The association between neuropathic pain and disability grades in leprosy

ROGÉRIO DEL’ARCO*, ADRIELI BARBOZA DE OLIVEIRA**, SUSILENE MARIA TONELLI NARDI*** & VÂNIA DEL’ARCO PASCHOAL****
*Santa Casa de Misericórdia de São José do Rio Preto, São Paulo, Brazil
**Academic of Nursing Course, Medicine School in São José do Rio Preto, São Paulo, Brazil
***Instituto Adolfo Lutz - São José do Rio Preto, São Paulo, Brazil
****Medicine School in São José do Rio Preto, São Paulo, Brazil

Accepted for publication 20 January 2016

Summary

Objective: To detect neuropathic pain in people who have had leprosy and correlate this association with the WHO Degree of Physical Disability classification (DPD-WHO).

Patients and Methods: Data were collected from medical records, interviews and physical examinations of patients treated in 2013 in a regional referral service that attends 102 municipals. Clinical and general data, the DPD-WHO classification and the Douleur Neuropathique 4 Questionnaire (DN4) were utilised to determine the profile and to diagnose neuropathic pain.

Results: Of 84 treated patients, 37 (44·1%) had leprosy-related pain at the time of the interview. The mean age was 53 years, 51·4% were women; 75·7% had multibacillary disease and 72·9% had some kind of reactional episode. Of the 37 patients with pain, 22 (59·5%) had neuropathic pain and 15 (40·5%) had nociceptive pain. The most frequently reported symptoms related to neuropathic pain, apart from numbness (64·9%), were tingling and touch hypoesthesia (56·8%). Of 22 patients with neuropathic pain, 20 had some physical disability; 14 (63·6%) had Grade I disability, six (27·2%) Grade II, and two (9·3%) Grade zero disability. An association was found between neuropathic pain and degree of disability ($P$-value < 0·05).

Conclusion: Of the patients who reported pain related to leprosy, 59·5% had neuropathic pain. The DN4 seems to be suitable for determining the presence of neuropathic pain in leprosy. There is an association between the degree of disability and neuropathic pain, i.e. patients with neuropathic pain tend to have a physical disability too.

Keywords: Leprosy, neuropathic pain, nociceptive pain, disability
Introduction

Neural damage may manifest as pain,\textsuperscript{1} with the main symptoms being impaired sensitivity and loss of motor force which may cause secondary injuries, such as burns, ulcers in insensitive regions and infection.\textsuperscript{2,3} These changes need to be diagnosed and treated early\textsuperscript{4} in order to avoid physical and psychological disabilities as well as impaired social participation of individuals.\textsuperscript{5–7} It is well known that patients with intense pain have limitations in their daily activities.\textsuperscript{2,8}

Inflammatory processes of the peripheral nerves in leprosy are caused by the direct action of the bacillus or by reactive states and can cause in addition to physical disability, intense pain which is classified as nociceptive (somatic or visceral) or neuropathic as a sequel of neuritis.\textsuperscript{9}

Nociceptive pain is the perception of stimulation of nociceptors, which when acute, alert the body to imminent danger and inform of injury or tissue damage.\textsuperscript{10–12} Moreover, neuropathic or neurogenic pain is defined as pain resulting from injury/dysfunction of peripheral nerves or the central nervous system. This is a poorly defined syndrome characterised by inflammatory and immune responses.\textsuperscript{13,14} The distinction between the two situations is important because specific treatment is indicated in each case\textsuperscript{15} and undesirable side effects with the frequent use of anti-inflammatory drugs can be avoided. Thus, the identification of neural damage in leprosy, including the type, the cause and the extent of damage requires careful attention from professionals to provide precise drug treatment, and to control the evolution of the condition to prevent the sensory and motor abnormalities that cause physical disabilities.\textsuperscript{5}

With the aim of reaching an accurate diagnosis of neuropathic pain and to understand the consequences of leprosy, the objective of this work was to detect neuropathic pain in patients treated for leprosy, determine its characteristics and substantiate whether pain is associated with the Degree of Physical Disability of the World Health Organization (DPD-WHO).

Patients and Methods

A database was created containing the data of patients treated in a leprosy service of a large city in the state of São Paulo, Brazil in 2013. This service is a regional referral centre for 102 adjacent towns with a total population of around one million. The referral service only treats patients with complications due to leprosy who, for different reasons, could not be treated by professionals in their home towns. The service receives about 15 patients with complications per month or an average of 180 leprosy patients annually. Most of the 102 municipals have eliminated leprosy as a public health problem (<1/10,000 inhabitants). This study was approved by the Research Ethics Committee of FAMERP (CAAE #02435412.0.0000.5415).

This is a descriptive cross-sectional investigation of data collected from medical records, interviews and physical examinations of patients who agreed to participate in the study. It was decided to determine the population of patients with pain, who were treated in the Dermatology Outpatient Clinic of Hospital de Base over a 1-year period (January 1st 2013 to December 31st 2013). Epidemiological data were collected from patient records, reporting forms, inclusion spreadsheets and follow up reports of leprosy cases. After this initial data collection, 84 patients (46.7\%) were called for interviews and those who agreed to participate in the study signed informed consent forms.
All patients who had completed multidrug therapy (MDT) and complained of leprosy-related pain of the arms and legs were included. Patients with diabetes, alcoholics and those who had reactional episodes [reversal reactions and erythema nodosum leprosum (ENL)] were excluded, as these are confounding factors in the diagnosis of neuropathic pain.

The anatomical plausibility of the affected area was respected to diagnose neuropathic pain; pain not caused by a stimulus attaining four or more points in the Douleur Neuropathic 4 Questionnaire (DN4). This questionnaire evaluates ten items: characteristics of pain (burning, painful sensation to cold, electric shock), symptoms in the region of pain (tingling, pins and needles, numbness, itching), localized pain (touch hypoesthesia, pricking hypoesthesia) and increased pain in the region on brushing.

The DPD-WHO was adopted to assess disability of the arms and legs.

Data collection included the interviewee’s personal data (name, address and telephone) and leprosy-related data (date of diagnosis, clinical signs, type of onset, duration of disease symptoms, type of treatment for leprosy, presence or absence of neuropathic pain according to the DN4 and the DPD-WHO classification).

Data analysis was based on the frequency of the studied variables with the chi-square or Fisher’s exact test, as appropriate, being employed to assess the association between the variables of interest. Statistical significance was set for \( P \)-values \( \leq 0.05 \).

Results

Of the 84 patients interviewed, 37 (44·1%) who filled the inclusion criteria made up the study population.

Table 1. Profile of the people who had leprosy

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>19</td>
<td>51.4</td>
</tr>
<tr>
<td>male</td>
<td>18</td>
<td>48.6</td>
</tr>
<tr>
<td>Profession</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>7</td>
<td>18.9</td>
</tr>
<tr>
<td>Home worker</td>
<td>8</td>
<td>21.6</td>
</tr>
<tr>
<td>Unemployed</td>
<td>4</td>
<td>10.8</td>
</tr>
<tr>
<td>Other professions</td>
<td>18</td>
<td>48.7</td>
</tr>
<tr>
<td>Clinical form</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL</td>
<td>4</td>
<td>10.8</td>
</tr>
<tr>
<td>TL</td>
<td>5</td>
<td>13.5</td>
</tr>
<tr>
<td>BL</td>
<td>15</td>
<td>40.5</td>
</tr>
<tr>
<td>LL</td>
<td>13</td>
<td>35.2</td>
</tr>
<tr>
<td>BAAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>positive</td>
<td>14</td>
<td>37.8</td>
</tr>
<tr>
<td>negative</td>
<td>23</td>
<td>62.2</td>
</tr>
<tr>
<td>Form of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MB</td>
<td>27</td>
<td>73.0</td>
</tr>
<tr>
<td>PB</td>
<td>6</td>
<td>16.2</td>
</tr>
<tr>
<td>alternative MB</td>
<td>4</td>
<td>10.8</td>
</tr>
<tr>
<td>Reactional episodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>neuritis</td>
<td>12</td>
<td>32.4</td>
</tr>
<tr>
<td>ENH</td>
<td>7</td>
<td>18.9</td>
</tr>
<tr>
<td>RR</td>
<td>4</td>
<td>10.8</td>
</tr>
<tr>
<td>ENH + RR</td>
<td>3</td>
<td>8.1</td>
</tr>
<tr>
<td>Lucio phenomenon</td>
<td>1</td>
<td>2.7</td>
</tr>
<tr>
<td>none</td>
<td>10</td>
<td>27.0</td>
</tr>
</tbody>
</table>

MB: multibacillary; PB: paucibacillary; IL: Indeterminate leprosy; TL: Tuberculoid leprosy; BL: Borderline leprosy; LL: Lepromatous leprosy; ENH: erythema nodosum leprosum; RR: Reversal reaction.
The mean age of the patients at the time of the interview was 53.2 years with a median of 56; 51.4% had ages between 51 and 60 years.

Most of the study sample (51.4%) was female. Retired men outnumbered retired women and most women were unemployed.

Considering the two types of treatment regimens, the mean number of supervised drug doses was 14 with a minimum of six and a maximum of 24 doses of MDT.

At the time of interview, none of the interviewees had any other leprosy-related complications, but 72.9% had already had some kind of reactional episode such as erythema nodosum leprosum (ENH) and/or reversal reactions (RR).

At the time of the interview, the mean time since completing MDT was 4 years, ranging from 1 year to 25 years.

Seventeen (45.9%) of the interviewees had no other associated disease. Of those with comorbidities, 20 (54.0%) reported more than one, with the most common being systemic arterial hypertension \((n = 7)\) and depression \((n = 3)\); patients also reported anemia \((n = 2)\), osteoarthritis \((n = 2)\), glaucoma \((n = 2)\) and osteoporosis \((n = 2)\). (Table 1)

According to the criteria of the DN4, neuropathic pain is characterized in patients who have scores \(\geq 4\) points.

The frequencies of neuropathic and nociceptive pain of the 37 patients in this study are shown in Figure 1.

On evaluating the ‘characteristics of pain’, all patients who felt burning also felt electric shock-type pain \((20; 54.1\%)\), with painful cold feelings being the least common \((10; 27.0\%).\)

The most common symptoms in the area of pain were numbness \((24; 64.9\%)\) followed by tingling \((21; 56.8\%);\) itching \((5.4\%)\) was the least frequent. Regarding the ‘location of pain’, touch hypoesthesia \((21; 56.8\%)\) was more common than pricking hypoesthesia \((19; 51.4\%).\)

### Table 2. Distribution of pain and related symptoms reported by people who had had leprosy \((n = 37)\)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics of pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burning</td>
<td>20</td>
<td>54.1</td>
</tr>
<tr>
<td>Painful cold feeling</td>
<td>10</td>
<td>27.0</td>
</tr>
<tr>
<td>Electric shock</td>
<td>20</td>
<td>54.1</td>
</tr>
<tr>
<td>Symptoms in the area of the pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tingling</td>
<td>21</td>
<td>56.8</td>
</tr>
<tr>
<td>Pins and needles</td>
<td>19</td>
<td>51.4</td>
</tr>
<tr>
<td>Numbness</td>
<td>24</td>
<td>64.9</td>
</tr>
<tr>
<td>Itching</td>
<td>2</td>
<td>5.4</td>
</tr>
<tr>
<td>Local pain- hypoesthesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Touch</td>
<td>21</td>
<td>56.8</td>
</tr>
<tr>
<td>Pricking</td>
<td>19</td>
<td>51.4</td>
</tr>
<tr>
<td>Increase in pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brushing</td>
<td>10</td>
<td>27.0</td>
</tr>
</tbody>
</table>
There was no increase in pain in 73·0% of the interviewees when the painful area was brushed (Table 2).

Twenty (90·8%) of the patients with neuropathic pain had a physical disability, 14 (63·6%) were classified as Grade I and six (27·2%) as Grade II with only two (9·2%) not having any disability (Grade 0; Table 3). Of the 15 patients diagnosed with nociceptive pain, 60% (n = 9) were classified as Grade 0 in respect to physical disabilities. There was an association between the degree of disability and neuropathic pain showing that patients with neuropathic pain tend to have a physical disability (P-value < 0·05). (Table 3)

Discussion

Pain is an important and worrying problem in the treatment of leprosy.18 In this study, neuropathic pain accounted for more than half of the evaluated cases. Studies in China and Brazil report similar incidences of patients with neuropathic pain of about 45·8% and 44·3%, respectively, highlighting a need for greater attention to be paid to this clinical condition.19,20

Given that the treatment is different in both types of pain, it is critical to recognise and differentiate the kind of pain in order to provide the correct treatment.11,13,21

On physical examination, sensory changes are strong evidence of neuropathic pain.22 Therefore, researchers strongly suggest that adequate and validated screening questionnaires are used to accurately identify the problem and define appropriate treatment.18,23,24

One study showed that on starting therapy in cases with altered nerve function, the risks of suffering further damage during treatment are up to 65% higher in multibacillary cases and 16% higher in paucibacillary cases.25 For this reason, it is essential that those responsible for leprosy control programmes are rigorous and require effective evaluations of physical disabilities during the monitoring of people with leprosy.

In this study, the physical examination used the DN4 Questionnaire; this showed a high frequency of symptoms such as tingling, burning and electric shock feeling, symptoms that are not routinely screened for in national leprosy protocols. Hence, these are important aspects to investigate in the physical examination of people who have or have had leprosy. The presence of more than six symptoms of pain in patients with Grade II disabilities can be attributed to chronic neuropathy, the physiological basis of which are the phenomena of

| Table 3. Degree of physical disability of patients with neuropathic pain according to the World Health Organization (DPD-WHO) classification

<table>
<thead>
<tr>
<th>Degree</th>
<th>Nociceptive</th>
<th>Neurpathic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>9</td>
<td>60·0</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>13·4</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>26·6</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100·0</td>
</tr>
</tbody>
</table>

P-value = 0·000457 (Chi-Square – Yate’s correction).
hypersensitisation and cellular memory, which act in perpetuating the pain making it chronic, and sometimes making it difficult to control.  

In a study from China, 126 (45.8%) of 275 leprosy patients reported symptoms suggestive of neuropathic pain and in Ethiopia, 29% of cases had neuropathic pain as identified using the Neuropathic Pain Symptom Inventory. The incidence was 44.3% in one other Brazilian study that used electrophysiological studies to identify neuropathic pain. 

According to this and other studies, the vast majority of patients, at least 70.3% after completing MDT, have at least some degree of disability, i.e., Grade I or II. It was also observed that a group of people (9.2%) after completing MDT had neuropathic pain even though they did not have physical disabilities (Grade 0).

The results of this study reinforce the recommendation that all healthcare professionals should employ the DN4 to precisely diagnose neuropathic pain, and quickly treat any indication of nerve damage in order to prevent future disability that greatly impacts on the quality of life of patients.

It is expected that this research will help to improve the diagnosis and treatment of neuropathic pain in leprosy, as this sequel can be intense and cause morbidities.

Conclusion

Neuropathic pain affects more than half of those who reported leprosy-related pain with most being multibacillary cases with physical disabilities and with leprosy reactions.

There is an association between the degree of disability and neuropathic pain, showing that patients with neuropathic pain tend to have a physical disability as well.

All interviewees who experienced Grade II disabilities reported more than six symptoms related to neuropathic pain. The most common symptoms in neuropathic pain are numbness, tingling and touch hypoesthesia.

The Douleur Neuropathic 4 Questionnaire (DN4) proved to be a robust tool to determine the presence of neuropathic pain in patients with leprosy.

References

Neuropathic pain and disability in leprosy


34. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m


40. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m


42. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m

43. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m

44. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m


47. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m


52. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m


60. Brasil. Ministério da Saúde. Manual de prevenc¸a˜o de incapacidades. Cadernos de prevenc¸a˜o e reabilitac¸a˜o m