Treatment of Paucibacillary Leprosy Patients with Dapsone and Rifampicin

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Dapsone resistance is found worldwide\(^{(1,2)}\) and resistance to other available drugs such as ciprofloxacin\(^{(3)}\) and rifampicin\(^{(4)}\) also occurs. It is known that paucibacillary leprosy patients harbour \(<10^6\) bacilli\(^{(5)}\). However, the treatment of paucibacillary leprosy is of long duration. It is psychologically undesirable for a symptom-free, paucibacillary patient to receive therapy for a long period of time\(^{(6)}\). In practice, many patients discontinue treatment prematurely although they may continue to attend the treatment services. The high failure rate of standard dapsone therapy in control programmes in the developing countries stems directly from the difficulty of persuading patients to remain under treatment for long enough\(^{(7)}\).

Concerned at the problem of high patient failure rate and high relapse rates in Nepal, we have instituted short course multidrug therapy (MDT) for leprosy in 1981. Administration of one dose of rifampicin every month was supervised. In this article, we review the progress made.

**Materials and Methods**

Five hundred and ninety patients were studied.

Group A, 222 patients with no history of previous treatment.

In Group B, 346 patients had received dapsone but did not complete the treatment advised. Twenty-two patients were referred to Anandaban as a referral centre and to its principal skin clinic at Patan. Most of the patients presented voluntarily. All patients were clinically classified on the Ridley-Jopling scale\(^{(8)}\). In particular emphasis was laid on peripheral nerve examination and deformities. From a majority of the patients, a skin biopsy was obtained. Skin smears were routinely taken, from four sites that is ear lobe, back of forearm, front of thigh and from a lesion. Skin tests with lepromin, leprosin A and tuberculin were undertaken. All the data were recorded.

**Drug Regimen:**

**Paucibacillary Patients (BI negative)**

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Rifampicin 600mg (2 doses monthly)
Dapsone 100mg daily.
Duration-Six months.

**Paucibacillary Patients (BI <2+)**
Rifampicin 600mg (2 doses monthly)
Dapsone 100mg daily
Duration-until skin smear negativity.

Patients failing to report on three consecutive occasions for collection of drugs were re-started on MDT.

**Results**

Of 568 patients belonging to Group A and B, 340 (60%) were male and 228 (40%) were female. 393 (69%) patients were classified BT; 108 (19%) TT; 17 (3%) patients had indeterminate leprosy and 50 (9%) had polyneuritic leprosy with no skin manifestations (Table 1).

Of 222, Group A patients, 122 were smear positive. The average pretreatment bacteriological index was 1.4. They were given MDT for ten months. At the end of treatment, the skin smears were negative. In 100 patients the bacteriological index was negative. MDT was administered for six months. In Group B, 346 patients received MDT for six months as the skin smears were negative. All patients did well. Erythema of the lesions disappeared and the lesions diminished considerably in size and number. Patients were followed for 28 months. In the smear negative patients the lesions regressed and wrinkling of the lesions was observed. In the smear positive group the regression of the lesions was relatively slow and the lesions persisted for longer. Enlargement of the peripheral nerves persisted on follow-up, but there was no tenderness.

32 patients developed the following complications during therapy:

- Tenosynovitis -1
- Foot drop, partial -10
- Foot drop, complete -3
- Jaundice -1
- Type 1 reaction with neuritis -17

They were admitted to the hospital and given standard medical and surgical treatment.

Of the 22 absconders, 8 patients were classified BT, 4 indeterminate, and polyneuritic. They were irregular in taking treatment and missed appointments regularly. Efforts to follow them were disappointing. Table 2 shows the clinical relapses recorded among TT-BT patients.

<table>
<thead>
<tr>
<th>Table 1 Showing distribution of patients according to sex and type of leprosy</th>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Total</td>
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</tbody>
</table>
following therapy with MDT. In the first 6 months, 6 patients developed new skin lesions. In the second 6 months, 19 patients developed new skin lesions, and in the third 6 months, 26 patients relapsed with new lesions.

At 18 months of post-MDT follow-up, 13% of smear positive patients and 9% of smear-negative patients clinically relapsed. Following the diagnosis of the clinical relapse, the patients were given treatment for a further six months. Fifty one relapsed, patients on completion of a second course of six months MDT, showed clinical improvement. There was no further deterioration and no neuritis was seen.

Table 2 Clinical relapse of paucibacillary leprosy patients in the first eighteen months after stopping MDT

<table>
<thead>
<tr>
<th>DURATION of MDT (Months)</th>
<th>No. of TT-BT Patients completed MDT</th>
<th>Clinical Relapses</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>First 6 months</td>
<td>Second 6 months</td>
</tr>
<tr>
<td>6</td>
<td>379</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>122</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>501</td>
<td>6</td>
<td>19</td>
</tr>
</tbody>
</table>

Discussion

The patients welcomed MDT of limited duration. Patient failure rate improved remarkably. Medical and paramedical staff were compelled to lay more emphasis on the detection of nerve damage at an early stage. Clinical lesions observed in TT-BT group of patients may possibly be due to two kinds of cellular function, cell-mediated immune response and delayed hypersensitivity\(^{10}\). The immune responses are variable as assessed by lymphocyte transformation test (LTT), lepromin and leprosin A skin tests\(^{11}\). Chemotherapy may possibly contribute to the killing of the existing bacilli which account for <10\(^6\). This may precipitate reversal reaction. These reactions may result in rapid and permanent damage to the peripheral nerves. In this group of patients inflammation of the nerves is associated with the death of the bacilli and the reactions triggered in the immunologic granulomas. These patients contribute to the bulk of the patient load in leprosy control programmes. The treatment of these patients is therefore very important. Thirteen patients developed rapid onset of foot drop, and 17 developed reversal reaction with severe neuritis in the course of MDT. The most commonly affected nerves were the ulnar and lateral popliteal. The patients had to be hospitalized.

The classification of borderline/tuberculoid patients into smear-positive and smear-negative is important as the administration of MDT differs in the two groups. In smear-positive patients, lesions regressed relatively rather more slowly in contrast to the lesions in smear-negative patients.

Most of the data in the literature on relapses pertain to dapsone monotherapy and the length of treatment necessary to prevent relapses\(^{12-14}\). A study from Ethiopia\(^{15}\) records that following administration of eight doses of 900mg rifampicin no relapses were recorded. In
another report\textsuperscript{(16)}, an eight-month follow-up of post-MDT patients shows a relapse rate of 1%. Revenkar\textsuperscript{(17)} reports that following MDT, 38.2\% skin lesions regressed and no case of upgrading reaction was recorded. The puzzling differences observed in clinically similar groups of patients may be either due to ethnic/geographic factors and/or to observer error.

In the present study, 35 smear-negative patients after six months of MDT, and 16 smear-positive patients after 10 months of MDT had clinically relapsed an overall rate of 10\%. Post-MDT relapses in paucibacillary patients occur within two years. Post-MDT follow-up of TT-BT patients should be undertaken every six months for a period of three years.

Three BT patients after successful completion of six months of MDT presented to the clinic with new lesions after 12 months. These patients are not included in 51 relapsed cases. The clinical diagnosis was a type 1 reaction without neuritis. Patients were hospitalised and standard therapy was instituted. The biopsy report on the new skin lesions was "borderline tubercloid with upgrading reversal reactions". Therefore a distinction has to be made during post-MDT follow-up between clinical relapses and upgrading reversal reactions. This is of paramount importance in documenting relapse rate following MDT in control programmes.

WHO\textsuperscript{(18)} recommendations of short course chemotherapy for paucibacillary patients in leprosy control programmes is welcomed because of its applicability in the field and because of the administrative and logistic advantages both for the leprosy control authorities and for the patients. We await with interest other reports of application of MDT and the relapse rates among paucibacillary patients.

**Summary**

Five hundred and ninety paucibacillary patients were administered multidrug therapy since 1981. Except for 22, all patients were regular for treatment. Thirty-two patients developed complications during therapy. All patients responded well to treatment. In the smear positive group, the regression of the lesions was relatively slow and the lesions persisted for longer. Patients were followed up for 28 months. At 18 months of post-MDT follow up, 13\% of smear positive patients and 9\% of smear negative patients relapsed. An overall relapse rate was 10\%.

**Acknowledgement**

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