CASE REPORT

Relapses in multibacillary leprosy patients after Multidrug therapy

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Summary

Objectives To determine the magnitude of relapses in multibacillary leprosy patients after multi-drug therapy and to determine the factors influencing the relapse.
Design A retrospective study pertaining to multibacillary leprosy patients treated with MBMDT as per WHO guidelines was carried out. The study included 300 MB patients who had successfully completed treatment during 1986–2002, of whom 163 patients were available for follow-up. Patients were examined clinically and bacteriologically to assess the present status of disease.
Results A total of three cases relapsed at 2, 4 and 11 years after being released from treatment which gives a crude cumulative relapse rate of 1.84% for the 18 year period of follow-up with a mean duration of follow-up 7.13 ± 1.25 years. It also gives the total follow-up period of 1163 person–years with the relapse rate of 0.26/100 person–years of follow-up (95% confidence interval is 0.235–0.285).
Conclusion Relapse rate after WHO recommended MDT leprosy is low. High bacterial load before initiation of therapy is an important factor which determines the relapse.

Introduction

The important development in the history of the control of leprosy was the introduction and implementation of multi-drug therapy (MDT) which was recommended by the World Health Organization (WHO) study group in 1982. Since then there has been a significant change in the leprosy scenario both at the global and national level, and the active case load came down drastically in India. There has been a dramatic downward revision of the estimated numbers
Relapses in multibacillary leprosy after MDT

Among the 163 followed-up cases, 121 (74.3%) leprosy patients were above 30 years, and 42 (25.7%) patients were below 30 years of age (with a mean age of 45.3 years). There were 126 male patients and 37 female patients. Their disease classification is shown in Table 1.

Out of 300 patients treated with MBMDT between 1986 and 2002, 163 patients were available for follow-up. Among 163 cases (as shown in Table 1), 59 (36.19%) were classified as lepromatous leprosy (LL), 48 (29.45%) as borderline lepromatous (BL), 12 (7.37%) as midborderline (BB) and 44 (26.99%) were borderline tuberculoid (BT). Forty-one patients (25.2%) were treated with 1 year MBMDT, 82 (50.3%) patients with 2 years of MBMDT and 40 (24.3%) patients treated up to smear negativity as shown in Table 1.
Among the 163 patients who were available for follow-up three patients were diagnosed as relapse, with a relapse rate of 0·26 per 100 person–years; 137 cases were lost to follow-up due to migration, death and other causes.

The first patient relapsed 11 years after release from treatment (RFT) (Table 2). He was diagnosed as LL in 1988 and became smear negative after 4 years of treatment. He was followed up for 11 years and during the follow-up in 2004, he was found to have new skin lesions that showed signs of activity; on smear examination he had an average BI of 2·00$^+$.  

The second patient was diagnosed as LL with a BI of 4$^+$ and was introduced to WHO MBMDT in 1988. The patient became smear negative after 3 years of treatment and followed-up for 5 years. In 1996 the patient relapsed both clinically and bacteriologically with new skin lesions and BI of 3$^+$. MBMDT was started and he became smear negative after 2$^\frac{1}{2}$ years of treatment. The third patient was treated with WHO MBMDT with a BI of 4·25$^+$ before the initiation of MB MDT till smear negativity for 4 years and relapsed 2 years after RFT in 2003.

All the relapse cases were males with LL disease. A follow-up of 1163 person–years had been made with a mean follow-up of 7·13 person–years (Table 3).

All the three patients with relapsed leprosy responded well to re-treatment with the MBMDT regimen.

In our study relapse occurred in patients who had received MB MDT till smear negativity, when compared to patients who received fixed duration therapy. However the duration of follow-up in patients who received fixed-duration therapy (FDT) is not long enough to highlight the efficacy and adequacy of FDT, hence caution has to be exercised to interpret this data.

Table 1. Classification of leprosy patients and duration of treatment

<table>
<thead>
<tr>
<th>Classification</th>
<th>Number of Patients*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LL</td>
<td>59 (102)</td>
</tr>
<tr>
<td>BL</td>
<td>48 (86)</td>
</tr>
<tr>
<td>BB</td>
<td>12 (25)</td>
</tr>
<tr>
<td>BT</td>
<td>44 (87)</td>
</tr>
<tr>
<td>Total</td>
<td>163 (300)</td>
</tr>
</tbody>
</table>

*Original no of cases are shown in brackets

Table 2. Profiles of relapsed patients

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Sex</th>
<th>Initial type</th>
<th>Initial BI</th>
<th>Duration of MDT (years)</th>
<th>Time of Relapse after RFT (years)</th>
<th>BI at relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>LL</td>
<td>1·75$^+$</td>
<td>4</td>
<td>11</td>
<td>2·00$^+$</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>LL</td>
<td>4·00$^+$</td>
<td>3</td>
<td>4</td>
<td>3·00$^+$</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>LL</td>
<td>4·25$^+$</td>
<td>4</td>
<td>2</td>
<td>4·00$^+$</td>
</tr>
</tbody>
</table>
Discussion

As in the cases of other infectious diseases, the relapse rate is a crucial parameter in assessing the long-term efficacy of chemotherapy. Though the earlier studies with short-term follow-up have shown a good response, it is the long-term outcome of the treated patients that determines the ultimate utility of the therapeutic regimens.\(^2\) Another aspect has been the continuously changing definitions of MB patients. Initially smear-positive patients with a BI \(>2\) at any site belonging to BT and all active patients with BB, BL and LL classification were included in the MB group.\(^1\) In view of the shortcoming in skin smear facilities at field level, the definition was later modified to include all AFB positive patients of BT (irrespective of BI) in addition to others.\(^9\) Subsequently the MB group was extended to include all leprosy patients with more than five lesions as per WHO guidelines and \(>10\) lesions are suggested by NLEP in India.\(^10\) For treatment purposes, WHO presently classify leprosy patients with \(1–5\) skin lesions as PB leprosy, and more than five lesions as MB leprosy.\(^11\)

Thus in contrast to earlier studies on the efficacy of MB treatment for MB leprosy, the later ones include a substantial proportion of smear-negative and low BI patients. Therefore the outcome of recent studies is not comparable with initial trials in MB patients.

The relapse after WHO-recommended MBMDT regimen is generally low. A WHO questionnaire survey reported that the cumulative risk of relapse was 0·77% for MB leprosy patients after 9 years of stopping MBMDT.\(^12\) Other follow-up studies have reported relapse rates varying from less than 1% to 20%.\(^13–15\)

The AMFES study reported no relapses after a mean duration of follow-up of 5 years.\(^16\) Another study reported that a group of MB patients was clearly at high risk for a relapse following 2 years of WHO MDT. Relapse is largely confined to BL or LL cases with a high BI initially and occurs long after the discontinuation of therapy.\(^15\)

The mean duration of follow-up was 7·13 \(\pm\) 1·25 years after RFT and the relapse rate in 0·26 per 100 person–years follow-up (confidence interval 0·235–0·285), which is lower than the acceptable relapse rate of 1·0 per 100 person–years and relapse rates reported in other studies.\(^15\)

Nevertheless, important aspects need to be considered while interpreting these findings. In this study more male patients were reported for follow-up than female patients. The relapse rate is governed by two factors: the high initial bacterial load and the long period of follow-up.\(^17\) In one study of patients treated up till smear-negativity, a higher relapse rate of 1·27 per 100 person–years was observed among patients with an initial BI of \(\geq 4·00\) as
compared to 0.46 per 100 person–years among patients with initial BI of \( \leq 4.00 \pm 2 \). In the present study also, two patients who relapsed had a high initial bacteriological index (BI \( \geq 4 \)) prior to the initiation of MB MDT. One patient relapsed 11 years after RFT, whereas other two patients at 4 and 2 years respectively. The relapse rate with reference to time-gap after RFT reveals most of the relapsed cases occur within 5 years after RFT and decline with the passage of time. It is inferred that the chances of relapse in the later years of RFT is less. It is also important to note that only 57% (107/188) of patients of LL and BL reported for evaluation. We presume that relapse rates would have been higher if all the patients were evaluated for relapse.

Age and sex are also known to influence the occurrence of relapse, but these do not act as independent factors.

Acknowledgements

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References