BORDERLINE TUBERCULOID LEPROSY: CLINICOPATHOLOGICAL EVALUATION OF MULTIDRUG THERAPY

Lt Col PK KAR^{*}, Lt Col RS DHAKA⁺

(Command Hospital Southern Command and Command Pathology Laboratory, Pune)

ABSTRACT

Efficacy of multi-drug therapy as per WHO recommendation in 125 fresh cases of borderline tuberculoid (BT) leprosy was evaluated. There were 116 (92.8%) male and 9 (7.2%) female patients. Age of the patients ranged from 18-50 years but the majority (80.8%) were young adults in the age group 21-35 years. The commonest site of lesion was the upper extremity in 65 (52%) cases. Skin smear for acid fast *Mycobacterium leprae* was positive in 11 (8.8%) patients. All patients were given multidrug therapy consisting of rifampicin 600 mg once a month and dapsone 100 mg daily for 6 months. At the end of 6 months, 42 (33.6%) patients had shown marked improvement, 14 (11.2%) had increase in activity, 51 (45.6%) had shown regression and 12 (9.6%) cases became clinically inactive. Histologically complete clearance of the infiltration was not observed in any patient. Compact granulomas persisted in 30 (24%) cases. In 1 (0.8%) patient *M. leprae* were found in the skin smear at the end of 6 months. This study indicates that treatment with MDT for 6 months is inadequate to treat all types of BT leprosy cases.

MJAFI 1997; 53 : 91-94

KEYWORDS : Drug therapy combination; Leprosy borderline; Leprostatic agents; *Mycobacterium leprae*.

Introduction

A leprosy patient is defined as one who is found to have clinical signs and symptoms of the disease and who requires chemotherapy [1]. As defined by WHO, paucibacillary leprosy (PBL) includes indeterminate (I), tuberculoid (TT) and borderline tuberculoid (BT) patients diagnosed clinically and histologically with the bacteriological index (Ridley's scale) less than 2 on at any site [2]. WHO has recommended a short course of multidrug therapy (MDT) for PBL cases. The meeting of a WHO study group reaffirmed that treatment of PBL should continue for 6 months [3]. This regimen consists of rifampicin 600 mg once a month and dapsone 100 mg daily for 6 months. Several workers from India have found that a total duration of 6 months of MDT in various PBL cases is inadequate [4,5]. Since, in India, BT is the commonest form of leprosy [6] a study was undertaken to evaluate the efficacy of MDT given to BT cases for a period of 6 months.

Material and Methods

One hundred twenty five fresh cases of BT leprosy attending a leprosy centre from July 1991 to June 1994 were included in the study. Complete clinical examination was done in each patient by recording the morphology and site of lesions, and thickening and tenderness of peripheral and cutaneous nerves. Skin smear examination for acid fast bacillus, *Mycobacterium leprae* (AFB(L)) and biopsy of the skin lesion were carried out before beginning MDT. The clinical and histopathological classification of leprosy was made according to criteria given by Ridley and Jopling [7]. Relevant laboratory investigations such as hemogram, urine examination, and assessment of renal and hepatic functions were carried out periodically during the period of the study.

All patients were given rifampicin 600 mg once a month and dapsone 100 mg daily. Each patient was reassessed clinically every month and histologically at the end of the 6 month treatment

^{*}Classified Specialist (Dermatology & Ven), 151 Base Hospital C/O 99 APO; ⁺Classified Specialist (Pathology), Military Hospital Jalandhar Cantt 144004.

period. Apart from ensuring regular intake of MDT, the patients were regularly tested for sensory acuity and motor power of hands and feet.

Clinical resolution was graded as (a) 'Marked improvement' if there was reduction of more than 1 cm in the size of lesions, disappearance of erythema and/or infiltration or disappearance of satellite lesions; (b) 'Increased activity', if erythema and/or infiltration increased, new lesions appeared, or if thickening and/or tenderness of peripheral nerves occurred; (c) 'Regression', if there was reduction up to 1 cm in the size of lesion, decrease in erythema and infiltration of the lesion; and (d) 'Inactive' when signs of activity subsided.

Histological resolution was graded as (a) 'Complete' when complete clearance of infiltration was seen; (b) 'Partial' if the density of infiltration was significantly reduced and; (c) 'Increased activity' if the size or density of granuloma was increased by outward infiltration or internal expansion by a preponderance of young and relatively healthy macrophages with few vacuoles (cellular activity).

Results

Out of 125 patients, 116 (92.8%) were male and 9 (7.2%) were female. In the majority of patients (78%) the duration of disease was less than 12 months. The age of patients ranged between 18-50 years and majority (80.8%) were in the age group 21-35 years.

Twenty six patients (20.8%) had single lesions and 99 (79.2%) patients had multiple patches less than 5 in number with features of BT leprosy histologically. Seventy six (60.8%) patients had multiple patches at more than one site. A total number of 18 (14.4%) cases did not have any peripheral nerve thickening. The commonest site of lesion was the upper extremity in 52 per cent of patients. Scalp and genitalia were not affected in any patient. Skin smears for AFB(L) were found to be positive in 11 (8.8%) patients with bacteriological index less than 2 on Ridley's scale. After 6 months of MDT, AFB(L) was found in skin smear in 1 patient. Out of 14 (11.2%) patients showing increased activity of the existing lesions 3 (2.4%) had developed Type 1 reaction during treatment. Fifty seven (45.6%) patients had shown regression and 12 (9.6%) cases became clinically inactive at the end of 6 months (Table 1). Histologically com-

plete clearance of the infiltration was not observed in any patient (Table 2). Compact granulomas persisted in 30 (24%) cases (Table 3).

TABLE 1

Clinical changes in BT leprosy after six months of MDT

Clinical changes	No. of patients
Marked improvement	42 (33.6)
Increase in activity (active)	14 (11.2)
Regression (active)	57 (45.6)
Inactive	12 (9.6)
Total	125 (100)

(Figures in parentheses denote percentage)

TABLE 2

Histological resolution of skin lesion after six months of MDT in BT leprosy

Histological resolution of skin lesion	No of patients
Complete	—
Partial	111 (88.8)
Increase in activity	14 (11.2)
Total	125 (100)

(Figures in parentheses denote percentage)

TABLE 3

Histological findings of skin lesion before and after initiation of MDT in BT leprosy

Histological findings of skin lesion	Percentage	
	Before initiation of therapy No.	After 6 months of MDT No.
Nerve infiltration	125 (100)	81 (64.8)
Skin infiltration	125 (100)	125 (100)
Epithelioid cells	65 (62)	18 (14.4)
Giant cells	15 (12)	—
Lymphocytes	125 (100)	125 (100)
Compact granuloma	56 (44.8)	30 (24)

(Figures in parentheses denote percentage)

Discussion

India is one of the countries where patients with PBL constitute more than 70 per cent of all leprosy patients [6]. The skin smear in BT leprosy is usu-

ally negative for AFB(L) or, at the most, only a few bacilli may be seen. Because of the low bacterial load most of these patients are not infectious and are not considered to be important in spreading leprosy in the population. However, these patients constitute a large percentage of the total leprosy population who have high rate of deformities [8]. By providing effective and appropriate treatment the deformities and the associated morbidity can be easily prevented [3].

For the success of any mass chemotherapeutic programme the duration of treatment is considered to be an important factor. It is now well accepted that for better drug intake compliance, short regimens would be greatly preferred. With the advent of potent bactericidal drugs like rifampicin and with the introduction of MDT, the WHO study group [3] advocated that treatment in PBL cases should consist of rifampicin 600 mg once a month and DDS 100 mg daily, unsupervised, for 6 months. The group advocated that treatment should be stopped at the end of 6 months irrespective of whether the patients became clinically inactive or not.

The recommendations of the study group were based on the following considerations :-

(i) The maximum bacterial load in a PBL patient is not above 10^6 organisms and therefore the drug resistant mutants arising as a result of treatment are insignificant.

(ii) This group of patients has some degree of cell mediated immunity (CMI) and persists, if any, are likely to be contained by the CMI.

(iii) Rifampicin is a potent bactericidal drug. The need for providing short course effective treatment to majority of patients is obvious. Many patients do not come for regular treatment if it is of long duration.

(iv) There is need for improving the cost-effectiveness of treatment and simultaneously easing the burden of disease on individual patients.

(v) There is also need for saving the working time of health personnel to enable them to devote more time to the treatment of multibacillary patients and other activities of the control programme.

In the present study, out of 125 patients treated with MDT, 71 (56.8%) had active disease after 6

months of treatment (erythema of the skin lesion had persisted at the end of 6 months of MDT). Twelve (9.6%) patients had peripheral nerve tenderness. However, partial resolution of skin lesion was observed histologically in most cases (88.8%) showing effectiveness of treatment.

Kaur et al [9] assessed the WHO multidrug therapy on patients of PBL and concluded that this regimen is safe and acceptable to patients. However, the skin lesions did not regress in 61.9 per cent of their patients at the end of 6 months of therapy. Revankar et al [10] showed that lesions in 36 per cent of untreated PBL patients remained active after 6 months of the same treatment. Bhate et al [11] studied 40 untreated PBL patients on WHO multidrug therapy. At the end of 6 months 50 per cent of the patients were active. The authors continued MDT for a further period of 12 months with dapsone and observed that 92.5 per cent of the patients became clinically inactive at the end of 1 year. In a study of MDT in hospitalized leprosy cases Tiwari et al [12] observed that activity of disease subsided in 65.5 per cent of PBL patients within 12 months and 70.5 per cent of PBL patients took more than 6 months to exhibit subsidence of activity.

The time taken for the disease to become inactive after MDT in BT cases was observed to be 8.4 months which is shorter than that taken for the disease to become inactive under sulphone monotherapy which was 12.2 months in a study by Girdhar et al [13]. The percentage of PBL patients remaining active at the end of 6 months therapy ranges from 4.3 per cent to 35 per cent [14,15]. The continuing activity in BT lesions may not be due to lack of therapeutic efficacy but may be due to continued presence of antigens of killed bacilli or the slowness of the resolution of the granuloma [3]. Therefore treatment can be stopped once regression commences. Regression continues after the treatment is stopped [3].

The MDT proposed by the WHO study group [2] has given impressive results. Since its implementation in 1982 approximately 5-6 million patients have been cured [16]. From a compilation of the data from 17 leprosy control programmes, it was observed that 0.5 per cent of the PBL cases relapsed after taking MDT as per WHO regimen

[17]. A recent meeting of a WHO study group reaffirmed that treatment duration for PBL should continue to be 6 months [3]. However some experts call for caution, arguing that the risk of relapse could be high, especially in multi-bacillary leprosy and a high proportion of cases may relapse 10 to 20 years after treatment [18].

The important parameter of bacteriological conversion from positivity to negativity as proof of efficacy of an antileprosy regimen is not available in PBL. In the absence of this, the 2 yardsticks of efficacy of therapy are (i) clinical regression and (ii) prevention of relapse. Since BT leprosy cases are potentially a serious form of disease both in respect of progress of the disease and propensity to develop deformities, treatment should be continued till all signs of activity have subsided and clinical regression has taken place [19]. Before stopping treatment it should be ensured that the lesions are regressing. If there is no regression treatment should be continued for another 6 months [20]. Regular follow-up (once in 6 months) of BT leprosy patients is necessary so that relapses are detected early [16,18-20].

REFERENCES

1. WHO. A Guide to leprosy control. Edn 2. World Health Organization 1988, Geneva.
2. WHO. Chemotherapy of leprosy for control programme. Report of a WHO study Group. WHO 1982 Tech Rep Ser 675.
3. WHO. Chemotherapy of leprosy. Report of a WHO Study Group. WHO 1994 Tech Rep Ser 847.
4. Chopra NK, Agarwal JS, Pandya GP. A study of relapse in paucibacillary leprosy in MDT project in Baroda District. *Lepr Rev* 1990; 61: 157-62.
5. Grugni A, Nadkarni NJ, Kini MS, Mehta VR. Relapse in paucibacillary leprosy after MDT - a clinical study. *Int J Lepr* 1990; 58: 19-24.
6. Rao PS, Subramanian M, Subramanian G, Parkash I. Prospects for elimination of leprosy in India by 2000 AD. *Indian J Lepr* 1995; 67: 285-92.
7. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five group system. *Int J Lepr* 1966; 43: 255-73.
8. Rao PS, Subramanian M, Subramanian G. Deformity incidence in leprosy patients treated with multidrug therapy. *Indian J Lepr* 1994; 66: 449-54.
9. Kaur S, Sharan VK, Bhushan Kumar, Kaur I. Experience with 2 drug regimen in paucibacillary leprosy. A preliminary report. *Indian J Lepr* 1984; 56: 48-52.
10. Revankar CR, Ganapati R, Naik DD. Multidrug therapy for paucibacillary leprosy: Experience in Bombay. *Indian J Lepr* 1985; 57: 773.
11. Bhate RD, Gupta CM, Chattopadhyay SP, Singh IP. Experience with multidrug therapy in paucibacillary leprosy. *Indian J Lepr* 1986; 58:244.
12. Tiwari VD, Tutakne MA, Singh G, Dutta PK. Multidrug therapy in hospitalized leprosy cases. *Indian J Lepr* 1988; 60: 71-6.
13. Girdhar BK, Girdhar A, Ramu G, Desikan KV. Short course treatment of paucibacillary (BT/TT) leprosy cases. *Indian J Lepr* 1985; 57: 491-8.
14. Boerrichter G, Ponnighaus JM, Fine PEM. Preliminary appraisal of WHO recommended multiple drug regimen in paucibacillary leprosy patients in Malawi. *Int J Lepr* 1988; 56: 409-17.
15. Katoch K, Ramu G, Ramanathan U, Desikan KV. Comparison of three regimens containing rifampicin for treatment of paucibacillary leprosy patients. *Int J Lepr* 1987; 55: 1-8.
16. WHO. Progress towards eliminating leprosy as a public health problem. *Weekly Epidemiological Record* 1994; No 20: 145-51; No 21: 153-7.
17. Naafs B. Features of relapse in PB leprosy after multi-drug therapy. *Indian J Lepr* 1995; 67: 61-7.
18. 14th International Leprosy Congress. Workshop 3: Chemotherapy. *Int J Lepr* 1993; 61: 729-30.
19. Ramu G. Problems of Multidrug Therapy. *Indian J Lepr* 1991; 63: 435-45.
20. Ramu G. Duration of MDT for paucibacillary leprosy. *Indian J Lepr* 1992; 64: 1-7.