Nerve conduction study in leprosy: a hearty need or a customary practice?

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Summary
Objective: To determine the diagnostic accuracy of the clinical tests like nerve palpation, monofilament test and voluntary muscle test for assessing peripheral nerve function impairment in leprosy.
Methods: In this comparative cross-sectional study, 74 newly diagnosed leprosy patients without lepra reaction were enrolled. They underwent a thorough evaluation for peripheral nerve function using the above-mentioned clinical tests and nerve conduction study. The diagnostic accuracy of the clinical tests was determined by sensitivity, specificity, positive predictive value and negative predictive value considering nerve conduction study as a gold standard test. Data analysis was performed using SPSS version 11.5.
Results: All clinical tests (nerve palpation, monofilament test and voluntary muscle test) were more specific but less sensitive. Amongst all, monofilament testing was the most specific one. Its specificity ranged between 93.54–100%, whereas its sensitivity was 38.46–68.75% only. Both nerve palpation and voluntary muscle testing had high specificity (>90%) for all nerves, except nerve palpation for ulnar nerve; whereas both the tests had very low sensitivity (<70%) for all the tested nerves.
Conclusion: Though these clinical tests had higher specificity, their sensitivity was very low. So, along with clinical tests, nerve conduction study should be considered in leprosy patients for early detection of nerve function impairment whenever feasible.

Introduction

Leprosy is one of the common causes of treatable peripheral neuropathy. Although leprosy has been eliminated from developed countries, it is still considered to be a major public health problem in developing countries of Africa, Asia, and Latin America. Every year thousands of
patients develop nerve damage as a result of leprosy.\(^1\) A total of 6,332 patients presented with Grade-2 disability in South East Asia during the year 2013, which is approximately half of the world’s data of 14,403.\(^2\) In Nepal, 3.38% of new leprosy cases presented with Grade-2 disability in a year.\(^3\)

Peripheral nerve enlargement is one of the cardinal signs and the most common physical finding in leprosy, which may even proceed to sensory-motor deficits.\(^4\) Monofilament testing and voluntary muscle testing (VMT) are two established tests for assessing sensory and motor functions of peripheral nerves respectively.\(^5\)

The role of electrophysiological evaluation of nerve function in the diagnosis and assessment of different neuropathies is well established.\(^6\) A stage of functional blockade of nerve conduction almost always precedes visible pathological changes in the nerve. A significant decline of motor nerve conduction velocities has been reported in clinically normal nerves in leprosy.\(^7\)

In less sophisticated settings where newer modalities of nerve function assessments are not available, nerve conduction study (NCS) is supposed to be a reliable technique.\(^8\) In a country like ours, where the majority of people live below the poverty line, we cannot impose NCS as a routine investigation. Therefore we conducted this study to determine the sensitivity and specificity of each of the clinical tests done in leprosy, considering nerve conduction study as a gold standard test.

### Materials and Methods

#### STUDY POPULATION

All newly diagnosed leprosy patients of age \(\geq 12\) years without lepra reaction attending the Dermatology department from May 2011 – April 2012 were enrolled in the study.

#### SAMPLE SIZE

Based on the previous study\(^9\) the sample size was taken as 74. For this odds ratio between two measurements (NCS and clinical assessment) was calculated as 2.66. Then we calculated the sample size for the study at 95% confidence interval (CI) and 80% power by using Epi Info software.

#### Methods

The patients were assessed at baseline for nerve function impairment using three clinical methods (nerve palpation, monofilaments testing and VMT). Informed written consent was taken from them. All the clinical tests were performed for bilateral sensory (ulnar, median and sural) as well as motor nerves (ulnar, median, common peroneal and posterior tibial). The results were compared with the obtained sensory nerve action potential (SNAP) and compound muscle action potential (CMAP) by sensory and motor NCS respectively. The findings of relevant examination were entered in the standardised pro-forma.
NERVE FUNCTION ASSESSMENTS

Clinical assessments

(a) Touch sensibility testing using monofilaments (MF)
Touch sensibility was tested with a standard set of five coloured Semmes–Weinstein monofilaments (MF) as described by Bell Krotoski. In our study, weight up to 200 mg for the hands and 2 gm for the foot were considered as normal values of the monofilament test.

TEST SITES

(1) Ulnar nerve – at hypothenar eminence, 5th metacarpal head and volar surface of the distal phalanx of the little finger
(2) Median nerve – at thenar eminence, volar surface of distal phalanx of the thumb and volar surface of distal phalanx of the index finger
(3) Radial nerve – over dorsum of the thumb at the site of motor point
(4) Sural – at dorsal lateral aspect of the foot

(b) Nerve palpation (NP)
All the major nerves listed above were palpated bilaterally to record the enlargement and were graded as normal or enlarged.

(c) Voluntary muscle testing (VMT)
Voluntary muscle testing was done using the modified Medical Research Council (MRC) scale. VMT score less than 4 was set as the criteria for motor impairment. Motor functions of all the nerves were categorised into: normal or impaired. All the clinical tests were confirmed by the consultant dermatologist. Muscles tested according to the nerves were: a) ulnar nerve (abductor digiti minimi), b) median nerve (abductor pollicis brevis), c) radial nerve (extensor carpi radialis and extensor carpi ulnaris), d) common peroneal nerve (tibialis anterior, peroneus longus and brevis) and e) posterior tibial nerve (small intrinsic muscles of feet).

ELECTROPHYSIOLOGICAL ASSESSMENTS

Nerve conduction study (NCS)
Nerve conduction study was performed at the Neuroelectrophysiology laboratory of Physiology department of BPNIHS using Digital Nihon Kohden Machine (NM-420S, H636, Japan). We commented on the functional impairment of the nerves based on standard criteria. Room temperature was maintained at the thermo neutral zone (26 ± 2°C). It was ensured that all the patients were relaxed and comfortable with the laboratory set up prior to the recording.

RECORDING PROCEDURE

(a) Motor nerve conduction study (MNCS)
Stimulator with water soaked felt tips were placed on the skin overlying the nerve at proximal and distal sites. The recording and reference electrodes were placed using belly tendon montage. The gain was set at 2–5 mV per division and stimulation duration in the range of
50–300 μsec. The nerves were stimulated with short burst of direct current, not exceeding 50 mA since it was the upper limit available in the machine. The current was initially set to zero, then gradually increased with successive stimuli up to the point that compound motor action potential (CMAP) no longer increases in size. Further, it was increased by another 20% to ensure the supra-maximal stimulation. For each stimulation site, CMAP latency, amplitude, duration and conduction velocity of median, ulnar, radial, common peroneal and posterior tibial nerves were recorded. F-waves were also recorded for all nerves except radial nerve.

(b) Sensory nerve conduction study (SNCS)
Ring and surface stimulating electrodes were used for orthodromic and antidromic (sural nerve) stimulation respectively. Electrodes were placed over a purely sensory portion of the nerves. Gain was set at 10–20 μV per division and an electrical pulse of either 100 or 200 μsec of duration was used. Current was slowly increased from a base line of 0 mA, usually by 3–5 mA at a time until the supra maximal stimulation of nerve was ensured. For each stimulation site, sensory nerve action potential (SNAP) amplitude, latency, duration and conduction velocity were measured.

Statistical Analysis
Data were entered in MS-Excel 2007, and were transferred into SPSS version 11.5 for statistical analysis. For descriptive statistics, percentage, proportion, median were calculated. The diagnostic accuracy of clinical tests was determined by sensitivity, specificity, positive predictive value and negative predictive value.

Ethical Clearance
Ethical clearance was obtained from institutional ethical review board.

Conflict of Interest
All authors declare that the answer to the question on competing interest form are all ‘No’, and therefore have nothing to declare.

Funding Source
There was no funding source for the study – the Institute considered free process for patients who couldn’t afford the procedural fees.

Results
Socio-Demographic Profile
Out of a total of 74 patients, the maximum (27·0%) were in the age group 30–39 years, with the mean age 35·09 ± 14·92 years. Males predominated with the ratio being 2:1. About 77·1% patients were literate, among which only one fifth 15/74 (20·3%) had studied more than 10th grade. The subjects in the study group had different occupations, but the majority
were housewives 15/74 (20.3%). Out of 74 subjects included in the study, 58/74 (78.4%) were of the multibacillary group and 16/74 (21.6%) were of the paucibacillary group. The presenting complaint of the maximum patients (50.0%) was loss of sensation, followed by hypopigmentation in 44.6% of patients. Most of the patients (31.0%) had 6–10 months of illness duration.

SUMMARY OF CLINICO-ELECTROPHYSIOLOGICAL FINDINGS

All the patients were subjected to a thorough examination, including clinical (i.e. nerve palpation, monofilament testing, VMT assessment) and NCS tests. Among the sensory nerves the sural nerve was found to be maximally affected (21.6%) followed by the ulnar (17.6%), radial (16.2%) and median (9.5%). Similarly, among the motor nerves, the ulnar was maximally affected (18%) followed by the common peroneal (16.2%), posterior tibial (13.5%), median (8.1%) and radial (8.1%) as detected by NCS (Table 1).

DIAGNOSTIC ACCURACY OF CLINICAL TESTS

For the calculation of diagnostic accuracy, nerve wise sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of clinical tests were calculated and nerve conduction study was taken as reference test.

(a) Monofilament test:
It was found to be important for its negative predictive value. Its specificity was high whereas sensitivity was low for all tested sensory nerves. Its overall specificity was 83.63%, sensitivity was 78.94%, negative predictive value was 92.00% and positive predictive value was 62.5%. Among all the tested sensory nerves, highest specificity was for monofilament test of the sural nerve (Table 2).

Table 1. No (%) of patients showing enlarged nerves, impaired clinical (monofilament test, VMT assessment) and nerve conduction (sensory and motor) tests

<table>
<thead>
<tr>
<th></th>
<th>Enlarged nerves on NP (%)</th>
<th>Impaired MF test (%)</th>
<th>Impaired VMT (%)</th>
<th>Impaired SNCS (%)</th>
<th>Impaired MNCS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>43 (58-1)</td>
<td>19 (25-7)</td>
<td>7 (9-4)</td>
<td>24 (32-4)</td>
<td>15 (20-3)</td>
</tr>
<tr>
<td>Sensory Nerves</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar</td>
<td>32 (43-2)</td>
<td>7 (9-1)</td>
<td>NA</td>
<td>13 (17-6)</td>
<td>NA</td>
</tr>
<tr>
<td>Median</td>
<td>6 (8-1)</td>
<td>5 (6-8)</td>
<td>NA</td>
<td>7 (9-5)</td>
<td>NA</td>
</tr>
<tr>
<td>Radial</td>
<td>6 (8-1)</td>
<td>9 (12-1)</td>
<td>NA</td>
<td>12 (16-2)</td>
<td>NA</td>
</tr>
<tr>
<td>Sural</td>
<td>4 (5-4)</td>
<td>11 (14-9)</td>
<td>NA</td>
<td>16 (21-6)</td>
<td>NA</td>
</tr>
<tr>
<td>Motor Nerves</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar</td>
<td>32 (43-2)</td>
<td>NA</td>
<td>6 (8-1)</td>
<td>NA</td>
<td>18 (24-3)</td>
</tr>
<tr>
<td>Median</td>
<td>6 (8-1)</td>
<td>NA</td>
<td>3 (4-1)</td>
<td>NA</td>
<td>6 (8-1)</td>
</tr>
<tr>
<td>Radial</td>
<td>6 (8-1)</td>
<td>NA</td>
<td>2 (2-75)</td>
<td>NA</td>
<td>6 (8-1)</td>
</tr>
<tr>
<td>Common Peroneal</td>
<td>20 (27-0)</td>
<td>NA</td>
<td>1 (1-4)</td>
<td>NA</td>
<td>12 (16-2)</td>
</tr>
<tr>
<td>Posterior Tibial</td>
<td>13 (17-5)</td>
<td>NA</td>
<td>1 (1-4)</td>
<td>NA</td>
<td>10 (13-5)</td>
</tr>
</tbody>
</table>

(Abbreviation: NA = Not applicable, NP = Nerve palpation, MF = Monofilament, VMT = Voluntary muscle test, SNCS = Sensory nerve conduction, MNCS = Motor nerve conduction).
(b) Nerve palpation test
It was also found to be important for its specificity and higher negative predictive value when individual nerves were considered. The overall sensitivity and specificity were 64.00% & 65.30% for sensory nerves; and 48.57% & 80.64% for motor nerves respectively (Table 3).

(c) Voluntary muscle testing
Overall, VMT has sensitivity: 14.28%, specificity: 79.10%, PPV: 6.66% and NPV: 89.83%. Here, median and radial nerves had high negative predictive value whereas common peroneal and posterior tibial nerves had 100% specificity and PPV (Table 4).

LOGISTIC REGRESSION ANALYSIS
On five step logistic regression analysis, a combination of occupation, monofilament test and nerve palpation test were found to be important determinants of abnormal nerve conduction study in leprosy patients. Variables intered in the first step of the analysis were occupation, monofilament testing, nerve palpation, voluntary muscle testing of ulnar nerve, grade of disability and bacillary index.

Discussion
Leprosy is a common treatable disease of peripheral nerves, but still remains a devastating disease in the developing world because of the potential deformities, disabilities and morbidity associated with it. It can be minimised if nerve damage is detected and treated early.

Monofilament testing is an inexpensive, easy-to-use and portable test for assessing the loss of protective sensation. Previous study had said that the monofilament testing can be one of the valid and standard screening tests for sensory nerve function assessment.14 While testing touch sensation by monofilament, out of 74 patients in our study, only 19 (25.7%) patients had impaired test, which is less (41%) then that found in a previous study.9 In our study, the sural nerve showed maximum impairment 11/74 (14.9%), followed by radial 9/74 (12.1%), ulnar 7/74 (9.1%), median 5/74 (6.8%) and the sequence was comparable to a previous study9 but frequency of impairment was less in our patients. It could be because of the inclusion of both paucibacillary and multibacillary patients in our study unlike in the study by Khambati et al. where only multibacillary patients were included.9
An effective diagnostic test requires an acceptable sensitivity and specificity. To find the accuracy of the monofilament test, we calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Overall sensitivity was 78·94% (53·90–93·02%), specificity was 83·63% (70·69–91·79%), PPV was 62·5% (40·75–80·44%) and NPV was 92·00% (79·89–97·40%). Sensitivity of the monofilament test was very low with a wide range for all nerves, whereas it showed good specificity and NPV. Among the individual nerves, the sural nerve was found to have the maximum specificity (100%). The PPV of the monofilament test was good only for the sural nerve (100%). So there is a high chance of missing patients with neuropathy if we rely only on the monofilament test. A similar result was found when Dros et al. conducted one systematic review for the accuracy of the 5/10 gram monofilament using nerve conduction as a reference standard in diabetic neuropathy; in which sensitivity ranged from 41% to 93% and specificity ranged from 68% to 100%. The authors stressed that monofilament testing should not be used as the sole test to diagnose peripheral neuropathy, whereas nerve conduction study could be of great help for the detection of peripheral neuropathy.

In our study, more than half of the patients (58·1%) had enlarged peripheral nerves. The ulnar nerve was the most commonly enlarged nerve in most of the patients (43·2%) followed by the common peroneal (27·0%), posterior tibial (17·5%) radial (8·1%), median (8·1%) and sural (5·4%) nerves. In another study done in Bangladesh, the most commonly affected nerve

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<th>Table 3. Diagnostic accuracy of nerves palpation</th>
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<tr>
<td>Nerves</td>
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<tr>
<td>Sensory nerves</td>
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<tr>
<td>Ulnar</td>
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<td>Median</td>
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<td>Radial</td>
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<td>Radial</td>
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<tr>
<td>Common peroneal</td>
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<td>Posterior tibial</td>
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(Abbreviation: PPV = positive predictive value, NPV = negative predictive value).

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<th>Table 4. Diagnostic accuracy of voluntary muscle testing</th>
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<tr>
<td>Nerves</td>
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<tr>
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<td>Posterior tibial</td>
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(Abbreviation: PPV = positive predictive value, NPV = negative predictive value).
was the posterior tibial nerve (9.38%), followed by the ulnar nerve (5.56%), median and common peroneal nerves. The ulnar nerve, however, being the most commonly involved nerve in our study, could be explained by the maximum number of patients having skin lesions on the forearm and hand.

Assessment using voluntary motor testing showed impaired motor nerve function only in seven (9.4%) patients. The ulnar nerve showed maximum impairment in 6/74 (8.1%) patients followed by the median in 3/74 (4.1%), the radial in 2/74 (2.7%), the common peroneal in 1/74 (1.4%) and the posterior tibial 1/74 (1.4%) patients. In a study by van Brakel et al., concordance between VMT results and motor nerve conduction was good for the ulnar nerve, but very few median and common peroneal nerves with abnormal conduction had an abnormal VMT. So they recommended that a more sensitive manual motor test may be needed for these nerves. Both nerve palpation and VMT had a high specificity (>90%) for all nerves, except nerve palpation for the ulnar nerve (sensory as well as motor i.e. 66% for both). But both tests had very low sensitivity with wide range. These findings also suggest that we should not depend only on these clinical tests; and these tests alone are not sufficient enough to detect peripheral neuropathy in the early stages.

The Nerve conduction study (NCS) is one of the established tools for the assessment of various peripheral neuropathies, including leprosy. van Brakel et al. reported that half of the INFIR cohort without clinical evidence of neuropathy had impaired NCS for the superficial radial and sural nerves. Similarly, monofilament-detected ulnar sensory neuropathy was preceded by abnormal SNCS in 100% of cases. Hence NCS may play an important role for the early detection of Leprosy neuropathy compared to clinical tests. This statement has also been supported by few other studies.

In our study 32/74 patients (43.2%) had impaired nerve conduction study at the time of disease diagnosis. However in a previous study more than 50% of the patients had NFI at the baseline. A lesser percentage of baseline neuropathy in our study could be because of: i) exclusion of patients in lepra reaction and ii) non-exclusion of paucibacillary leprosy patients. Out of them, 24/74 (32.4%) patients had abnormal sensory NCS and 15/74 (20.3%) patients had abnormal motor NCS. So sensory neuropathy was found to be more common in leprosy patients. One of the studies from western Nepal also found more of sensory neuropathy (11.90%) then the motor one (7.39%). Similar was the report from Brown et al. with sensory neuropathy in 42.89% and motor neuropathy in 21.42% of the leprosy patients. In contrast to our study, in the study by Ramadan et al. motor nerve conduction was found to be more impaired than the sensory one.

When concordance was assessed between different clinical tests and the gold standard test in our study; between nerve palpation and NCS tests, the maximum concordance was observed for ulnar nerve (motor-14.9%, sensory-12.2%), followed by the common peroneal nerve (10.8%). Between monofilament test and SNC tests, concordance was maximum for the sural nerve (14.9%). Similarly between VMT assessment and MNC, concordance was maximum for the ulnar nerve (2.7%). Hence 4.1–18.9% of patients with impaired nerve conduction can be missed by nerve palpation. Similarly, subclinical neuropathy ranging from 6.7–21.6% can be missed by VMT and that from 5.4–10.8% may be missed by monofilament test. For the peripheral nerves (both sensory and motor), the impairment observed by SNC as well as MNC may be preclinical and may translate into obvious weakness (i.e. sensory and motor respectively) late in the disease. Similar opinion was given by the authors in few of the previous studies.
Conclusion

Though all the clinical tests i.e. monofilament testing, nerve palpation and voluntary muscle testing assessment have higher specificity, they have very low sensitivity for assessing peripheral nerve damage in leprosy. So along with clinical tests, nerve conduction studies should also be considered in leprosy patients for the early detection of nerve function impairment whenever feasible.

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References

Shetty VP, Khambati FA, Ghate SD et al. The effect of corticosteroids usage on bacterial killing, clearance and nerve damage in leprosy; part 3- study of two comparable groups of 100 multibacillary (MB) patients each, treated with MDT + steroids vs MDT alone, assessed at 6 month post – release from 12 months MDT. *Lepr Rev*, 2010; 81: 41–58.


