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Can addition of test sites for monofilament testing improve detection of nerve function impairment?

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Summary

Background: In a multi-centre study titled 'Treatment of Early Neuropathy in Leprosy' ('TENLEP'), monofilament testing (MFT) was used for the detection of touch pressure sensibility impairment (TPSI). It was recommended to use three test sites each for median, ulnar, radial cutaneous, sural and posterior tibial nerves.

Aim: To assess the possible increase in detection rate of TPSI by increasing test sites for ulnar, median and posterior tibial nerves.

Method and subjects: For the ulnar nerve, two sites were added in the area supplied by its dorsal cutaneous branch. For the median and posterior tibial nerve, one site each was added on dorsum of the index finger and heel respectively. Bilateral nerves were tested in a total of 70 leprosy patients.

Findings: The addition of two extra test sites on the ulnar nerve resulted in the detection of TPSI in an additional 41 (29%) of the 140 nerves tested. Similarly for the median and posterior tibial nerves, the addition of one test site each detected TPSI in an additional 21 (15%) and 23 (16%) nerves respectively.

Conclusion: The study showed that the addition of five test sites divided over three nerves, the ulnar, median and posterior tibial nerves, improved the detection of TPSI by 20%.

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Introduction

Sensory, motor and autonomic functions of peripheral nerve trunks can be assessed by testing the functions of end organs such as muscles and sensory mechanoreceptors supplied by nerves. The level of impairment that is clinically detectable depends on the sensitivity of the testing instruments used. The use of standardised, graded, nylon monofilaments is accepted as a reliable, quick, safe and reproducible method to evaluate touch–pressure sensibility (TPS) at the skin sites innervated by the respective peripheral nerves.[1–3] In the context of leprosy, its advantages are a) ease of use under field conditions, b) personnel can be trained quickly in its use and c) results are quantifiable for comparison at various stages of the disease and over time.[4,5]

Thus far, optimisation of test sites has been recommended empirically.The standard sites tested are: on hands three sites each on the palm for ulnar and median nerves, one for the radial nerve; on the feet seven sites on the sole for the posterior tibial nerve and one site on the dorsum of the foot for the deep peroneal nerve.[6,7] Anderson *et al.* using a maximum of five test sites each on palm and sole, detected 95% of patients whose loss of TPS was detected by a longer test using up to 12 sites.[8] The dorsal aspects of the hand and foot were not examined in that study. A sensory conduction velocity study by Gaurie-Devi showed frequent impairment of the dorsal cutaneous branch of the ulnar nerve in leprosy. In that study for the ulnar nerve, abnormality seen by motor conduction velocity was identified in 28%, sensory antidromic conduction velocity using digit five in 46% and orthodromic sensory conduction of the dorsal cutaneous branch in 82%.[9]

Although the radial cutaneous and sural nerves are the most frequently involved nerves in leprosy, they are either not tested or tested at one site only, probably because of their lower propensity to cause deformity.[10,11]

In January 2011, a multicentre randomised, double-blinded, placebo-controlled study entitled 'Treatment of Early Neuropathy in Leprosy' ('TENLEP') was launched, in which The Foundation for Medical Research (FMR) was one of the participating centres. In this study graded monofilament (MF) was the main tool for detecting and monitoring sensory nerve function impairment in the limbs. The protocol recommended that three sites should be tested for each of the nerves commonly affected in leprosy, namely the median, ulnar, radial cutaneous, sural and posterior tibial nerves.[12] Using this opportunity, FMR independently incorporated additional MF test sites for the ulnar (dorsal aspect of the hand), median (dorsum of the distal phalanx of the index finger) and posterior tibial (heel), to determine whether this resulted in enhancement of TPSI detection rates.

In this study a comparison is made between the outcome results of sites used in the TENLEP protocol hereafter termed as Method A and the additional sites tested in FMR termed as Method B.

Methods

Seventy subjects in the age group of 15–60 years were recruited. These were newly detected or previously treated leprosy patients with at least one nerve with NFI of less than 6 months' duration. There were 65 MB (including 60 smear negative borderline tuberculoid BT and five smear positive BL cases) and five PB (all BT) cases (as per WHO operational classification)[13] including 58 males (average age 31 $\pm$ 10·8 years) and 12 females (average age 35 $\pm$ 9·4 years).

DETERMINATION OF NORMAL THRESHOLD FOR THE NERVES UNDER STUDY

Validation of the scoring was obtained by testing 50 control subjects (age group 25–60 yrs) in the same way. These were subjects who did not have any sensory complaints and were not leprosy patients or relatives of a leprosy patient.

The test was carried out by one of two trained assessors from TENLEP (KP & GC) with the standard monofilament set. All five nerves (median, ulnar, radial, posterior tibial and sural) were tested. Acceptable inter-tester reliability for MFT was demonstrated prior to the recruitment of patients.[14] The testing room was well lit, quiet, and the fan was switched off to prevent any draft affecting the readings.

The monofilament testing set and scoring method are shown in Figure 1 and Table 1 respectively.

The examinationof the hand was initiated with the lightest filament, the blue (0·2 gm); while for the foot it was the next heavier filament, the purple (2·0 gm), indicating normal TPS threshold for hands and feet respectively.

If the subject felt (responded to the touch positively) the lightest filament, the score for that particular site was '0'. As shown in Table 1, the score at any point on the hand ranged from 0 to 5 (indicating complete loss of sensation), while on the foot, it ranged from 0 to 4.

Figure 1. Monofilaments for hands and feet. The markings are for ease of scoring – e.g., H2 means that if the patient felt touch with that filament then the score for that site was 2 for the hand. F2 means the same for the foot.

Table 1. The scoring system of the monofilament test

Monofilament weight with score	
Hand	Foot
0·2 gm = 0 (Blue) 2·0 gm = 1 (Purple) 4·0 gm = 2 (Red) 10 gm = 3 (Orange) 300 gm = 4 (Pink) No sensation with 300 gm = 5 (Pink)	2·0 gm = 0 (Purple) 4·0 gm = 1 (Red) 10 gm = 2 (Orange) 300 gm = 3 (Pink) No sensation with 300 gm = 4 (Pink)

Method A (TENLEP) A total of three test sites each for all the five nerves. The total number of sites by this method = 30 (9 for each hand and 6 for each foot). In this case for the median, ulnar and radial nerves, the maximum possible score for each abnormal nerve was 15 while for the posterior tibial and sural nerves it was 12.

Method B (FMR) A total of five sites for ulnar, four each for median and posterior tibial, and three sites each for radial cutaneous and sural nerves (as in the TENLEP protocol). This method tested a total of 38 sites (24 sites in the hands and 14 in the feet). Here the maximum score for each abnormal nerve was: 20 for median, 25 for ulnar, 15 for radial, 12 for sural and 16 for posterior tibial.

Figures 2 and 3 depict the scoring sites under method A (white circles) and B (Black circles) for the ulnar median and radial nerves and for the sural and posterior tibial nerves respectively.

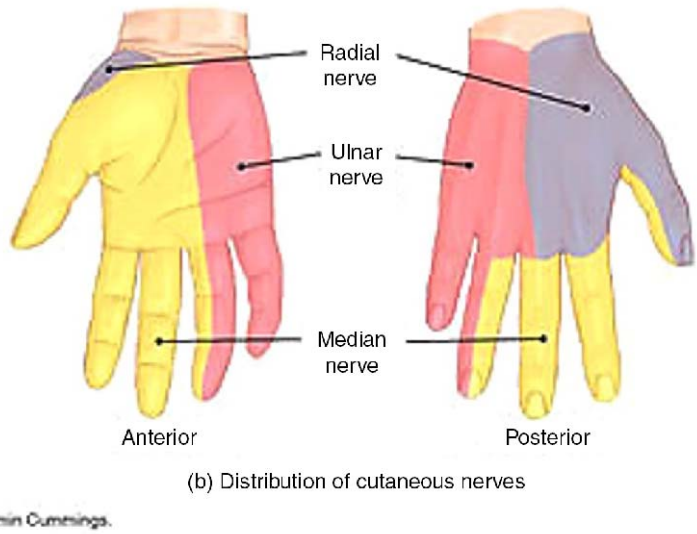

Figure 2. Sites for MFT in the hands. White circles denote Method A. Black circles show additional sites used in Method B.

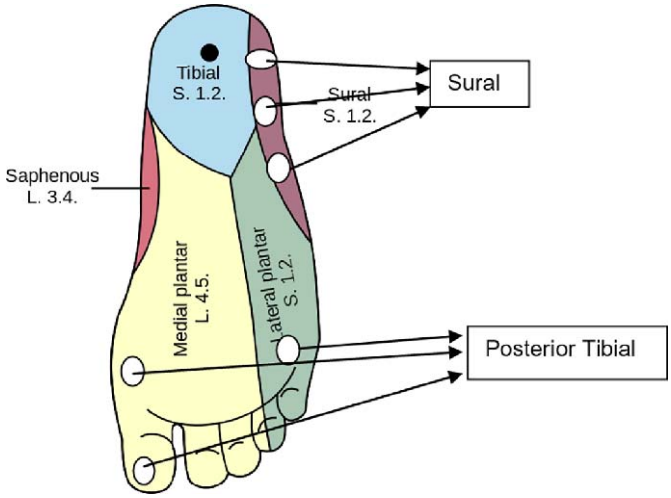

Figure 3. Sites for MFT in the feet. White circles denote Method A. Black circle denotes additional site used in Method B.

All patients and controls were tested by Method B only and the scores compared for yield of impairment with Method A, by computing the concordance and discordance between the two.

ANALYSIS

The results were analysed for concordance and discordance between the two methods, A and B.

Concordance: If for both methods- a nerve was *normal* for all the test sites (a score of 0), then it was depicted under the heading 'NN'. Similarly, if a nerve was *abnormal* using either method (any site had a score of 1 or more), then it was depicted as 'AA'.

Discordance: If the three sites (Method A) of any nerve were *normal* but the additional site/s (Method) B were *abnormal*, this was depicted as 'NA'. Similarly when the three sites of any nerve were abnormal (i.e., score ≥ 3) and the extra site/s were *normal* ($=0$), then it was depicted as 'AN'. It may be noted here that for the extra site on the heel (posterior tibial nerve) we took a value of 2 or more to be considered as abnormal, keeping in mind the thickness of the callus on the sole.

Ethics clearance

The study followed International Ethical Guidelines for Biomedical Research involving human subjects (CIOMS/WHO, 1993). The study received clearance from the institutional Ethical Committee of the Foundation for Medical Research (IEC NO-FMR/IEC/L01/2011). Written consent was obtained from individual study subjects. No financial incentives were given to the patients, only travel expenses were reimbursed to the patients. TENLEP is registered with Clinical Trials Registry India (CTRI/2011/09/002022).

Table 2. Concordance and discordance score (%) between Methods A and B for ulnar, median and posterior tibial nerves by MFT

Nerves	Concordance		Discordance		
Pts=70 Nerves=140	NN	AA	NA	AN	Total abnormal nerves %
ULNAR	61 (44%)	37 (26%)	41 (29%)	1 (1%)	79 (56%)
MEDIAN	103 (74%)	12 (9%)	21 (15%)	4 (2%)	37 (26%)
POST.TIBIAL	65 (47%)	46 (34%)	23 (16%)	6 (4%)	75 (54%)

Key: NN – Normal Normal, AA – Abnormal Abnormal, NA – Normal Abnormal, AN – Abnormal Normal.

Results

None of the 50 control subjects studied showed scores greater than zero. As depicted in Table 2 there was concordance between the Methods A & B to the extent of 70% for ulnar nerve, 83% for median nerve, 81% for posterior tibial nerve.

On the other hand 41 ulnar nerves (29%), 21 median nerves (15%) and 23 posterior tibial nerves (16%) showed abnormal scores only in the FMR-added site (discordance).Thus use of the extra sites in these three nerves increased the overall detection of NFI by 20%.There was also a small proportion of nerves that were abnormal only in the TENLEP sites (1%, 2%, 4%, for ulnar, median and posterior tibial respectively, average $= 2{\cdot}3\%$). For the radial and sural nerves only the TENLEP method was followed and showed abnormal scores in 52/140 (37%) and 84/140 (60%) of these nerves respectively.

Discussion

Nerve function impairment (NFI) is a serious complication of leprosy. Early detection of NFI and timely intervention can minimise or reverse the effects of this complication. Moreover recording of NFI also serve as a tool in monitoring the effect of interventions.

Nerve conduction studies and thermal testing are well-accepted techniques for detection of NFI.[15–17] but their drawback is the cost of equipment, reliable electricity supply, acclimatised rooms and the requirement of specially qualified personnel.

Touch pressure sensibility (TPS) of peripheral nerves is known to be affected early in leprosy, and can be detected and monitored, using a set of five graded monofilaments (MF) at the field level by any field personnel after some training. The present study looks at the scope of improving/optimising the detection of abnormal TPS using MF.

As seen in Table 2, over all 56% of ulnar, 26% of median and 54% of posterior tibial nerves were detected with abnormal TPS.We show that the addition of two sites for the ulnar nerve to cover the distribution of the dorsal cutaneous branch and also one site for the median nerve on the mid-dorsum of the index finger (digital branch) enhanced the detection of abnormal TPS by 29% and 15% respectively.

Notably for the ulnar nerve, the use of only the two points supplied by the dorsal cutaneous branch detects abnormality in 56% of nerves (78/140) whereas use of three points on palm (Method A) detects abnormality in 27% of nerves (38/140), showing that the dorsal branch of the ulnar is more frequently impaired than the palmar branch. A study carried out in

Israel also showed that sensory impairments on the dorsum of a limb occurs more frequently than on the palm or sole.[18]

The TPS of the posterior tibial nerve has been evaluated using from three to as many as 12 sites in various studies. The test sites included in the protocol followed by TENLEP (Method A) were recommended by Anderson *et al.*[8] In Method B one more site on the heel was added and additional gain by this site alone was 16% (despite using a higher cut of value of 2), thus showing that the frequency of impairment is higher on the heel.

The radial cutaneous and sural are sensory nerves and a number of NCV studies have shown that they are frequently affected in leprosy.[10,11,15] In keeping with this, using method A, abnormalities were detected in 60% of sural and 37% of radial nerves respectively.

In view of these findings we recommend:

Firstly additional testing sites on dorsum of limbs. In leprosy control programmes when expertise is available and feasible, addition of test sites on the dorsum could improve the detection rate of NFI by 20%.

Secondly, include sural and radial cutaneous nerves in routine detection and monitoring of TPS.

The set of five monofilaments is convenient to use in the field, can easily be used with a fair amount of accuracy by any trained field worker therefore should be made available.

Thirdly, inter-tester reliability studies and validation of the findings using NCV and TSA as gold standards in a randomised study design, should be done.

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Competing Interest Statement

The author(s) declare that they have no competing interests.

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