A Sensory Nerve Conduction Study of Sural Nerve Among Leprosy Patients

P. H. Gandhi[*], C. B. Desai[*], H. H. Mehta[**], H. B. Mehta[***], V. P. Nikam[****], B. N. Astik[*****] C. J. Shah[*****]

*3rd Year PG Student; Dept of Physiology, **Prof. & Head, Dept. of Skin & VD, *** Prof. & Head, Dept. of Physiology, **** 3rd Year PG Student, Dept. of Skin & VD, ***** Asso. Prof, Dept. of Skin & VD; ******Asso. Prof. Dept of Physiology, Govt Medical College & Sir T Hospital, Bhavnagar, 364001

Abstract: Background: Leprosy neuropathy is characterized by initial involvement of the small nerve fibers, later followed by involvement of the large fibers, when routine nerve conduction studies become abnormal. Sural nerve is main sensory supplying of the foot. Mostly, ulcer occurs in foots due to neuropathy of lower limb which is most early & neglected complication of lower Limb among leprosy Patients. Early assessment of Sural nerve is more important in leprosy. The results of Nerve Conduction Studies are closely parallel to the structural abnormality of Nerve. Aim**:-**To assess the sensory nerve conduction study parameters of the Sural nerve in cases of clinically manifest leprosy with or without nerve damage. Method: To increase the diagnostic yield, we applied the Antidromic SNCS near nerve technique to the Sural nerve of 42 leprosy patients. Result: Sural Nerve was not detected by NCS in 11(26.19%) Leprosy patient out of 42. This may be due to conduction block. Mean Latency of Bilateral Sural nerve was prolonged and SNCv was reduced. That represented demyelinating type of Neuropathy of Sural Nerve. Conclusion: Demyelinating neuropathy of Sural Nerve is more common than Axonal Neuropathy in Leprosy cases. Total nerve conduction block might be developed in early stage. Axonal Neuropathy may develop with or without conduction block. To better understand the neurophysiology and physiology of leprosy and to increase the accuracy and precocity of the diagnosis, it will be necessary to investigate patients in the very early stages of the disease and to correlate these findings with the corresponding nerve pathology.

Key Words: Sensory Nerve Conduction Study, Leprosy, Sural Nerve

Author for correspondence: Dr. Pritesh Gandhi, Department of Physiology, Government Medical College, Bhavnagar–364001.e- mail: priteshgandhi2@gmail.com

Introduction: The main target of Mycobacterium Leprae is the peripheral nerve[1].Neuropathy is the hallmark of the leprosy diseases as the three Physiological functions of nerves- motor, sensory or autonomic may equally affected but usually the sensory component is the earliest and the most severely affected[2]. Sensory neuropathy is far more common than motor neuropathy[2]. Neuropathy associated with leprosy is Small Fibre Neuropathy/ Diffuse Sensory Neuropathy due to direct invasion of the Nerve trunks by the bacillus[3].The small nerve fibers conducting pain and temperature sensations are affected significantly before the large myelinated fibers that conduct vibration sense, position sense, and motor impulses[4,6]. NCV study is used mostly to diagnose the neuropathy which can be degenerative or demyelinating. The results of NCS are closely parallel to the structural abnormality of Nerve[4,5]. NCSs consist of stimulating a peripheral nerve and recording the response elsewhere on contiguous nerve or from a skeletal muscle innervated by the nerve. Sural nerve is main sensory supplying of the foot and mostly ulcer occurs due to neuropathy of lower limb. So early assessment of Sural nerve are more important in leprosy. Selective sequential involvement of the nerve fibers impairs the detection of leprosy neuropathy at the initial stages of the disease by neurophysiological evaluation since routine nerve conduction studies only record potentials originating from fibers wider than 7 mm in diameter[7,8].

Materials and Method: The permission was taken from Institutional Review Board (IRB) and Human Ethics Committee before starting this study. Leprosy patients were enrolled from the leprosy clinic held on every Friday at Department of Skin & V.D. This study was carried out at EMG/NCV Lab at Department of Physiology.

Participants: The present study was carried out in 42 Leprosy patients of newly diagnosed or on treatment cases.

Preparation of Subjects and Precautions: Subject was informed about this study in local language with written Subject Information Sheet. Informed Written Consent was taken in the presence of subject relative. All leprosy subjects taking medication was informed to take regular morning dose. Subject Informative, Anthropometric data (age, height and weight), brief clinical history, vital data and examination, personal history, family history was taken according to standard protocol.

This study was taken between 9am to 1pm in air conditioned Lab and Room temperature was keep at around 25^0c. Patients were asked to avoid prior application of topical creams as these may increase skin resistance to the applied current. The skin surface temperature was in all cases between 31^oc to 34^0c. Participants' skin surface was kept clean with spirit swab and let them to become dry to avoid any error before placing electrodes on upper limbs. Earthling should be kept in position as it passes extra current to the earth. Supramaximal stimulation (up to 50 mA) was used to stimulate Sural nerves for sensory recording

Instrument: RMS Aleron EMG/NCV EP II MARK 401: 4 channels instrument was use for this study. This machine is manufacture by RECORDERS & MEDICARE SYSTEMS (P) LTD.
Settings Filters for sensory recording are LFF = 20Hz, HFF= 2 kHz and Sweep Speed for SNCS was 2ms/ division

Terminologies and Technique for electrode placement and recording of Sural Nerve Sensory Studies for type of Stimulus[9]:

Supra-maximal Stimulation for Sensory recording: Stimuli are those that do not produce any further increase in the response and a stimulus delivered at approximately 20-30% above maximal intensity is supra-maximal threshold.

Antidromic Stimulation: Propagation of an impulse in the direction opposite to physiologic conduction. The basic technique of antidromic SNCS involved the active recording electrode and reference electrode are mounted 4 cm apart over the Sural Nerve on lateral aspect of foot near lateral melleolus. Antidromic evoke response can be recorded with surface stimulus 14, 18 cm proximal to the active electrode, distal to the lower border of gastrocnemius at the junction of middle and lower third of leg during the recording, the leg should be relaxed and lateral position is convenient.

The most reproducible results are obtained when stimulating over 14 cm & 18cm distance. A nerve action potential produced produce by the electrical stimulation of the afferent nerve may be recorded over peripheral sensory nerve in a number of areas. The response obtained is called Sensory Nerve Action Potential.

Latency: It is "time interval b/w the onset of the stimulus and the initial deflection of the response." It is measured in milliseconds.

Amplitude: It is measured from baseline to peak to peak. It is measured in µV.

Conduction Velocity: Speed of propagation of an action potential along a nerve is called conduction velocity. When the latency is measured to the peak of the SAP, an average conduction of the group Ia fibers are obtained rather than the CV of the fastest fibres. It is measured in m/sec.

CV = distance between stimulus and recording electrode / onset latency.

Fig 1: Electrode placement for Sural Nerve Sensory Nerve Conduction study at 14 cm distance.

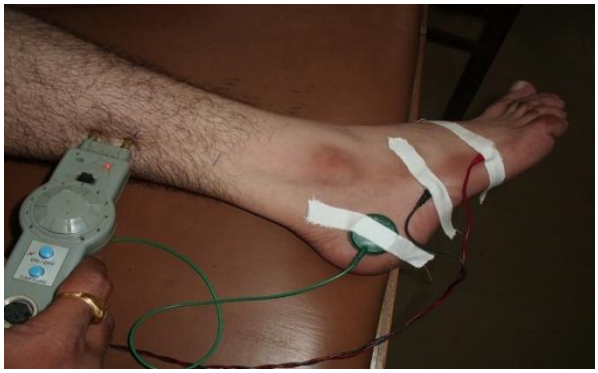

Table 1: References Values of Sural nerve conduction (SNCS) for this study

	Latency(ms), (Range)	Amplitude (µV) (range)	NCV(m/sec), Mean ±SD
Kimura (14cm)a	2.4 – 3.0	12.9-28.9	54.8±15.3
Kimura (18cm)a	3.4 – 4	12.2 – 25.6	NA
Mishra &Kalita(b)	2.83 – 4.0	18.0 -30.5	50.9 ±5.4
Di Benedetto	2.27±0.43	23.7±3.8	46.2±3.3
Waniapel et al	3.7±0.3	18.9±6.7	41.0±2.5

a=61individuals, age 11-74 years (average 40), onset latency, b=30 individuals (60 limbs), age 11-57years (average 36), onset latency, base to peak amplitude;

Result: This study was conducted among 42 leprosy patients. 14 patients of paucibacillary and 28 patients of multibacillary were diagnosed base on their clinical presentation and serological or biopsy examination.

In Paucibacillary group, 4 patients were tuberculoid leprosy, 3 patients were Borderline tuberculoid Leprosy with Pure Neural Leprosy and 7 patients were Borderline tuberculoid Leprosy.

In Multibacillary group, 11 patients were of lepromatous leprosy, 12 patients of Borderline Lepromatous Leprosy with pure neural leprosy and 5 patients were of Borderline lepromatous Leprosy. Out of the multibacillary, 4 patients have trophic ulcer on foot and one patient has ulnar abscess. They were also divided in subgroup like Newly Diagnosed cases (n=31) and Old cases or on treatment cases (n=11), Smear positive cases (n=19) and Smear negative cases (n=23).[Table-3]

Table 2: Anthropological measurement of Leprosy Cases (n=42)

Age	Male	Female	Ht (m)	Wt(kg)	BMI
39.93	26	16	1.59	53.74	21.27

Table 3: Leprosy cases classify as their presentation (n=42)

Smear +Ve	Smear-ve	New Case	On treatment	PB	MB
19	23	31	11	14	28

PB- Paucibacillary**, MB-** Multibacillary

All the data were enter in Microsoft Excel sheet. The mean and SD taken with the Help of Graph pad InStat software and Student t- test and ANOVA were applied to for statistical significance. P-value < 0.05 shows as significance of the values. Both of Sural Nerve was not detected in 11(26.19%) Leprosy patient out of 42 leprosy patients. This might be due to conduction block.

Table 4: Comparision of Sural Nerve Values between Leprosy patients and reference values

	Latency(ms) (Range)	Amplitude (µV) (range)	NCV(m/sec) Mean ±SD
Kimura (14 cm)a	2.4 – 3.0	12.9-28.9	54.8±15.3
Kimura (18cm)a	3.4 – 4	12.2 – 25.6	
Mishra &Kalita(b)	2.83 – 4.0	18.0 -30.5	50.9 ±5.4
Present Study values of bilateral sural nerve (n=31)			
RtSural Nerve (14cm)	5.99±2.56	37.73±25.27	25.60±9.85
Left Sural Nerve (14cm)	5.27±2.22	38.73±27.07	25.80±13.78

Above table 4 shows bilateral sural nerve have prolonged latency with reduced SNCV among leprosy patients. In smear positive leprosy cases, conduction block was higher as 8 out of 19 patients have not detected sural nerve bilaterally, whereas in smear negative cases, 3 out of 23 leprosy patients hvae not detected sural nerve. This present the effect of smear positivity on conduction block.

Table:5 Comparison of Sural Nerve Conduction studies Values (Mean±SD) between Paucibacillary (n=11) and Multibacillary (n=20) Leprosy patients.

	Paucibacilary	Multibacilary	P-value
Rt Sural Nerve			
Latency(ms)	5.56±2.40	6.22±2.68	0.5036
Ampli. (μV)	64.76±62.11	53.67±55.30	0.6192
NCV(m/sec)	23.40±11.04	22.16±9.41	0.7439
Rt Sural Nerve			
Latency(ms)	5.70±2.24	5.04±2.24	0.4342
Ampli. (μV)	64.01±44.67	60.33±64.55	0.8681
NCV(m/sec)	24.72±11.49	24.84±15.18	0.9809

Table 6: Variation of values among smear +ve (n=11) and smear-ve (n=20) leprosy cases

	Latency(ms) Mean ±SD	Amplitude (μV) Mean ±SD	NCV(m/sec) Mean ±SD
Smear +ve Rt Sural N	6.41±3.23	42.22±23.18	20.47±9.34
Smear -ve Rt Sural N	5.75±2.17	35.26±26.59	23.77±10.16
Smear +ve Lt Sural N	5.12±2.32	36.80±23.24	19.30±8.23
Smear -ve Lt Sural N	5.35±2.23	39.79±29.48	27.82±15.40

Table 7: Variation of values of newly diagnosed (n=23) and On treatment (n=8) leprosy cases

	Latency(ms)	Amplitude (μV)	NCV(m/sec)
Newly Diagno. Rt Sural N	6.20±2.43	60.14±64.18	21.76±10.05
On treat. Rt Sural N	5.37±3.0	50.81±30.19	25.01±9.49
Newly Diagno. Lt Sural N	5.15±2.31	72.68±59.67	26.30±15.04
On treat. Lt Sural N	5.61±2.07	39.79±38.05	20.47±8.63

Discussion: In leprosy patients, it is important to recognize that, nerve damage may occur with or without symptoms from the very beginning of infection[2]. There is considerable evidence to suggest that the peripheral nervous system plays an important role in day to day activity[3].

The Neuronal status of leprosy patients can be evaluated by Nerve Conduction Study, one of the most reliable Neuropathy assessments Tests[4]. Distal Latency, Amplitude of SNAP and Sensory Nerve Conduction are the parameters of Antidromic Sensory Nerve Conduction Study of bilateral Sural nerve were evaluated in both the groups in this study.

By applying student t-test to the values and ANOVA analysis, p value was <0.05 shows statistically significance of difference of values.

Antidromic Sensory Nerve Conduction Study was done for Bilateral Sural Nerve at stimulus of

14 cm distance for active electrode. As per table no. 4, The Mean values of Right Sural Nerve Distal Latency (ms) 5.99±2.56whereas in Left Sural Nerve distal Mean latency (ms) were5.27±2.22, the Mean values of Right Sural Nerve Distal Amplitude (μV)was 37.73±25.27whereas Left Sural Nerve Distal Amplitude (μV)were38.73±27.07, the values of Right Sural Nerve SNCV (m/sec) was 25.60±9.85whereas in Left Sural Nerve SNCV (m/sec) were25.80±13.78. All values were differing from the reference values.

Shefner et al.[10] applied the near nerve technique to patients with peripheral neuropathy and found that in 31% of them the only electrophysiological abnormality present was an abnormal late component of the SNAP,

demonstrating the efficacy of this technique in the study of potentials arising from nerve fibers ranging from 3 to 6 mm diameter, that are not recorded in routine nerve conduction studies[11,12]. Considering that in the initial phases of leprosy there is a predominant involvement of unmyelinated fibers, following impairment of small myelinated nerve fibers[2,12], we decided to investigate the nerve conduction of sural nerve only as it specifically carrying sensation of lower limb and most deformities occur to lower limb. To increase the diagnostic yield of nerve conduction studies in early Diagnosed leprosy cases, it results in early treatment, the best measure to avoid the feared consequences of leprosy neuropathy, including painless ulcerations, and muscle atrophy and weakness[13].

Recently, Marques et al.[8,11] applied the near nerve technique to study the sensory fibers of the median nerve is newly diagnosed leprosy patients. Unfortunately, the median nerve is not accessible to biopsy, preventing morphological analysis in those cases with detected neurophysiological abnormalities. This is not the case for the sural nerve, an exclusively sensory nerve whose morphology has been extensively studied in peripheral neuropathies, including leprosy.

In this study, 11 Leprosy patient had no SNAP was recorded, suggesting complete axonal degeneration or conduction block of all nerve fibers of Sural nerves.

The abnormalities found in the main component were relatively homogeneous, always suggesting axonal loss, a finding already reported by many authors[5,8-16], but is not in perfect agreement with the proposed physiology of this neuropathy since Schwann cells are the first to be involved by the bacilli[17,18]. This theoretically implies that demyelination should be the first abnormality detected, as was reported by Tzourioet al.[19] for the superficial radial nerve from recently diagnosed patients.

As an affected nerve may function normally in leprosy[20], it is possible that all patients studied in this series had advanced disease, even those with mild manifestations. If this assumption is true, we may be studying nerves that show a significant degree of axonal degeneration, regeneration and even remyelination. The definitive understanding of all these findings and assumptions will probably be reached with the evaluation of patients in the very early stages of the disease, studied not only distally but also at the topography were the initial attack occurs, and with studies analyzing both morphology and electrophysiology.

Conclusion: Demyelinating neuropathy of Sural Nerve is more common than Axonal Neuropathy in Leprosy cases. There is also chance that lead to total conduction block later or might be developed in early stage also. To better understand the neurophysiological status of leprosy and especially of lower limb and to increase the accuracy of the diagnosis; it is to be necessary to investigate patients in the very early stages of the disease and periodically. Smear positive case are more prone to develop the conduction block than smear negative cases.

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