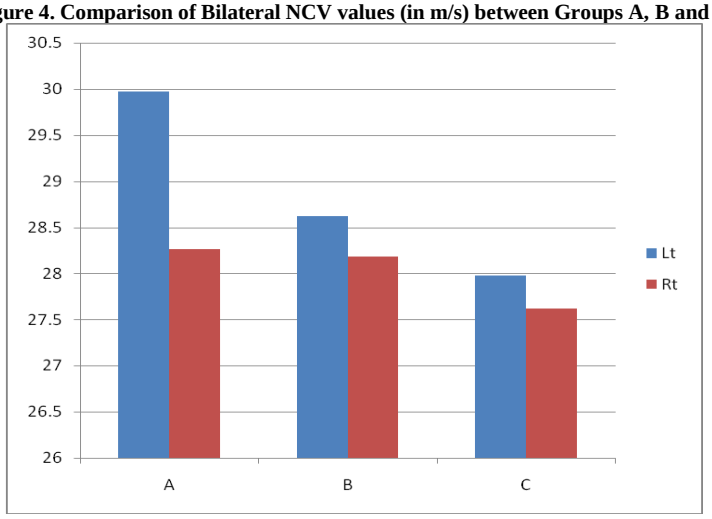


Figure 4. Comparison of Bilateral NCV values (in m/s) between Groups A, B and C.



DISCUSSION

The present study was undertaken to determine the effect of duration of diabetes on Sural nerve conduction parameters in subjects with type-II Diabetes mellitus having varying duration of diabetes. Subjects were divided into three groups based on Duration of Diabetes. Group A, B and C having <5,5-10 and >10 years of duration, respectively. The subjects in all three groups had comparable baseline parameters. There was no statistically significant difference in Age and BMI, while Males predominated in all the three

groups. Room temperature was maintained at 26+/- 2 degree Celsius throughout the process. Hence, alteration of Nerve conduction parameters due to temperature variation was minimized.

Sural nerve was considered for evaluation as this nerve is first affected and is also a prevalent indicator of peripheral nerve dysfunction. [16] Sural nerve was analyzed bilaterally in all subjects. Sensory nerve conduction velocity (SNCV in m/s) and Sensory nerve action potential (SNAP in micro volt) parameters were considered for analysis. It was found that while SNCV did not decreased significantly, but SNAP showed significant reduction ($p<0.05$) with increase in duration of diabetes.

Pathogenesis of Diabetic Neuropathy

Dyck et al proposed that Endoneurial microangiopathy accounts for diffuse fibre loss leading to Axonal degeneration in distal nerve fibres in Diabetes. [17] However, other mechanisms have also been proposed. Increased polyol flux results in accumulation of sorbitol in cytoplasm leading to cell lysis (osmotic theory). [18,19] Advanced glycation end products (AGE) have also been implicated to cause injurious effects on the endoneurium. Axonal transport system is disrupted resulting in distal fibre degeneration. On the other hand, Regeneration efforts of Diabetic nerves have also been found to be impaired by AGE. [20,21]

Generation of increased free radicals is also proposed to be a major factor causing peripheral neuropathy. Free radicals induce a cascade of events in mitochondria that lead to programmed cell death. [22]

Enhance pro-inflammatory processes and lack of neurotropism further enhances the development of Neuropathy. [23]

Zahed et al 2008, conducted a study to evaluate the efficacy of electrodiagnostic tests to detect Diabetic neuropathy at its subclinical stage. It was found that among the Sensory nerve conduction parameters, Sensory nerve action potential amplitude (SNAP) was affected more than conduction velocity. [14] This finding is parallel to the current study findings. Amina Zaidi et al, in their study, explored the correlation between Duration of diabetes and SNCS parameters of Median, Ulnar, Sural and Superficial peroneal nerves; and a significant negative correlation ($p<0.05$) was found. [13] Similar findings were found by Raju Panta et al 2017, Ahsan Numan et al 2021, [11, 12]

On the contrary, Pastore C et al, 1999 and Senhamil et al, 2021 did not find any significant difference in the nerve conduction attributes in type-II Diabetic individuals with dissimilar duration of diabetes. [24, 25]

In conformity with the previous studies on Sural nerves in Diabetic individuals, the current study suggests that Diabetic nerves become more liable to lesion as the duration of Diabetes increases. However, other factors like the level of Physical activity, any form of addiction, HbA1c level, cholesterol and triglyceride level should also be taken into consideration. This forms one of the limitations of this study.

CONCLUSION

Duration of Diabetes has a significant detrimental effect on Sural nerve. The result of present study has strong implications for early diagnosis of neuropathy in diabetic individuals, which in turn, aids in preventing many long term complications, thus decreasing the economic burden on society and family. Hence, NCS should be made an essential investigation during DPN screening.

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Conflict of Interest: None

Ethical Approval: Approved

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