Nerve conduction studies in early tuberculoid leprosy

Deepak Vashisht, Arjun Lal Das[1], Sanjeev S Vaishampayan[2], Surbhi Vashisht[3], Rajneesh Joshi[4]

Department of Dermatology, [1]Armed Forces Medical College, Pune, [2]Army College of Medical Science, New Delhi, [3]Department of Dermatology and Physiologist, Base Hospital, Srinagar, [4]Department of Community Medicine, Symbiosis International University, Pune, India

ABSTRACT

Context: Hansen's disease is a chronic illness; besides involving skin and peripheral nerves, it affects multiple organs. Nerve involvement is always present in leprosy, and it may be present much before the patient manifests clinically. **Aims:** To assess nerve conduction parameters in thickened and contralateral non-thickened nerves in early tuberculoid leprosy **Materials and Methods:** Fifty new untreated male patients with tuberculoid and borderline tuberculoid leprosy in the age group of 15-50 years with thickened peripheral nerves on one side were included in the study. Nerve conduction studies consisting of sensory and motor velocity (NCV), distal latencies, and amplitude were carried out on thickened ulnar, common peroneal, and posterior tibial nerves and contralateral normal nerves. **Statistical Analysis Used:** Mean values along with coefficient of variation were obtained for various parameters. These were compared with normal values of the control population. P value was used to verify statistical significance. **Results:** Nerve conduction parameters were deranged in most of the thickened nerves. Sensory parameters were affected early in the disease process. **Conclusion:** Additional parameters are required to assess nerve damage in early cases, where it is more in slow conducting fibers (average velocity fibers). Change in conduction velocity may not be marked; this calls for the measurement of fast fibers separately because potentials recorded are mainly from myelinated fibers.

Key words: Leprosy, neuropathy, nerve conduction

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.146164

Quick Response Code:

Address for correspondence:
Dr. (Lt Col) Deepak Vashisht, 92 Base Hospital, c/o 56 APO, Srinagar, India.
E-mail: deepak3975@gmail.com

INTRODUCTION

Hansen's disease primarily affects the skin, the peripheral nerves, the upper respiratory tract, and the eyes.[1] Nerve involvement may vary from involvement of intradermal nerves in a cutaneous patch to a major lesion in the peripheral nerve trunk,[2] with a predilection for the cooler parts of the body. Patients with skin lesions overlying peripheral nerve trunks are more prone to the development of sensory or motor impairment.[3] The nerve lesions may be insidious without any clinical manifestations, with mild clinical manifestations, or a sudden event, especially during reactions. In addition, nerve involvement may be present much before the patient manifests clinically. Nerve conduction studies (NCS) help in early diagnosis in suspected/doubtful cases that enables timely treatment and prevention of disabilities.

MATERIALS AND METHODS

Fifty new untreated male patients with tuberculoid and borderline tuberculoid leprosy in the age group of 15-50 years with thickened peripheral nerves on one side were included in the study. None of the patient had nerve abscesses. Patients with pure neuritic leprosy were not included in the study as it is not possible to determine the pole of leprosy in these cases. All the patients were right handed.

Clinical, bacteriological and histopathological diagnoses were carried out. Patients with deformities, nerve thickening on both the sides, those with implanted devices (such as cardiac pacemaker) and diseases like diabetes mellitus, alcoholism, or other cause of neuropathy were excluded from the study. Nerve conduction studies consisting of sensory and motor velocity (nerve conduction velocities-NCV), distal latencies, and amplitude were carried out on thickened ulnar, common peroneal, and posterior tibial nerves and contralateral normal nerves. Sensory nerve conduction studies were performed only on ulnar nerve, whereas motor nerve conduction studies were performed on ulnar, common peroneal and posterior tibial nerves. These nerves are easily

accessible for NCS and normal reference values for NCS in healthy individuals are available for comparison. The statistical significance was calculated by paired *t*-test.

Nerve conduction parameters studied

Motor Conduction Studies

The latency is the time between the stimulus and the response. In motor nerve studies, this latency includes the nerve conduction time and the neuromuscular transmission time. Distal latency is measured from the distal stimulation point to the first deflection from the baseline. The amplitude of the evoked motor response carries important information. It is dependent on the number of axons that conduct impulses from the stimulus point to the muscle, the number of functioning motor endplates and the muscle volume. Proximal latency starts at the proximal stimulation point and ends at the first deflection from the baseline. The amplitude is measured from the baseline to the negative peak. The conduction velocity (CV) is calculated by dividing the length of the nerve segment between the two stimulation points by the difference between the proximal and distal latency. In this way the slow distal conduction and any delay in the neuromuscular transmission is eliminated. It is calculated as follows:

$$CV\,(m/s) = \frac{\text{Distance}\,(mm)}{\text{Proximal latency - distal latency}}$$

When motor conduction velocity is calculated in this manner, it reflects the conduction in the fastest motor axons.

Sensory Conduction Studies

Sensory nerve conduction studies consist of either the stimulation of the digital nerves for recording an orthodromic sensory potential at a more proximal site or the stimulation of the nerve trunk for recording an antidromic digital potential. Latency is the time from the stimulus to the first positive peak of sensory nerve action potential (SNAP). The onset latency corresponds to the large diameter sensory fibers that conduct faster than motor fibers by 5-10%. Amplitude of the SNAP should be measured from the first positive peak to the highest negative peak. SNAPs are small and signal averaging is usually necessary. Sensory nerve conduction in peripheral nerves does not involve synaptic transmission so stimulation of the nerve at a single site suffices to calculate CV. The CV is calculated by dividing the length of the nerve segment from the stimulus point to the recording point by the positive peak latency.

$$CV\,(m/s) = \frac{\text{Distance}\,(mm)}{\text{Latency}}$$

RESULTS

A total of 50 male cases were studied. Age of patients ranged from 17 yrs-44 yrs, with mean age being 31.9 years and the maximum of 16 cases (32%) were in the age group of 25-29 yrs. The probable duration of illness varied from 1 month to 18 months with a mean of 4.9 months. Maximum number of patients 25 (50%) had illness for less than three months. Total of 47 cases (94%) were diagnosed as borderline tuberculoid leprosy and 3 cases (6%) as tuberculoid leprosy. Ulnar nerve was the most common nerve thickened in 36 cases (72%). Total of 30 (60%) cases had more than one nerve thickened, 12 (24%) cases demonstrated thickening of all three nerves, 20 (40%) cases had thickening of only one nerve. All together 92 thickened and 208 non-thickened nerves were studied. These patients had unilateral thickening of ulnar, common peroneal and the posterior tibial. Patients with bilateral thickening of nerves were excluded from the study.

Sensory deficit in the distribution of thickened ulnar nerve was seen in 31 (86%) out of 36 thickened nerves, whereas only 16 (66.7%) of thickened posterior tibial nerves had any sensory deficit. Out of 92 thickened nerves, 70 (76%) demonstrated sensory deficit along the distribution. Clinical examination of the non-thickened nerves revealed sensory deficit along the distribution in 4 (1.9 %) nerves. Altogether 204 (98.1%) of non-thickened nerves showed no sensory deficit along the distribution of the nerve.

Conduction velocity of thickened ulnar (sensory) nerve was 21.53 m/s, which was comparatively less than that of non-thickened ulnar nerves, but this difference was not statistically significant (P = 0.11). Motor conduction velocity in the thickened ulnar nerve was 53.48 m/s, which was comparatively lesser than that in non-thickened ulnar nerves but again statistically not significant (P = 0.056). Similarly, motor conduction velocity in the thickened and non-thickened common peroneal nerve was statistically insignificant [Table 1].

Comparisons of the number of thickened and non-thickened nerves with reduced NCV showed a significant difference P < 0.01, i.e. more number of thickened nerves had reduced NCV as compared to non-thickened nerves. This statistically

Table 1: Nerve conduction velocities of thickened and non-thickened nerves

Types of nerve	NCV in thickened nerve		NCV in non-thickened nerve		*P* value
	Mean+SD	Coeff var. (%)	Mean+SD	Coeff var. (%)	
Ulnar					
Sensory	21.53±10.91	50.7	26.41±12.06	45.7	0.11
Motor	53.48±7.12	13.3	56.84±6.05	10.6	0.056
Common peroneal	53.55±9.12	17.0	51.12±8.36	16.3	0.42
Posterior tibial	43.68±5.89	13.5	44.37±6.56	14.8	0.056

SD: Standard deviation, NCV: Nerve conduction velocities

significant difference was observed in both sensory as well as motor nerve conduction velocity. Total of 58.3% thickened ulnar sensory nerves had reduced NCV as against 4.7% of non-thickened nerves ulnar sensory [Table 2].

Latency in thickened ulnar nerve (sensory) was 2.77 m/s and non-thickened nerves was 2.58 m/s. This difference was statistically not significant (P = 0.35). Distal latency in thickened ulnar nerve was also statistically insignificant (P = 0.81).

Comparisons of the number of thickened and non-thickened nerves with distal latency showed a significant difference (P < 0.01), i.e. more number of thickened nerves had increased distal latency as compared to non-thickened nerves [Table 3]. The difference observed was found to be significant in all the nerves with (P < 0.01).

The difference in mean sensory amplitude (SNAP) in thickened ulnar nerve was statistically not significant (P = 0.11). The mean compound muscle action potential (CMAP) in thickened ulnar nerve when compared with non-thickened ulnar nerves was statistically insignificant (P = 0.50). Analysis of the number of cases showing decreased amplitude (SNAP and CMAP) in thickened and non-thickened nerves showed significant statistical difference with P < 0.01 [Table 4].

Sensory nerve conduction studies also correlated well with the observed sensory deficit. Total of 31 (91.1%) ulnar nerves with sensory deficit along the course demonstrated abnormal studies at least in one parameter as against 4.5% in patients without sensory deficit P < 0.01.

Overall analysis of nerve conduction studies i.e. NCV, latency and amplitude when compared with thickened and non-thickened nerves revealed a significant association between deranged parameters and nerve thickness. At least a single parameter was found deranged in NCS (sensory) in 27 (75%) of thickened ulnar nerve. Whereas, only 3 (4.6 %) of non-thickened ulnar nerves showed any derangement in NCS. This difference was statistically highly significant P value < 0.01 [Table 5].

Motor nerve conduction studies also showed a significant association between deranged parameters and nerve thickness. Maximum abnormalities in NCS were observed in posterior tibial nerve, 21 (87.5%) of thickened nerves showed derangement of at least one parameter of NCS (NCV, distal latency and amplitude). Differences observed in all the three thickened and non-thickened nerves were statistically significant P value < 0.01.

Table 2: Reduced NCV in thickened and non-thickened nerves

Types of nerve	Reduced NCV in thickened nerve		Reduced NCV in non-thickened nerve		*P* value
	Number	Percent	Number	Percent	
Ulnar					
Sensory	21/36	58.3	3/64	4.7	<0.01
Motor	14/36	39	2/64	3.1	<0.01
Common peroneal	16/32	50	0	0	<0.01
Posterior tibial	13/24	54	0	0	<0.01

NCV: Nerve conduction velocities

Table 3: Increased distal latency in thickened and non-thickened nerves

Types of nerve	Increased latency in thickened nerve		Increased latency in non- thickened nerve Thickened nerve		*P* value
	Number	Percent	Number	Percent	
				3.1	
				3.1	
Ulnar					
Sensory	12	33.3	2	3.1	<0.01
Motor	12	33.3	2	3.1	<0.01
Common peroneal	15	46.8	3	4.4	<0.01
Posterior tibial	6	25	0	0	<0.01

Table 4: Mean amplitude in thickened and non-thickened nerves

Types of nerve	Amplitude in thickened nerve		Amplitude in thickened non-thickened nerve		*P* value
	Mean+SD (μV)	Coeff var. (%)	Mean+SD (μV)	Coeff var. (%)	
Ulnar					
Sensory	21.5+10.9	51	26.4+12	46	0.11
Motor	4.9+3.42	70	5.3+2.74	52	0.50
Common peroneal	4.57+2.88	63	4.17+2.29	54	0.58
Posterior tibial	5.4+2.42	45	4.52+2.46	54	0.38

SD: Standard deviation

DISCUSSION

Leprosy is one of the leading causes of severe neuropathies in developing countries.[4] Diagnosis of leprosy can be challenging especially, neuritic leprosy. Nerve conduction studies provide us a non-invasive modality, to assess the peripheral nerve involvement in leprosy.[5] Conduction studies have the merit that they are quantitative observations, which depend neither on the cooperation of the patient nor the subjective impressions of the observer. They help in evaluating patients with peripheral neuropathy, assessing disease progression and monitor therapeutic intervention. The only disadvantage is the cost factor and the expertise involved in carrying out the investigation.

Whenever possible a baseline nerve conduction test should be performed. The NCS should be repeated every year if the

Table 5: Overall number of cases with abnormalities in NCS (NCV, latency, amplitude) in thickened and non-thickened nerves

Types of nerve	Abnormal NCS in thickened nerve		Abnormal NCS in non-thickened nerve		*P* value
	Number	Percent	Number	Percent	
Ulnar					
Sensory	27	75	3	4.6	<0.01
Motor	28	77.7	3	4.6	<0.01
Common Peroneal	20	62.5	2	2.9	<0.01
Posterior tibial	21	87.5	0	0	<0.01

NCV: Nerve conduction velocities, NCS: Nerve conduction studies

patient is on long term thalidomide, when new symptoms of neuritis, or findings of nerve function impairment occur after MDT completion.

In this study, the ulnar nerve was the most common nerve to be thickened in 72% of cases, which was closely followed by the common peroneal nerve in 64% of cases, in accordance with findings by Rao *et al*.[6] and Mc Leod *et al*.[7] Sensory nerves are involved much earlier in leprosy.[4] Ulnar (sensory) nerve conduction velocities in thickened and non-thickened nerves did not reveal any statistically significant difference, (P = 0.11). However, comparison of number of cases with reduced ulnar (sensory) conduction velocities in thickened and non-thickened nerves revealed significant differences. Similar findings were recorded by Mc Leod *et al*.[7], Gourie Devi[5] and Singh *et al*.[8] Latency in sensory nerves, distal latency in motor nerves, SNAP and CMAP in thickened and non-thickened nerves showed a similar trend. Findings of this study support the views of Rao *et al*.[6] and Verghese *et al*.[9] that there was no statistically significant difference in the electrophysiological parameters examined between clinically thickened nerve and their non-thickened contralateral counterparts, in early stages of the disease. Clinically thickened nerves also had normal NCS in some cases primarily because the nerve involvement is patchy in leprosy; however, as segmental demyelination progresses in an increasing number of fibres, besides the amplitude, even the CV is altered due to distorted conduction along small segments of demyelination in majority of fibers. Secondarily, a significant number of nerve fibers have to be involved to cause a change in electrophysiological studies. Finally, NCV represents only the function of the large myelinated fibers. Various authors studying histopathological changes have observed that the earliest changes in leprosy occur in the non-myelinated fibers.[10-13]

Mshana *et al*.[14] mentioned that some nerves that appeared to be clinically normal have been shown to have pathological changes. This study also showed abnormal conduction studies in some of the non-thickened nerves similar to other studies.[8,15,16] McLeod *et al*.[7] has suggested that if the nerve is thought to be thickened, and conduction studies are normal, a further period of observation is indicated before other investigations or treatment are instituted. However, normal conduction may be present in a diseased nerve.

Electrophysiological abnormality in ulnar (sensory) was well correlated with hypoesthesia along the course of the nerve, similar to findings of Ramadan *et al*.[16]

In this study, statistically no significant difference in nerve conduction parameters could be due to early detection of leprosy. At such an early stage, there may not be enough damage to significant number of nerve fibers to cause conduction changes. Altered nerve conduction parameters in non-thickened nerves could be attributed to preclinical disease. Overall analysis of nerve conduction studies i.e. NCV, latency and amplitude when compared with thickened and non-thickened nerves revealed a significant association between deranged parameters and nerve thickness.

It is further suggested that combining this modality with other non-invasive modality like USG of nerves will help in diagnosis of doubtful cases, much earlier. This will provide information on nerve morphologic alterations, echotexture and location of nerve enlargement, the limitations being availability of high-resolution ultrasound machine, technical expertise and cost.

To conclude, it may be stated that nerve conduction studies are helpful in early tuberculoid leprosy as they provide us non-invasive methods to assess the degree of nerve dysfunction and type of fibers involved (motor or sensory). In early cases where damage is more in slow conducting fibers (average velocity fibers) the change in conduction velocity may not be marked. This calls for the measurement of fast fibers separately because potentials recorded are mainly from myelinated fibers. This modality is quite sensitive and subclinical changes can be picked up early even in clinically uninvolved nerves. Further, sensory parameters are affected early in the disease process.

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Cite this article as: Vashisht D, Das AL, Vaishampayan SS, Vashisht S, Joshi R. Nerve conduction studies in early tuberculoid leprosy. Indian Dermatol Online J 2014;5:71-5.

Source of Support: Nil, **Conflict of Interest:** None declared.