

Original Research Article

Nerve conduction study: can it diagnose leprosy early?

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ABSTRACT

Background: Leprosy is a chronic infectious disease which predominantly involves skin and peripheral nerves. Most important consequences of leprosy are due to the involvement of peripheral nerves which leads to gross deformities and disabilities. Detection of preclinical nerve function impairment can help in the prevention of deformities and disabilities. The objective of the study was role of nerve conduction study (NCS) to detect nerve function impairment (NFI) in leprosy.

Methods: An electrophysiological study was conducted for 50 newly diagnosed cases of leprosy from December 2017 to July 2019 at Department of Dermatology, Osmania Medical College, Hyderabad. Nerve conduction velocities, amplitude, and latencies of ulnar, median, common peroneal, posterior tibial, sural nerves are measured.

Results: 10 nerves in each patient with a total of 500 nerves were studied by NCS. Only 8 (16%) cases had totally normal NCS. And rest 42 (84%) cases have abnormal NCS. Most common pattern observed is sensory motor axonal neuropathy. A total of 268 (53.6%) nerves were normal before starting multidrug therapy and 232 (46.4%) nerves have abnormal NCS. Among these nerves the involvement of Sensory nerves (49%) are more than motor nerves (42%).

Conclusions: NCS is a reliable and reproducible test to detect the early NFI. Though it cannot directly diagnose leprosy, it can be used in suspected cases, newly diagnosed cases, and household contacts to detect the NFI early and prevent the complications associated with it.

Keywords: Leprosy, Nerve conduction study, Detect nerve function impairment

INTRODUCTION

Leprosy is the most common treatable cause of neuropathy in the world.¹ In all patients with leprosy, the nerve tissue is involved. The dermal nerves are infected in all skin lesions, including those due to indeterminate leprosy of childhood. Clinical examination is often sufficient to reliably diagnose leprosy neuropathy. Nerve damage in non-lepromatous leprosy and in 'reversal' reactions is the result of an immune response to

the presence of antigenic material derived from leprosy bacilli within nerves. This immune response damages nerves by intraneural epithelioid cell formation, and by compression of Schwann cells due to inflammatory oedema. In lepromatous leprosy the presence of leprosy bacilli induces slow damage to both perineurium and Schwann cells.

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 or doubtful cases that enables timely treatment and prevention of disabilities.²To assess the role of NCS, in detecting nerve function impairment (NFI) in leprosy.

METHODS

The study group is drawn from patients attending the outpatient and inpatient, Department of Dermatology, Venereology and Leprology at Osmania medical college, Hyderabad from December 2017 to July 2019. Samples were collected after obtaining ethical approval.

Method of collection of data

50 newly diagnosed cases with proven leprosy belonging to all age groups between 12 to 60 years and both sexes were included in the study after taking their consent. In each case detailed history, thorough general physical, local and systemic examination with relation to neuropathy in leprosy will be recorded. In all cases necessary investigations and skin biopsy for histopathological confirmation was taken from those patients who had a well-defined cutaneous patch or a well-defined area of sensory deficit.

Inclusion criteria

Age above 12 years, newly diagnosed patients with pauci and multi bacillary leprosy were included.

Exclusion criteria

Already treated cases, children below 12 years of age, pregnant women and lactating mothers, diabetics, HIV positive cases, patients with neuropathy due to other causes and patients under recent treatment with neuromuscular blockers were excluded.

A detailed history was taken with particular reference to neuropathy, reactions and complications, the presenting complaints like exacerbation of the skin lesions, appearance of fresh lesions, shooting pain in the limbs, fever, malaise, muscle pain, pain in the lesions, bone, joints and neuralgia, pain in the testis (in case of males) were noted down.

An attempt was made to find out the precipitating factors if any like concomitant infections or infestations, physical and psychological stress, menstrual periods, vaccinations or injections, hot foods, extremes of climate and drugs.

Examination

A detailed general examination was carried out in all cases with particular reference to the number of skin lesions, distribution of skin lesions, type of skin lesions,

lymph node enlargement, mucous membrane involvement (oral, pharynx, larynx etc.), eye involvement, and oedema of extremities were also noted.

Local examination was carried out methodically in every patient with particular stress laid on the extent of the skin lesions, type of skin lesions, sensation over the lesions, over the normal skin and over extremities were tested and the changes if any were carefully noted down.

In every patient, the extent of nerve involvement was noted whether a single nerve or multiple nerves.

All the systems were carefully examined and systemic involvement if any was noted down.

All the cases who were clinically and provisionally diagnosed as cases of reactions in leprosy were investigated as follows.

Routine investigations

All the patients diagnosed were investigated routinely like blood Hb%, total white blood cell count, different count, ESR, urine for albumin, sugar and microscopy and stool for ova and cyst. Liver function tests and renal function tests to rule out any underlying systemic disorders.

Diagnosis of type of leprosy was confirmed by slit smear examination.

Slit smear examination

Slit and scrape smear was done for the demonstration of acid fast bacilli. Sites chosen were 2 ear lobes, 2 eyebrows and an active lesion.

Procedure

The selected sites were cleansed with spirit. The skin was held firmly between thumb and index finger and the pressure was maintained until the skin became pale. An incision, 5 mm long and 3 mm deep was made and the blade was turned through 90° and the tissue material was scraped from the sides and the floor of the incision. This material was then smeared on to the slide and a uniformly thick smear was made. The smear was allowed to dry and fixed by passing the slide over the top of a flame. The fixed smear was stained with Ziehl-Neelsen stain.³

Procedure of Ziehl-Neelsen staining

After placing on the staining rack, the whole slide was covered with carbol fuchsin and heated with a spirit lamp till it caused steam to rise from all parts of the slide, but boiling was avoided. The slide was left for 10 min without further heating. The plain was tipped away and the slide was held under a gentle stream of tap water. The slides were decolorized by adding 5% of H₂SO₄ for 20

seconds or until the smear became light pink in color and was again washed with gentle running water and counter stained with 1% methylene blue for about 1 minute and washed in running water and allowed to dry.

The bacteriological index (BI) and the morphological index (MI) were calculated according to Ridley's scale.

Bacteriological index

It is a method for assessment of the mycobacterial load. The bacterial load is graded as detailed below.⁴

0: No bacilli observed after searching at least 100 microscopic fields.

1+: 1-10 bacilli in 100 microscopic fields

2+: 1-10 bacilli in 10 microscopic fields

3+: 1-10 bacilli in an average microscopic field

4+: 10-100 bacilli in an average microscopic field

5+: 100-1000 bacilli in an average microscopic field

6+: Many clumps of bacilli in an average microscopic field (over 1000).

Morphological index

It is the percentage of solid stained bacilli. This was calculated after examining 200 red staining elements lying singly.⁴

Biopsy

Specimens from 19 patients were studied for histopathological changes.

After local infiltration of 1cc to 2 cc of xylocaine to the edge of the lesions, a piece of skin consisting of both involved and uninvolved skin was taken for histopathological study. The tissue was preserved in 10% formalin before it was processed for histopathological study at the Department of pathology, Osmania general hospital, Hyderabad. The sections were stained with the Haematoxylin and Eosin and fite faraco stains.

Nerve conduction study

The electrophysiological nerve conduction assessment was done for all the patients using RMS-EMG EP Mark 2 machine. Filters were set at 2 to 5 Hz and sweep speed was 5ms per division for motor study and the corresponding settings for sensory study were 20 to 3 kHz and 2 ms per division. The duration for both the recordings was taken to be 100 μ sec. The room temperature for the study was set at 30°C.⁵

The parameters studied for motor nerves were distal motor latency, compound muscle action potential, and conduction velocity while for sensory nerves sensory nerve action potential (SNAP), onset latency, and conduction velocity were recorded. The sites for stimulation for median and ulnar nerves were the wrist

and the elbow, and the recording sites were motor point of abductor pollicis brevis and abductor digiti minimi, respectively.

Reference electrode was placed at 4 cm distally over first metacarpopharyngeal joint for median nerve and over fifth metacarpopharyngeal joint for ulnar nerve.



Figure 1: Stimulation of ulnar nerve.



Figure 2: Distal stimulation of peroneal nerve.

Belly-tendon montage was used with cathode and anode set 3 cm apart. Antidromic study was done for sensory nerves by placing the electrodes at index and little finger for median and ulnar nerves, respectively. SNAP amplitude was taken from peak to base and the ground electrode was placed between stimulation and recording electrode.

Compound muscle action potential

Normal values: Latency (distal) <4 ms, amplitude >10 mV.

Conduction velocity: Upper limbs >50 m per seconds, lower limbs >45 m per seconds

SNAP

Normal values: Latency (distal) <4 ms, amplitude >20 mV.

Conduction velocity: Upper limbs >50 m per second, lower limbs >45 m per second

Statistical analysis

The recorded observations were analyzed using the SPSS Version 18. (SPSS 18- IBM Corp. Armonk, NY). Categorical variables were expressed as counts and percentages

RESULTS

This study included study of electrophysiological changes in 50 cases of leprosy over a period of 18 months (December 2017 to July 2019) in the Department of Dermatology, Osmania Medical College, Hyderabad.

10 nerves in each patient with a total of 500 nerves were studied by NCS. Only 8 (16%) cases had totally normal NCS. And rest 42 (84%) cases have abnormal NCS. Most common pattern observed is sensory motor axonal neuropathy. A total of 268 (53.6%) nerves were normal before starting multidrug therapy (MDT). And 232 (46.4%) nerves have abnormal NCS. Among these nerves the involvement of sensory nerves (49%) are more than motor nerves (42%).

Table 1: Age and sex distribution in years.

Variable	Number of patients	Percentage (%)
Age group in years		
12-20	2	4
21-30	23	46
31-40	11	22
41-50	7	14
51-60	7	14
Gender		
Males	40	80
Females	10	20

Age distribution

Cases had a wide range of age distribution from 12 to 60 years. Youngest patient seen was 17 years and oldest 60 years. Peak incidence was seen in 21 to 30 years (23 cases of 46%), followed by 31 to 40 years (11cases of 22%), 41 to 50 years (7 cases of 14%), 51 to 60 years (7 case of 14%) and 12 to 20 years (2 cases of 4%).

Sex distribution

Males (40 to 80%) are more frequently involved than females (10 to 20%) as shown in Table 1.

Maximum number of cases were found to be in lepromatous spectrum (46%), followed by tuberculoid (44%), indeterminate (6%) no cases of borderline leprosy are observed in study.

Table 2: Disease spectrum in present study.

Types of leprosy	Number of cases	Percentages (%)
Indeterminate	3	6
Tuberculoid	22	44
Lepromatous	23	46
Pure neuritic	2	4

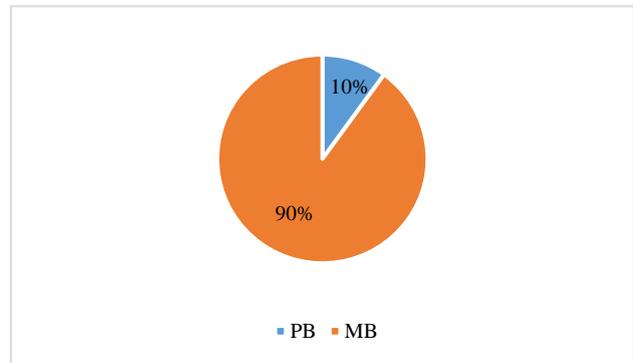


Figure 3: Distribution according to the WHO category.

Five cases belonged to pauci-bacillary category and 45 cases belonged to multi-bacillary category.

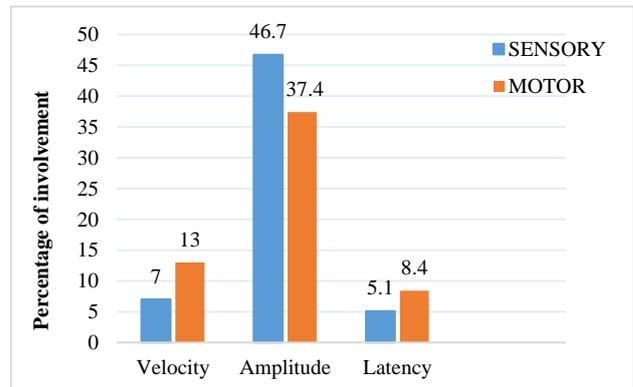


Figure 4: Nerves involvement before MDT.

Amplitudes are the most affected parameter among both sensory and motor nerves. In sensory nerves amplitudes (46.7%) are most effected followed by their velocities (7%) and latencies (5.1%). In motor nerves amplitudes (37.4%) are more effected followed by their velocities (13%) and latencies (8.4%).

DISCUSSION

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. 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 patient is on long term thalidomide, when new symptoms of neuritis, or findings of nerve function impairment occur after MDT completion. It is well known that the sensory nerves are first to be affected in leprosy. But Sadly, by the time it becomes clinically apparent, the nerve damage is already quite advanced. However, if the preclinical damage is detected early, the nerve damage can be prevented to a large extent.

Nerve functioning is assessed using distal latency (myelination), amplitude (number of axons), velocity (myelination).

Slowing nerve conduction is a reflection of demyelination rather than axonal degeneration. In majority of cases, amplitude and the duration of action potential are within the normal range, but it is the sensory velocities that are impaired. Suggesting that leprosy results in diffuse neuropathy even in a stage when it cannot be detected by routine clinical testing. Detection of preclinical nerve function impairment can help in prevention of deformities and disabilities.

In present study 10 nerves in each patient with a total of 500 nerves were studied by NCS. Only 8 (16%) cases had totally normal NCS and rest 42 (84%) cases have abnormal NCS. Most common pattern observed is sensory motor axonal neuropathy. A total of 268 (53.6%) nerves were normal before starting MDT. And 232 (46.4%) nerves have abnormal NCS. Among these nerves the involvement of sensory nerves (49%) are more than motor nerves (42%). Cases had a wide range of age distribution from 12 to 60 years in which Peak incidence was seen in 21 to 30 years. Most of the cases occurred in the 3rd decade, similar to other studies as well. Roy et al and Kadam et al found most of their cases to be between the ages of 35 to 55 years.^{6,7} Incidence in younger age group could be due to the endemic nature of leprosy.

In present study males (40 to 80%) are more frequently involved than females with ratio of male to female is 4:1. Similar as Roy et al 4.5:1 being the male to female ratio.⁶ Similar findings have been observed in other studies as well.⁷ The male majority has been attributed to more chance of contact in males due to occupation, and social inhibition and occupational factors regarding less reporting of cases in females in India.

Maximum number of cases were found to be in lepromatous spectrum (46%) and we have no cases of borderline leprocy. Khamankar et al found lepromatous leprosy to be the commonest histological type.⁸ Pokhrel et al found borderline tuberculoid to be the least common

(1 case) and tuberculoid to be the most common (14 cases) type.⁹ Thapa et al found the most common types to be tuberculoid in their study.¹⁰

5 cases belonged to pauci-bacillary category and 45 cases belonged to multi-bacillary category are found in our study. In study done by Roy et al 30 cases (60%) cases in our study were paucibacillary and 20 (40%) cases multibacillary which is agreed with other studies.⁶

In our study 10 nerves in each patient with a total of 500 nerves were studied by NCS. Only 8 (16%) cases had totally normal NCS. And rest 42 (84%) cases have abnormal NCS. Most common pattern observed is sensory motor axonal neuropathy. A total of 268 (53.6%) nerves were normal before starting MDT, and 232 (46.4%) nerves have abnormal NCS. Among these nerves the involvement of sensory nerves (49%) are more than motor nerves (42%). Amplitudes are the most affected parameter among both sensory and motor nerves. In sensory nerves amplitudes (46.7%) are most effected followed by their velocities (7%) and latencies (5.1%). In motor nerves amplitudes (37.4%) are more effected followed by their velocities (13%) and latencies (8.4%). In the study by Ramadan et al, significant reduction in motor nerve conduction velocity, prolongation of distal latency and reduction of amplitude was 72%, 70% and 80% for median, ulnar and common peroneal nerves respectively.¹¹ Marahatta et al showed NCS can detect subclinical leprosy neuropathy, which may be helpful for the prevention of clinical neuropathies.¹² Mshana et al 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.^{13,14} McLeod et al 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.¹⁵

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.

CONCLUSION

NCS is a reliable and reproducible, diagnostic & prognostic indicator to detect the early NFI. Though it

cannot directly diagnose leprosy, it can detect the NFI, which is an early manifestation of the disease. It can be used in endemic areas, suspected cases, newly diagnosed cases, and household contacts to detect NFI early and manage efficiently.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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