Early diagnosis of leprosy and the care of persons affected by the disease in a low endemic area
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CHAPTER 5

Inter-observer reliability in assessment of sensation of skin lesion and enlargement of peripheral nerves in leprosy patients

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SUMMARY

The accurate diagnosis of leprosy is important to both individuals and to the community. The diagnosis of leprosy is based on clinical examination. However, the reliability of the clinical assessment of sensation in skin lesions and thickness of peripheral nerves on palpation has not been well studied, due to lack of a gold standard. We report an inter-tester reliability study of the clinical assessment of skin lesions and thickness of ulnar and popliteal nerves in leprosy patients by different staff. For sensory testing of skin lesions, the agreement between the leprologist and leprosy control staff, and between one student and leprosy control staff, was poor (kappa values < 0.4). The agreement between the leprologist and the two students, between the two students, and between the other student and local leprosy control staff were fair (kappa values > 0.4 but < 0.6). For the palpation of ulnar and popliteal nerves, the agreement ranged from 0.36 to 0.52 and from 0.02 to 0.29 in different pairs of testers, respectively. The reliability of clinical diagnostic skills based on both sensory testing of skin lesions with the cotton wool method and palpation of superficial peripheral nerves was unsatisfactory.
INTRODUCTION

The diagnosis of leprosy must be established as early as possible and must be accurate, because misdiagnosis (both under- and over-diagnosis) will lead to undesired consequences for both individuals and the community.\(^1\) Accurate diagnosis of leprosy is also of vital importance to all aspects of the leprosy control programme and research, such as epidemiology, chemotherapy, prevention of disability and assessment of interventions.\(^2,3\)

Leprosy used to be endemic in Shandong province, located in the northeast part of China, with a population of 90 million. The goal of elimination of leprosy was achieved in 1994 after more than 50 years of effort in combating the disease. Almost all active case-finding activities have been stopped since then, except for contact examination, because it was no longer cost-effective in terms of identifying the few incident cases of leprosy in a very low endemic situation.\(^4\) This situation may persist till the eradication of leprosy is achieved, as was the case in Norway.\(^5\)

The diagnosis of leprosy remains based on the clinical examination. Three cardinal signs still form the basis of the clinical diagnosis of leprosy, as affirmed by WHO Expert Committee on Leprosy in 1997: anaesthetic skin lesions, enlarged peripheral nerves and acid-fast bacilli in the skin smear.\(^6\) Based on the analysis of 594 leprosy patients, the data of Saunderson \textit{et al}\(^7\) support this method of diagnosis. The most likely source of error, using the anaesthetic skin lesions and enlarged peripheral nerve to diagnose leprosy, is the reliability of the examination of the individual patients, referred to as inter-observer reliability. In another words, the clinical diagnosis of leprosy depends on the examiner’s knowledge and skills in identification of anaesthetic skin lesions and peripheral nerve enlargement. The assessment anaesthetic skin lesions and peripheral nerve enlargement is of particular importance for the diagnosis of paucibacillary (PB) and neuritic leprosy,\(^8\) because skin smear examination is often negative in theses cases. However, these clinical signs in the diagnosis of leprosy have not been extensively tested for sensitivity, specificity and inter-observer agreement, and studies that have been published give equivocal results.\(^9\)

The aim of the study was to test the repeatability of testing sensation of the skin lesion with the cotton wool method and the repeatability of testing for thickening of nerve trunk in leprosy patients on multidrug therapy (MDT).

MATERIALS AND METHODS

Since the prevalence of leprosy is very low and new leprosy cases diagnosed are scattered in the province, it was impossible to recruit all the new patients into the
study, due to the limitation of time and financial constraints. We selected the leprosy patients newly diagnosed in the last 2 years in two formerly endemic prefectures, roughly accounting for 80% of the total new cases detected in the province. All selected patients were invited for the assessment when they came to the clinics for the collection of monthly MDT medications.

The assessment of sensory loss and nerve thickening was performed by three categories of testers. Two were postgraduates who were trained in the methods of sensory testing of skin lesions and palpation of peripheral nerves. They represented new trainees working in the dermatological field. The second group was local leprosy control staff, representing the level of clinical knowledge and skills in sensory testing of skin lesions and palpation of peripheral nerve in the current leprosy control programme in the province. The results of assessment obtained by a leprologist from the provincial leprosy control programme were taken as the reference (gold standard).

The tool for the examination of sensation of skin lesion was cotton wool, because it is easily available in the field and a common practice in sensory testing of skin patch(s) in Shandong, as well as elsewhere in China. The method for the sensory testing with cotton wool has been described elsewhere. Briefly, the individuals were shown cotton wool which was rolled into a point, and the threshold was tested at which they could just feel the wool’s touch on normal skin in the vicinity of the lesion. After the test had been explained and understood by the individuals tested, the patient was asked to close his/her eyes so that he or she could not see the examiners’ hand. After repeatedly touching the tested lesion and normal skin, it was decided whether there was anaesthesia to light touch. As recommended in other studies, only ulnar and popliteal nerves were palpated because they are involved most often in leprosy and easily palpated clinically. When palpating, left and right nerves were compared to assess which was enlarged.

For PB leprosy patients, a visible patch on any part of the body, except for a lesion on the face (sensation loss usually occurs latter than lesions on other parts of the body), was selected. For multibacillary (MB) leprosy patients, a lesion on the forearm was selected first and the lesion on the leg was selected as the second choice, if there was no visible lesion on forearm, because the patients could easily point the skin lesions in these areas. The site and the skin lesion, which were to be tested, were decided by all the examiners before the assessment started.

The duration of examination between the postgraduate, the leprologist and the local leprosy control staff was 30 min for each individual. The sequence of examination was randomly arranged. For example, for the first individual, the postgraduate was the first examiner, the next was the local staff, and finally, the leprologist; for the second individual, the local staff was the first, the leprologist was the second and the postgraduates were last. The examiners recorded their findings independently on a separate pre-coded sheet without knowing each other’s findings. Sensory test was
performed, followed by palpation of peripheral nerves. The results of the tests were compared between the leprologist, two dermatological postgraduates and the local leprosy control staff using the kappa tests for agreement. A value of 1 for kappa indicates complete agreement. A value of 0 implies agreement no better than chance. Negative values indicate more disagreement than expected by chance.\textsuperscript{10}

**RESULTS**

In total, 27 leprosy patients on MDT were examined, including 22 newly diagnosed cases and five relapsed; 18 males and nine females. Out of the 27 patients, six were borderline tuberculoid (BT), three were borderline borderline (BB), nine were borderline lepromatous (BL) and seven were lepromatous leprosy (LL). The diagnosis of all the 27 leprosy cases was confirmed by skin smear examination and biopsy. Two patients without visible skin lesions were only assessed for nerve thickness. Five patients with two skin lesions were tested, thus a total 30 skin lesions were assessed for the sensory loss. All 27 patients were tested for nerve thickness, thus giving a total of 108 nerves assessed.

Table 1 showed the agreement between sensory testing results. While the agreements between leprologist and leprosy control staff, and between student 2 and leprosy control staff were poor (kappa values < 0.4), the agreement between the leprologist and the two students, between the two students, and between student 1 and local leprosy control staff was fair (kappa values > 0.4, but < 0.6). The table 2 shows the comparison of palpation of peripheral nerves between the different pairs of testers. For ulnar nerve assessment, the agreement between leprologist and the two students were poor (kappa value < 0.4), while agreement between the other pairs of testers were fair (kappa values > 0.4, but < 0.6), with the highest kappa value between student 2 and local leprosy control staff. For the popliteal nerve, the kappa values between all pairs of the testers were < 0.4. Generally, the agreements on palpation of the ulnar nerve were better than the agreements on the palpation of popliteal nerve between different pairs of testers (Table 2).

<table>
<thead>
<tr>
<th>Pairs of testers</th>
<th>Concordance</th>
<th>Kappa value (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A vs B</td>
<td>0.733</td>
<td>0.450 (0.154-0.746)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>A vs C</td>
<td>0.767</td>
<td>0.533 (0.260-0.802)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>A vs D</td>
<td>0.633</td>
<td>0.310 (0.040-0.580)</td>
<td>0.04</td>
</tr>
<tr>
<td>B vs C</td>
<td>0.700</td>
<td>0.400 (0.073-0.727)</td>
<td>0.03</td>
</tr>
<tr>
<td>B vs D</td>
<td>0.700</td>
<td>0.405 (0.086-0.547)</td>
<td>0.02</td>
</tr>
<tr>
<td>C vs D</td>
<td>0.600</td>
<td>0.200 (-0.14-0.547)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

A: Leprologist; B: Student 1; C: Student 2; D: Leprosy staff
Table 2 Comparison of peripheral nerve enlargement between different staff

<table>
<thead>
<tr>
<th>Pairs of testers</th>
<th>Concordance</th>
<th>Kappa value (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulnar nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A vs B</td>
<td>0.685</td>
<td>0.358 (0.139-0.578)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>A vs C</td>
<td>0.741</td>
<td>0.387 (0.130-0.644)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>A vs D</td>
<td>0.722</td>
<td>0.455 (0.259-0.651)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>B vs C</td>
<td>0.759</td>
<td>0.513 (0.292-0.734)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>B vs D</td>
<td>0.741</td>
<td>0.482 (0.249-0.715)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>C vs D</td>
<td>0.759</td>
<td>0.524 (0.310-0.738)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Popliteal nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A vs B</td>
<td>0.677</td>
<td>0.270 (0.005-0.535)</td>
<td>0.05</td>
</tr>
<tr>
<td>A vs C</td>
<td>0.667</td>
<td>0.285 (0.022-0.548)</td>
<td>0.04</td>
</tr>
<tr>
<td>A vs D</td>
<td>0.648</td>
<td>0.253 (-0.01-0.516)</td>
<td>0.06</td>
</tr>
<tr>
<td>B vs C</td>
<td>0.630</td>
<td>0.189 (-0.08-0.458)</td>
<td>0.16</td>
</tr>
<tr>
<td>B vs D</td>
<td>0.574</td>
<td>0.080 (-0.187-0.347)</td>
<td>0.55</td>
</tr>
<tr>
<td>C vs D</td>
<td>0.537</td>
<td>0.017 (-0.252-0.283)</td>
<td>0.90</td>
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</tbody>
</table>

A = Leprologist; B=Student 1; C = Student 2; D = Leprosy staff

DISCUSSION

Anaesthesia of a skin lesion is one of the three cardinal signs of leprosy. Assessment of anaesthesia to light touch is a common practice for the diagnosis of leprosy, although it is recommended that the diminished pain sensation and the loss of thermal sensation can be used also as diagnostic tools in the diagnosis of leprosy.11 In one exercise conducted in India it was found that the pain sensation test had a higher sensitivity compared with the touch sensory test.12 However, a study conducted in Malawi demonstrated that the three tests had the similar sensitivity and specificity for the diagnosis of PB patients when pathological diagnosis was used as a reference.10 In Shandong as well as in China in general, sensation test to touch with cotton wool is the most common practice in the clinical diagnosis of leprosy, and the pain and thermal sensory tests are not used routinely. Our interest in the current study was to compare the reliability of a test between different testers, rather than to compare the different tests.

There is no standardized method in sensory testing of a skin lesion and the judgment of a test result is subjective rather than objective. Therefore, several factors will have an impact on the result of the testing.9,13 Sensory testing with cotton wool is the test of choice, but it may not be used in a standardized way globally. One study conducted in Nepal showed that the agreement in the reliability test of sensation testing was much better in the trained physio-technician group than in the paramedical worker group, reflecting that the skill and experience of the testers are the most important factors in
the inter-tester reliability test. Unlike another study conducted in India in which the agreement on sensory test of skin lesion between different pairs of staff were judged as fair or good, the results of the current study show the agreements on sensation test between the different pairs of testers were unsatisfying (kappa values are around 0.4). The difference between the study conducted in India and the current study is probably due to the different experiences in the examination of leprosy patients among the testers and the method used in sensory test.

The agreement on palpation of nerves in the current study is also unsatisfactory. Generally, the agreement on palpation of ulnar nerve is better than that on palpation of popliteal nerves. This is in contrast to a previous study conducted in India, in which the agreement on palpation of popliteal nerves was better than the agreement on palpation of ulnar nerve. In that study, the kappa values ranged from 0.45 to 0.54 and from 0.52 to 0.69 for the thickness of ulnar and popliteal nerves respectively. In clinical practice we found that it is more difficult to palpate the popliteal nerve than the ulnar nerve because the ulnar nerve is much more superficial than the popliteal nerve. The discrepancy of the results on palpation of peripheral nerves between the two studies needs to be clarified in the future.

The study conducted in India showed that not only did the paramedical workers had difficulty in diagnosing early leprosy, but the senior medical officers also had difficulty in eliciting the thickening of peripheral nerves, which resulted in a moderate level of intra-tester agreement. As pointed out by Nagaraju et al, eliciting clinical signs such as sensory loss of a patch and thickening of a nerve trunk could be correlated. This kind of bias cannot be avoided completely, and therefore, is likely to be responsible for variation in both intra-tester and inter-tester agreement. Apart from this, lack of standardization of the testing, especially the force applied on the lesion by the individual examiners, would be an important contributing factor for the disagreement in the current study.

In previous training programmes for leprosy, only lectures were given and practical skills were less often taught. Whenever training for dermatologists or leprosy control staff is arranged, especially for the new staff, as much practice as possible should be given. Besides this, careful standardized written instructions on how a test should be performed should be developed and given to all involved in diagnosing leprosy. Regular supervision with refresher training would also play an important role.

It should be emphasized that the sensory test of a skin lesion for the diagnosis of leprosy is more suitable for PB patients than for MB patients, because the sensation loss of skin lesions in MB patients occurs later than that in a PB patient, if it all. Apart from ulnar and popliteal nerves, other superficial nerves, such as the greater auricular nerves, the supraorbital nerves and radial cutaneous nerves are also can be enlarged and can assist in the diagnosis of leprosy. In Shandong province, more that 80% of
newly diagnosed cases of leprosy are MB. Therefore, whenever a patient is suspected to have leprosy, skin smear examination should be performed, no matter whether the sensation of the skin lesions is lost or not.²

ACKNOWLEDGEMENTS

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REFERENCES


