

Nerve conduction studies in paucibacillary and multibacillary leprosy: a comparative evaluation

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Involvement of peripheral nerves in patients with leprosy results in sensory, motor and autonomic dysfunctions along with deformities and disability. Pattern of nerve involvement is different for different forms of leprosy. In this study, we evaluated and compared the nerve conduction parameters of paucibacillary leprosy with that of multibacillary leprosy. In this study, 40 consecutive patients of leprosy (19 cases of paucibacillary and 21 cases of multibacillary leprosy) were included. Nerve conduction studies were performed according to the standard procedure described in the manual of the machine. We observed that patients with multibacillary leprosy had significantly more severe changes in nerve conduction parameters as compared to that of paucibacillary leprosy. In paucibacillary leprosy, the dominant pattern of nerve involvement was that of mononeuropathy, however, in 6 paucibacillary cases the nerve involvement was in form of mononeuritis multiplex. Electrophysiological assessment also revealed involvement of clinically uninvolved nerves. Nerve conduction parameters were suggestive of mixed axonal as well as demyelination of the peripheral nerves.

Key words: Axonal neuropathy, Electrophysiology, Mononeuritis multiplex, Leprosy

Introduction

Leprosy is still one of the most prevalent and treatable causes of neuropathy in the world. Neuropathy in leprosy is important because it is often associated with severe disability and handicap. World Health Organization classifies leprosy, on the basis of findings from skin smears, as paucibacillary and multibacillary leprosy. In World Health Organization classification, patients showing negative skin smears for acid-fast bacillus at all sites examined are grouped as paucibacillary leprosy whereas patients having

positive skin smear for acid-fast bacillus from any site are grouped as multibacillary leprosy. For field surveys, patients having 5 or fewer skin lesions are grouped in paucibacillary leprosy whereas patients having more than 5 skin lesions are grouped in multibacillary leprosy (WHO 1998). According to data from the World Health Organization, among newly detected cases in 2002, approximately 39% of patients were clinically classified as having multibacillary leprosy (WHO 2004).

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In leprosy, all physiological functions (sensory, motor and autonomic) of a peripheral nerve are likely to be affected. Sensory functions are most severely affected. Patterns of nerve involvement are different for different forms of leprosy. In tuberculoid leprosy, involvement of small dermal nerves of cooler parts of the body produces patchy areas of sensory loss. Patients with lepromatous leprosy have progressive symmetrical, distal peripheral neuropathy; damage to nerve trunks may superimpose a picture like mononeuritis multiplex. Borderline leprosy has a high propensity to involve nerve trunks, producing a picture of multiple mononeuropathies or mononeuritis multiplex (Ooi and Srinivasan 2004).

Electrophysiological assessments of leprosy reveal varied patterns of nerve involvement. Typically electrophysiological assessment in leprosy reveals both axonal loss and demyelination (Ooi and Srinivasan 2004).

In this cross-sectional comparative study, we evaluated the nerve conduction parameters in patients with paucibacillary and multibacillary leprosy (as per World Health Organization classification of leprosy) patients.

Materials and Methods

The study was conducted from March 2009 to February 2010 at the Department of Neurology, Chhatrapati Shahuji Maharaj Medical University, Lucknow, Uttar Pradesh. This is a tertiary medical referral center in the north-central part of India. Written informed consent (from the patient or their legal guardian) was obtained after explaining the procedure and the purpose of the study. The Institutional Ethics Committee approved the study.

Patient population

We included 40 consecutive newly-diagnosed patients of leprosy who attended Neurology outpatient department (OPD). Diagnosis of leprosy was based on its cardinal features. These cardinal features of leprosy were hypaesthetic skin

lesions, thickened peripheral nerves and positive skin smear for bacilli. The diabetic patients, patients with non-leprosy related peripheral neuropathies, chronic alcohol intake or poliomyelitis were excluded. Patients who were non-cooperative with nerve conduction studies were also excluded.

Initial evaluation

A detailed clinical evaluation was performed at enrollment in the study. The location and appearance of skin lesions and whether they were overlying the course of a peripheral nerve trunk were recorded. Particular attention was given to signs and symptoms of type 1 reactions and erythema nodosum leprosum. Slit-skin smears examination was performed in all cases. Nerve biopsy could be performed in 3 patients.

Patients were classified as per the Ridley-Jopling classification. In the present study, clinical classification was used in which lepromatous, borderline-lepromatous and mid-borderline in the Ridley-Jopling classification were classified as multibacillary leprosy and tuberculoid and borderline-tuberculoid leprosy were all classified as paucibacillary leprosy (Jopling 1981, Bartt 2004). The World Health Organization field criteria divide leprosy into paucibacillary or multibacillary type. Paucibacillary leprosy when number of skin lesions was 5 or less. Multibacillary leprosy when number of skin lesions was 6 or more (Jacob and Mathai 1998, WHO 2002).

All patients were also subjected to complete blood count, erythrocyte sedimentation rate, blood sugar, blood urea nitrogen, creatinine, antinuclear antigen, chest radiograph at the time of enrollment. Enzyme linked immunosorbent assay (ELISA) for human immunodeficiency virus was performed in each patient. None of the patients was human immunodeficiency virus positive. Detail drug history was also recorded. All patients received World Health Organization multidrug therapy for appropriate duration (Ooi and Srinivasan 2004).

Nerve conduction studies

Nerve conduction studies were performed using Medelec Synergy 5 channel EMG and EP systems machines (VIASYS Healthcare System, USA). Standard procedures were used for evaluation and recording as described in the accompanying manual of the machine. Procedure was explained to the patients to obtain their full cooperation. Room temperature was kept at around 25°C. The skin surface temperature was in all cases between 31°C and 33°C. Supramaximal stimulation was used to stimulate all the nerves. Values of conduction velocity, distal latency and amplitudes were analyzed and compared with our own laboratory values obtained from healthy subjects.

Motor nerve conduction parameters were measured on four nerves bilaterally (ulnar, median, lateral popliteal or common peroneal, and posterior tibial nerves), similarly sensory nerve conduction parameters measured bilaterally on three nerves (ulnar, median and sural nerves).

Motor conduction recording of median, ulnar, lateral popliteal and posterior tibial nerves was obtained from abductor pollicis brevis, abductor digiti minimi, extensor digitorum brevis and abductor hallucis brevis muscles respectively.

Sensory nerve conduction velocity was measured with ring electrodes placed around the thumb (median and radial nerve), middle finger (median nerve) and little finger (ulnar nerve) and stimulation at the wrist. Sural nerve was tested at both sides after stimulation lateral of the Achilles tendon, 10-12 cm proximal from the active electrode. Monopolar surface recording electrodes and bipolar hand held stimulating electrodes were used to obtain the sensory nerve action potentials. All the sensory nerve conduction testing was antidromic. The filter setting was 20 Hz for low frequency and 2 kHz for high frequency. The sensitivity and sweep velocity was set at 10 μ V and 20 ms respectively.

Values for the lower limits of normal correspond to mean values minus 2 SD of a historical series of

50 healthy subjects (age range 21-82 years, mean 35 years) studied by the same methods. A difference of at least 50% in sensory nerve action potential and compound motor action potential amplitude was required to define a significant asymmetry between two sides.

Definitions

Mononeuropathy was defined as disorder of a single nerve or nerve trunk. Polyneuropathy was defined as simultaneous involvement of multiple nerve trunks. Mononeuritis multiplex was defined as damage to at least two separate nerve areas presenting as asymmetric neuropathy. Demyelinating neuropathies demonstrate slow nerve conduction velocities, prolonged distal latencies and features of conduction block. By contrast, axonal neuropathies typically demonstrate normal nerve conduction velocities with low amplitudes of sensory/motor nerve conduction (Camdessanché et al 2002, Misra et al 2008).

Statistical analysis

Qualitative data have been presented in form of number and percentage and quantitative data have been presented in mean and standard deviation. Minimum and maximum values have also presented. Student t-test was used to find out significance difference in mean level of paucibacillary and multibacillary group. Fisher's exact probability test (P) was used to find out significant difference between two proportions. Significance level was taken 0.05% at two tailed test. The data were analyzed using the statistical package for the social science software (SPSS version 16.0).

Results

As per World Health Organization classification, number of patients in paucibacillary leprosy group was 19 (47.5%) and in multibacillary leprosy group the number was 21 (52.5%). Among multibacillary group, 3 patients were determined to have lepromatous leprosy and 5 patients borderline lepromatous leprosy and remaining 13 patients had borderline leprosy. Among

paucibacillary group 7 patients had borderline tuberculoid leprosy and 12 patients had tuberculoid leprosy.

Demographic data

The age of the patients ranged from 12 to 75 years. Mean age of onset was significantly higher in multibacillary group as compared to that of paucibacillary group. Other epidemiological characteristics have been given in Table 1.

Clinical characteristics of leprosy patients

Six patients had presented with acute illness. Thickened nerves were present in 35 (87.5%)

patients. Most common thickened nerve was ulnar nerve (65% cases) followed by common peroneal nerve (25%). There was bilateral 7th cranial nerve involvement in 2 patients, radial nerve in 1 patient and great auricular nerve in one patient of multibacillary group (Table 2). Mutilation of right index finger was noted in one patient.

Mononeuritis multiplex form of neuropathy was present in 40% of the patients, mononeuropathy was seen in 40% while rest 20% patients had symmetrical sensory motor polyneuropathy. Two patients (5%), in the multibacillary group, had

Table 1 : Epidemiological and clinical characteristics in patients with leprosy

Characteristics	Paucibacillary group (n=19)	Multibacillary group (n=21)	P value
Age in years (Mean±SD)	27.0±11	40.5± 13.8	0.002
Range	(12- 55)	(19-75)	
Male =34	17 (42.5%)	17 (42.5%)	0.664
Female=6	2 (5.0%)	04 (10.0%)	
Duration of illness in months (Mean±SD)	11.6±21.6	16.8±14.7	0.368
Range	(1-96)	(0.5- 60)	
Number of skin lesions (Mean±SD)	3±0.9	10.1±5	0.001
Range	(2 - 4)	(6 - 24)	

Table 2 : Clinical presentations of patients with leprosy

Features	Paucibacillary (n=19)		Multibacillary (n=21)		Total (n=40)		P value
	No.	%	No.	%	No.	%	
Weakness	9	22.5	13	32.5	22	55.0	0.52
Amyotrophy	9	22.5	9	22.5	18	45.0	1.00
Loss of sensation	19	47.5	20	50.0	39	97.5	1.00
Paresthesia	8	20.0	10	25.0	18	45.0	0.32
Thickened nerve	16	40.0	19	47.5	35	87.5	0.21
Ulcer	2	5.0	7	17.5	7	22.5	0.13
Deformity	9	22.5	11	27.5	20	50.0	0.70
Disability	12	30.0	15	37.5	27	67.5	0.73

Table 3 : Nerve conduction parameters of ulnar and median nerve in patients with paucibacillary and multibacillary leprosy

Electrophysiological function	Normal value	Paucibacillary (n=19)		Multibacillary (n=21)		P value	Paucibacillary (n=19)		Multibacillary (n=21)		P value
		Right	Left	Right	Left		Right	Left			
Motor function											
Ulnar nerve											
Mean latency (ms)	≤3.3	2.93±0.90	3.11±1.45	3.11±1.12	3.07±0.91	0.64	2.53±1.12	3.07±0.91	3.07±0.91	0.10	
Mean NCV (m/s)	≥49.0	55.12±8.42	40.54±16.57	46.62±19.58	49.38±12.60	0.00	46.62±19.58	49.38±12.60	49.38±12.60	0.59	
Mean amplitude (µV)	≥6.0	6.88±2.77	4.29±3.40	4.72±3.08	5.32±2.97	0.01	4.72±3.08	5.32±2.97	5.32±2.97	0.51	
Median nerve											
Mean latency (ms)	≤4.4	3.33±0.67	3.17±1.25	3.11±1.12	3.32±1.20	0.63	3.11±1.12	3.32±1.20	3.32±1.20	0.58	
Mean NCV (m/s)	≥49.0	56.00±5.40	46.70±17.40	52.54±14.31	49.80±13.82	0.03	52.54±14.31	49.80±13.82	49.80±13.82	0.92	
Mean amplitude (µV)	≥4.0	10.16±3.57	7.38±3.37	8.31±3.30	8.43±4.08	0.01	8.31±3.30	8.43±4.08	8.43±4.08	0.54	
Sensory function											
Ulnar nerve											
Mean latency (ms)	≤3.1	2.45±1.28	1.24±1.86	2.18±1.72	1.35±1.41	0.02	2.18±1.72	1.35±1.41	1.35±1.41	0.10	
Mean NCV (m/s)	≥50.0	37.90±19.19	15.89±22.38	35.17±24.44	25.92±26.53	0.00	35.17±24.44	25.92±26.53	25.92±26.53	0.26	
Mean amplitude (µV)	≥17.0	15.73±11.04	6.64±11.35	11.37±10.04	9.38±10.56	0.01	11.37±10.04	9.38±10.56	9.38±10.56	0.54	
Median nerve											
Mean latency (ms)	≤3.5	2.82±0.53	2.21±1.52	2.30±1.18	2.41±1.12	0.10	2.30±1.18	2.41±1.12	2.41±1.12	0.77	
Mean NCV (m/s)	≥50.0	51.08±9.61	37.92±23.97	45.31±21.43	40.96±19.08	0.03	45.31±21.43	40.96±19.08	40.96±19.08	0.50	
Mean amplitude (µV)	≥20.0	25.60±10.52	13.75±11.71	21.23±13.22	14.72±10.14	0.00	21.23±13.22	14.72±10.14	14.72±10.14	0.08	

Table 4 : Nerve conduction parameters of posterior tibial, common peroneal and sural nerves in patients with paucibacillary and multibacillary leprosy

Posterior tibial nerve	Normal values	Right	Right	P value	Left	Left	P value
Mean latency (ms)	≤5.8	4.23 ±1.22	4.24±2.41	0.99	4.26±0.68	4.02±1.83	0.59
Mean NCV (m/s)	≥41.0	46.52±4.51	34.62±17.64	0.00	47.61±4.81	38.29±13.45	0.00
Mean amplitude (µV)	≥4.0	7.39±2.87	4.14±3.46	0.00	7.94±4.34	4.85±3.09	0.01
Common peroneal nerve							
Mean latency (ms)	≤6.5	6.88±10.81	3.71±3.05	0.20	4.35±1.03	4.26±2.58	0.88
Mean NCV (m/s)	≥44.0	47.47±10.24	31.01±20.93	0.00	48.85±5.45	35.56±18.60	0.00
Mean amplitude (µV)	≥2.0	5.05±2.15	2.38±2.16	0.00	4.71±2.24	4.02±5.28	0.60
Sural nerve							
Mean latency (ms)	≤4.4	2.87±2.25	1.28±1.59	0.01	2.76±0.98	1.67±1.72	0.02
Mean NCV (m/s)	≥40.0	40.48±19.46	19.46±23.68	0.00	44.37±12.58	22.40±22.92	0.00
Mean amplitude (µV)	≥6.0	13.29±8.67	4.30±6.09	0.00	14.38±7.18	5.97±7.82	0.00

generalized areflexia and abnormal joint position sense. Other neurological manifestations such as weakness (55%), amyotrophy (45%), sensory impairment (97.5%), paresthesia (45%), nerve tenderness (20%), ulcer (22.5%), deformity (50%) and disability (67.5%) were present in both the groups but the differences between two groups were not statistically significant ($p>0.05$) (Table 2).

Slit-skin smear examination done in all cases. It was positive in 5 cases (12.5%), out of which 3 in multibacillary group and 2 cases in paucibacillary cases. Nerve biopsy was performed in 3 cases and all were non-contributory.

Nerve conduction parameters

On the basis of sensory nerve conduction studies, the most commonly affected nerves were the ulnar nerve (77.5%) followed by sural nerve (45%). Electrophysiological assessment revealed that in leprosy there were features suggestive of mixed axonal (decrease in amplitudes) as well as demyelination (decrease in velocity). In paucibacillary group, the dominant pattern of nerve involvement was mononeuropathy type. However, 6 paucibacillary cases the involvement was in pattern of mononeuritis multiplex. In multibacillary leprosy group, electrophysiological evaluation revealed that these patients either had mononeuritis multiplex or a picture consistent with distal polyneuropathy. Patients with multibacillary leprosy had significantly more severe changes in nerve conduction parameters as compared to that of paucibacillary leprosy. Nerve conduction studies revealed that patients with multibacillary group had significantly lower motor nerve conduction velocities and amplitude of motor unit potential as compared to that of paucibacillary group. Sensory nerve conduction study of median nerves showed significantly decreased conduction velocity and amplitude in multibacillary group than paucibacillary group. (Table 3, 4, 5).

Table 5 : Pattern of nerve involvement in patients with leprosy (n=40)

Pattern	Clinical		Electrophysiological	
	No.	%	No.	%
Mononeuropathy	21	52.5	9	22.5
Mononeuritis multiplex	12	30.0	27	67.5
Polyneuropathy	2	5.0	3	7.5
No definite pattern of nerve involvement	5	12.5	1	2.5

Discussion

In majority of patients with paucibacillary leprosy the pattern of nerve involvement was in form of mononeuropathy, however, in some paucibacillary leprosy patients the pattern of involvement was in the form of mononeuritis multiplex. Electrophysiology revealed involvement of clinically uninvolved nerves. The most commonly affected nerves on sensory nerve conduction studies were ulnar nerve followed by sural nerve. Patients with multibacillary leprosy had significantly more severe and extensive changes in nerve conduction parameters as compared to that of paucibacillary leprosy. In a recent study, a group of authors demonstrated that in patients with multibacillary leprosy nerve conduction abnormalities were seen in 92% of patients and majority of the patients had involvement of more than five sensory and motor nerves. Sensory nerve abnormalities were higher than motor. Affection of sensory and motor nerves was higher in patients showing evidence of reactions. Nerve damage was more widespread than anticipated (Capadia et al 2010). We observed that even patients of paucibacillary leprosy had more extensive involvement.

Nerve conduction studies, in past, revealed reduced nerve conduction velocities and reduced amplitudes of compound action potentials. Focal slowing of impulse conduction across thickened nerve segments had been observed (Ramadan et al 2001). Partial conduction block suggestive of segmental demyelination had been demon-

strated (Ghiglione et al 2004). In contrast to our findings a group of authors showed that leprosy produced a predominantly axonal polyneuropathy (Soysal et al 2004). Consistent with previous studies, our study also revealed that in leprosy the electrophysiological features were suggestive of evidence of axonopathy as well as demyelination.

All electrophysiology based studies have observed dominant involvement of sensory nerves. Sensory nerve action potentials are frequently absent or reduced. In routine studies, of sensory nerve conduction, only large fibres are evaluated. The late components, which originate from thinner fibers, are not detected. A near-nerve recording technique that records potentials from small nerve fibers has been found useful.

It has been observed that changes are more severe in the lower extremities (Soysal et al 2004). However, in our study, there was an equal involvement of upper and lower limbs which suggest that leprosy is not a length dependent neuropathy and motor and sensory conduction were equally affected.

Reversal reactions of leprosy cause greater electrophysiological abnormalities both in clinically-and subclinically-affected nerves (Thacker et al 1996). Near nerve potential recording increases the sensitivity of nerve conduction studies (Marques et al 2003).

In conclusion, electrophysiological tests provide valuable information for detecting nerve function impairment. Electrophysiological assessment

suggested that both in paucibacillary as well as multibacillary leprosy there were mixed involvement of axon as well as myelin sheath. Electrophysiologically, patients of leprosy had more extensive and more severe involvement of peripheral nerves. Nerve conduction studies in paucibacillary leprosy revealed involvement of nerves which were apparently normal on clinical examination.

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