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Original article:

Thickened and Contralateral Non-Thickened Nerves Conduction Studies in Early Tuberculoid Leprosy

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Abstract:

Introduction: Leprosy is a chronic infectious disease that primarily affects the peripheral nerves, skin, upper respiratory tract, eyes, and nasal mucosa. The aim of this study is to assess nerve conduction parameters in thickened and contralateral non-thickened nerves in tuberculoid leprosy.

Materials and Methods: The study population included 60 newly untreated leprosy and borderline tuberculoidleprosy patients in age group of 20-60 years. The statistical significance was calculated by paired t-test. Statistical significance was set at $p<0.05$.

Results: Comparisons of the number of thickened and non-thickened nerves with reduced NCV showed a significant difference $P<0.05$. This statistically significant difference was observed in both sensory as well as motor nerve conduction velocity. Comparisons of the number of thickened and non-thickened nerves with distal latency showed a significant difference ($P < 0.05$).

Conclusion: In conclusion this study proves that the nerve conduction studies are helpful in early tuberculoid leprosy.

Keywords: Tuberculoid Leprosy, Peripheral Nerves, Nerve Conduction.

Introduction

Leprosy also known as Hansen's Disease is a chronic infectious disease that primarily affects the peripheral nerves, skin, upper respiratory tract, eyes, and nasal mucosa.[1] The disease is caused by a bacteria known as *Mycobacterium leprae*.

Damage caused to the nerves by leprosy causes loss of sensation, this means that people with the disease cannot feel the affected areas making it easy for them to sustain injuries even from something as simple as a stone in their shoe.

Without treatment, injuries can become infected and ultimately can lead to life-changing disabilities. It is thought that four million people are currently living with a disability caused by leprosy.

Patients with skin lesions overlying peripheral nerve trunks are more prone to the development of sensory or motor impairment.[2]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.

There are very few organisms which enterperipheral or dermal nerves, and amongstmycobacteria, the leprosy bacillus is unique inthis respect. Since the early days of clinicalobservation in leprosy, it has been obvious thatnerves are heavily involved and some authorshave stated that neural tissues, and particularlySchwann cells, are the most heavily and consistentlyaffected; others consider that bacillifirst

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enter nerves in the genesis of all leprouslesions, and that they persist in them long afterdisappearance from other tissues as a result oftreatment.

More sophisticated methods for assessing nerve function such as vibrometry,[3] laser Doppler flowmetry[4,5] and thermal threshold testing have been shown to detect different modalities of leprous neuropathy.The most commonly used methods are thermal testing and testing ofvibration sense. Thermal testing assesses small, unmyelinated C-fibres that mediate warmsensation and small unmyelinated and myelinatedfibres mediating cold sensation.[6] Vibration 'sense' is mediated by large afferent A fibres.[7]

Around 10% of the 300,000 new leprosy casesregistered every year have signs of sensory, motor or autonomicneuropathy at diagnosis. The highest rates of impairment werereported from Ethiopia (55%),[8] while studies in Thailand andBangladesh reported rates of 18% and 12%, respectively.[9]New neuropathy may develop both during and after effectivemulti-drug therapy.[10]A substantial proportion of people withleprosy-related nerve damage will have life-long functional and/orsocial disability.[11]

The aim of this study is to assess nerve conduction parameters in thickened and contralateral non-thickened nerves in early tuberculoid leprosy.

MATERIALS AND METHODS

The study population included 60 newly untreated leprosy and borderline tuberculoid leprosy patients in age group of 20-60 years. The study was conducted at department of Dermatology, Era's Lucknow Medical College & Hospital, Lucknow in Uttar Pradesh, India. Written consent was obtained from individual study subjects before inclusion in the study, using a standard consent form.Details of the project were presented to andapproved by the Ethical Committee of the university, and all potential subjects were required to sign an appropriate form containing the Terms of Consent prior to the commencement of the study.

Inclusion Criteria:

- Age group between 20-60.
- Thickened peripheral nerve on one side.
- The patient with no nerve abscesses
- All the patients were right handed.

Exclusion Criteria

- Patients with pure neuritic leprosy
- Patients with deformities,
- Patients with nerve thickening on both the sides,
- Those with implanted devices (such as cardiac pacemaker)
- Diseases like diabetes mellitus,alcoholism, or other cause of neuropathy were excluded from the study.
- Patients who were non- cooperative with nerve conduction studies were also excluded.

Clinical, bacteriological and histopathological diagnoses were carried out. 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 nerveconduction 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 inhealthy individuals are available for comparison. The statisticalsignificance was calculated by paired t-test.Statistical significance was set at $p<0.05$.

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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 themuscle, 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.

Sensory Conduction Studies

Sensory nerve conduction studies consist of either the stimulation of the digital nerves for recording an orthodromicsensory 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.

Results:

Sixty subjects were enrolled in the study. Their mean age was 48.9 years.Total of 58 cases (96.6%) were diagnosed as borderline tuberculoid leprosy and 2 cases (3.33%) as tuberculoid leprosy. Nerve conduction velocities of thickened and non-thickened nerves are summerised in table 1. Ulnar nervewas the most common nerve thickened in 38 cases (63.3%). In which 63.5 % were Reduced NCV in thickened nerve and 6.9 % Reduced NCV in non thickened nerve in sensory conduction. And in motor 39.5 % were Reduced NCV in thickened nerve and 4.2% Reduced NCV in non thickened nerve. Reduced NCV in thickened and non-thickened nerves are summerised in table 2. Comparisons of the number of thickened and non-thickened nerves with reduced NCV showed a significant difference$P < 0.05$. This statistically significant difference was observed in both sensory as well as motor nerve conduction velocity. Comparisons of the number of thickened and non-thickened nerves with distal latency showed a significant difference ($P < 0.05$), 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 ($P < 0.05$). The difference in mean amplitude in thickened and non thickened nerve was statistically not significant in all the nerve. (Table 4)

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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	19.36±11.41	53.0	30.21 ± 11.0	39.6	0.24
Motor	48.91±3.11	16.8	60.3 ± 4.6	12.1	0.023
Common peroneal	54.46±11.16	13.6	50.9 ± 9.8	18.5	0.11
Posterior tibial	37.78±91	19.2	39.29 ± 7.29	16.3	0.058

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

Types of nerve	Reduced NCV in thickened nerve		Reduced NCV in nonthickened nerve		P value
	Number	Percent	Number	Percent	
Ulnar					
Sensory	24/38	63.5	5/72	6.9	<0.02
Motor	15/38	39.5	3/72	4.2	<0.01
Common peroneal	20/36	55.6	0	0	<0.01
Posterior tibial	12/28	42.9	0	0	<0.03

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	
Ulnar					
Sensory	16	42.1	3	4.2	<0.02
Motor	14	36.8	3	4.2	<0.01
Common peroneal	19	52.8	0	0	<0.01
Posterior tibial	8	28.6	0	0	<0.01

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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	20.36 ± 19.1	49	29.0 ± 9	50	0.19
Motor	5.2 ± 9.36	69	4.8 ± 3.49	48	0.39
Common peroneal	3.98 ± 8.1	58	5.38 ± 1.19	56	0.46
Posterior tibial	7.1 ± 3.86	47	3.47 ± 4.96	58	0.29

Discussion

Comparisons of the number of thickened and non-thickened nerves with reduced NCV showed a significant difference $P < 0.05$. This statistically significant difference was observed in both sensory as well as motor nerve conduction velocity. Comparisons of the number of thickened and non-thickened nerves with distal latency showed a significant difference. i.e. more number of thickened nerves had increased distal latency as compared to non-thickened nerves. The difference observed was found to be significant in all the nerves with ($P < 0.05$). The difference in mean amplitude in thickened and non thickened nerve was statistically not significant in all the nerve.

In leprosy, the sensation in the skin may bereduced due to dermal and truncal nerve fibre involvement.[12-16]On grounds of histopathological evidence, indicating that small, unmyelinatedfibres arethe first to be affected in leprosy.[17-19]

Many nerve conduction (NC) studies of subjects with leprosy have been reported, particularly in the 1960's and 1970's. Among the earliest were those of Hackett et al.,[20]Magora et al.,[21]Verghese et al.,[22]Antia et al.,[23] McLeod et al.,[24] and Singh et al.[25] With the exception of the studies of Magora et al. and Samant et al.,[26] all these studies were crosssectional in nature. The great majority of the studies were small and often a limited number of nerves was studied, e.g. only ulnar nerves in the study of Hackett et al., the radial cutaneous nerve by Antia et al.,[27] the ulnar and median nerves by Verghese and colleagues or singlesidednerves, as in the more recent study of Brown et al.,[28]Samant et al. did not find parameters in NC studies that helped predict reactions.[29]

In this study, the ulnar nerve was the most common nerve to be thickened, which was closely followed bythe common peroneal nerve, in accordance with findings by Raoet al.[30] and McLeodet al.[24] Sensory nerves are involved much earlier in leprosy.[31]

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 Raoet al.[30] that there

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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. In this study, statistically no significant difference in nerve conduction parameters could be due to early detection of leprosy.

However, this study had a smallsample size, so associations may have been present, but not statistically significant. Generally, investigators concluded that nerve conduction studies were very useful and could potentially detect pre-clinical neuropathy.

Conclusion:

In conclusion this study proves that thenerve 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). Generally, investigators concluded that nerve conduction studies were very useful and could potentially detect pre-clinical neuropathy.

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