

Clinical Evaluation of Multibacillary Leprosy Patients after Fixed Duration Multidrug Therapy (FD-MDT) of One Year: A Hospital Based Study

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ABSTRACT

Introduction: The fixed duration multidrug therapy (FD-MDT) of one year and relapses in multi-bacillary cases raise a few basic issues regarding the clinical activity and the bacillary index changes which occur in patients on multibacillary multidrug therapy.

Aims and Objectives: The aim of the study was to assess the impact of FD-MDT of one year in terms of clinical improvement and changes in Bacillary Index (BI) of skin smear for acid fast bacilli (AFB), and to find out the patients who were at risk of relapse and therefore need prolonged follow up.

Materials and Methods: In total of 100 multibacillary Leprosy patients, attending the urban leprosy Centre, who were on fixed duration multidrug therapy (FD-MDT), a hospital based study has been conducted. Patients were evaluated clinically by Ramu's clinical score and bacteriological index was estimated by taking slit skin smear (SSS) using Ridley's log scale. The clinical score and BI at the completion of FD-MDT of one year were compared with the scores at the time of Presentation.

Results and Observations: The mean clinical score of 100 patients before treatment was 14.69 while as after treatment it became 7.25. The mean reduction in clinical score after 12

months of treatment was 7.44 which were found to be statistically significant. The mean bacterial indices of 100 patients before treatment was 3.29 while as after treatment it became 2.28, hence there was a reduction of 1.01 units in the mean bacterial indices at the completion of 1 year. The difference was statistically significant.

Key words: Mycobacterium Leprae, Multibacillary Leprosy, Fixed Duration Multidrug Therapy, Bacillary Index, Acid Fast Bacilli.

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INTRODUCTION

Leprosy, also called Hansen's disease is a chronic infection. Mycobacterium leprae is an acid and alcohol fast, rod shaped, intracellular bacillus belonging to the family Mycobacteriaceae. It multiplies very slowly with an optimal doubling time of 11-13 days during the logarithmic phase of growth.¹

Human cases of lepromatous leprosy carry the largest load and the nasal mucosa of healthy contacts has also been reported to contain M. leprae.² The incubation period of leprosy is variable and usually ranges from 2-7 years, on an average of 3-5 years. Depending upon the clinical, pathological, immunological and bacteriological features, leprosy can be classified into the indeterminate and determinate leprosy.³ Determinate leprosy has five subtypes: 2 Polar types i.e. tuberculoid (TT) and lepromatous (LL) leprosy and 3 borderline types i.e. borderline tuberculoid

(BT), borderline (BB) and borderline lepromatous (BL) leprosy. At one pole is Tuberculoid Leprosy (TT) where no acid fast bacilli are found in the lesion(s) and the patients have high level of cell mediated immunity (CMI) to M. Leprae, number of lesions is 1-3, of any size and can occur anywhere on the body. They are in the form of well-defined hypo pigmented macules or plaques with raised edges. Surface is irregular or scaly with absent or deficient hair growth. At the other pole is lepromatous Leprosy (LL) where patients experience selective unresponsiveness to M. Leprae and have a very high bacterial load. There are multiple lesions in the form of macules, papules, plaques or nodules or a combination. Advanced disease may present with diffuse symmetrical infiltration and anaesthesia of distal part of limbs in a glove and stocking distribution. Between the polar groups are border line types

(BT, BB, BL), in which the immunological status lies in between and it may increase or decrease over the time, there-by allowing the patient to shift to either TT or LL.

For field workers, WHO has classified leprosy based on the number of skin lesions into single lesion leprosy (1 skin lesion), pauci bacillary (PB) (2-5 skin lesions), and multi bacillary (MB) leprosy (>5 skin lesions). For the purpose of therapy, leprosy is classified into paucibacillary and multibacillary.⁴ Paucibacillary leprosy includes only smear negative indeterminate, TT and BT leprosy. Multibacillary leprosy includes; a) all cases of LL, BL and BB leprosy b) smear positive indeterminate, TT and BT leprosy. Until 1980, when MDT was introduced, both multibacillary and paucibacillary patients were treated with dapsone monotherapy. Paucibacillary patients were released from treatment after varying periods of dapsone monotherapy⁵ and multibacillary patients were treated for life.⁶ Various studies have been conducted on fixed duration multidrug therapy in case of paucibacillary leprosy.^{7,8} The fixed duration multidrug therapy of one year and relapses in multibacillary cases raise a few basic issues regarding the clinical activity and the Bacillary index changes which occur in patients on multibacillary multidrug therapy. To assess the impact of fixed duration multidrug therapy of 1 year in multi-bacillary leprosy in terms of clinical improvement, and changes in bacillary index of skin smear for acid fast bacilli. Present study was carried out to elucidate such changes.

MATERIALS AND METHODS

A hospital based study regarding the clinical and bacillary index evaluation of 100 multibacillary leprosy patients attending the urban leprosy center of SMGS Hospital/Govt. Medical College, Jammu has been conducted. A detailed history and a thorough clinical and bacteriological evaluation were done. The findings at the end of treatment were compared with the findings already recorded at the time of presentation.

Multi-drug therapy (MDT): All patients took standard multi-drug treatment of (WHO 1997)⁹ for multibacillary (MB) patients, consisting of 600 mg of Rifampicin, 300 mg of Clofazimine and 100 mg of Dapsone on 1st day of every month, followed by 100 mg of Dapsone and 50 mg of Clofazimine on all other days of the month for 12 consecutive months.

Criteria for Evaluation

(A) Clinical: Patients were evaluated clinically by Ramu's Clinical score. The clinical score at the completion of multidrug therapy of one year was compared with the clinical score at the time of presentation.^{10,11} In this scoring system, the body is divided into seven regions i.e. face, head and neck, right and left upper limb, chest and abdomen, back and buttocks, right lower limb and left lower limb. Each region was independently scored. A score of 1 was given to predominantly macular lesions, 2 to diffuse infiltration, 3 to few papules or plaques and 4 to predominantly papulonodular lesions. Each of the seven regions received a score of 1-4. The score may range from 0-28.

Reduction of clinical score at the end of treatment was done in the following way:

- Reduction of score by one-regression up to 30%
- Reduction of score by two-regression of 31-60%
- Reduction of score by three regression of 61-90%
- Reduction of score by four regression of > 90%

(B) Bacteriological: Bacteriological index (B1) was estimated by taking slit skin smear (SSS) using Ridley's log scale³ from 4 sites one ear lobule, one eye brow, 2 from most active skin lesions. The resultant bacterial index was compared with bacterial index at the time of presentation.

Statistical Analysis

The reduction in Ramu's clinical score, Bacteriological index was analyzed by applying wilcoxon signed test.

Table 1: Frequent chief complaints at presentation.

S. No.	Chief Complaints	No.* (%)
1	Peripheral anesthesia in glove and stocking distribution	36%
2	Multiple nodules	30%
3	Multiple erythematous plaques	26%
4	Multiple wide spread symmetrical hypopigmented macules or patches	20%
5	Annular lesions	15%
6	Diffuse infiltration	12%
7	Reactions	6%

*Majority of patients had more than one chief complaint.

Table 2: Distribution of clinical scores among 100 patients before and after MDT.

Clinical Score	Before treatment (%age patients)	After treatment (%age patients)
0-4	0	24
5-9	15	51
10-14	41	19
15-19	24	5
20-24	19	1
>25	1	0
Total	100	100

Table 3: Changes in BI before and after treatment.

BI	Pre-treatment	Post-treatment						
		Negative	1+	2+	3+	4+	5+	6+
Negative	0	-	-	-	-	-	-	-
1+	11	11	-	-	-	-	-	-
2+	21	8	10	3	-	-	-	-
3+	23	2	5	14	2	-	-	-
4+	23	-	-	-	16	7	-	-
5+	17	-	-	-	1	11	5	-
6+	5	-	-	-	-	-	5	-
Total	100	21	15	17	19	18	10	0

RESULTS AND OBSERVATIONS

100 patients including 15 females and 85 males with multi-bacillary leprosy were selected for the study with age range between 16 and 65 years. The mean age of the patients was 36.5 years and the maximum patients were in the range of 21-50 years. Duration of the disease in the patients ranged from 2 months to 10 years. However, in majority of patients it was 6 months to 2 years. The mean duration of the disease was 1.41 ± 1.55 .

Thickening with or without tenderness of peripheral nerves was seen in most of the patients. Ulnar nerve was the most common nerve involved. Out of 100 patients, it was involved in 87% of patients, followed by lateral popliteal nerve in 68% patients, radial cutaneous nerve in 48%, posterior tibial in 48%, greater auricular in 36%, supra orbital in 11%, median in 6%, facial in 3% and sural nerve in 2% patients. Majority of patients had more than one nerve trunk involved.

Out of 100 patients, 48% had BL type of leprosy followed by LL (42%), BB (7%), histoid (2%) and BT (1%).

Clinical improvement in the disease was judged by reduction of infiltration of skin, flattening of papulonodular lesions and disappearance or diminution of hypo-pigmented lesions. The improvement was reflected in the change in Remu's clinical score (0-28). Before treatment, the minimal clinical score was 7 and the maximum clinical score was 25. Overall, 85% patients had clinical score of more than 10. After treatment, the minimal clinical score was 0 and the maximum was 21. Overall, 75% patients had clinical score of less than 10. The mean clinical score of 100 patients before treatment was 14.69 (S.D. 4.53) and after treatment it was 7.25 (S.D. 3.75). Hence there was a significant reduction of 7.44 in the mean clinical score after therapy.

Before treatment, all patients were bacteriologically positive, out of 100 patients, 11% had BI of 1+, 21% had BI of 2+, 23% had BI of 3+, 23% had BI of 4+, 17% had BI of 5+ and remaining 5% of patients had BI of 6+. After treatment, out of 100 patients, 21% became bacteriologically negative, 15% had BI of 1+, 17% had BI of 2+, 19% had BI of 3+, 18% had BI of 4+ and remaining 10% of patients had BI of 5+.

All the patients who tested negative after therapy (21%) had actually BI ≤ 3 at the start of therapy, whereas those patients with BI ≥ 4 did not test negative after therapy.

The mean BI of 100 patients before treatment was 3.29 (S.D. 1.39), while as after treatment it was 2.28 (S.D. 1.65), hence giving a significant mean reduction of 1.01 after 12 months of treatment. The BI before and after therapy was analyzed by applying Wilcoxon Signed Test and the Z value was found to be

7.9, which is highly significant at $p=0.005$. Therefore, the reduction in bacteriological index was found to be significant with respect to clinical improvement in the disease. The mean reduction in BI is more in those patients with BI ≤ 3 as compared to those with initial BI ≥ 4 . Before treatment, MI ranged from 0-80% with a mean MI of 35.36%. After treatment MI was zero in all the patients.

DISCUSSION

Fixed duration multi drug therapy (FD-MDT) for MB cases is effective, acceptable and safe, and the clinical and smear positivity have no bearing on the efficacy of FD-MDT, and relapses are low.¹² Multidrug therapy has been a very successful development in the treatment of leprosy with rapid killing of bacilli. With 2 years of MDT MB regimen, relapse rate reported was as low as 0.77%.¹³ On the basis of this and other available information, WHO reduced the recommended length of treatment from 24 to 12 months.^{9, 14} The present study was carried out to find out the effectiveness of 12 months FD-MDT in case of multibacillary by analyzing clinical improvement and bacteriological clearance. The findings at the time of completion of treatment were compared with the findings at the start of treatment. In the present study, the clinical spectrum of 100 multibacillary patients was: 2 Histoid, 42 LL, 48 BL, 7 BB and 1 BT. Majority of our patients belonged to LL and BL, BB and BT were rare. The reason being that BB leprosy is very unstable and the patients rapidly downgrade to BL or LLs (Lepromatous leprosy sub polar) without treatment. With effective treatment, BB is rapidly converted to BT or TTS (Tuberculoid leprosy sub polar). We have included one case of BT as per clinical picture which was smear positive (BI +) at the time of presentation. We had also 2 cases of histoid leprosy, which is rare and can be considered a severe variant of lepromatous leprosy.¹⁵ The ulnar, lateral popliteal and posterior tibial nerves were most commonly involved. All these findings are in agreement with other studies.^{16,17}

Clinical Improvement

The improvement was reflected in the change in Ramu's clinical score which may range from 0-28.¹⁰ In the present study, clinical score at the time of presentation ranged from 7-25; however in 85% of patients it was between 10-25. After treatment clinical score ranged from 0-21, however in 75% of patients it was less than 10. The mean clinical score of 100 patients before treatment was 14.69 while as after treatment it became 7.25. The mean reduction in clinical score after 12 months of treatment was 7.44 which were found to be statistically significant. Katoch K¹⁸

reported a fall of 7.0 and De Sarkar et al.,¹¹ reported a fall of 6.75 in the mean clinical score of patients of MDT group at 12 months of treatment. The average bacteriological index (BI) declined with MDT has been reported to be 0.57-1.01 log units /year, however, the rate of decline of BI in first 2 years after diagnosis is higher than overall rate.¹⁹ Whereas De Sarkar et al.¹¹ reported a fall of 1.05, Narang et al.,²⁰ reported a fall of 0.85 in the mean bacterial indices (BI) of patients of MDT group at 12 months of treatment. In our study the mean bacterial indices of 100 patients before treatment was 3.29 while as after treatment it became 2.28, hence there was a reduction of 1.01 units in the mean bacterial indices at the completion of 1 year. The difference was statistically significant when compared to the base line. Smear negativity: after one year of MDT was observed in 21% patients. Interestingly, all of these patients had initial BI \leq 3. Though highly bacilliferous cases with initial BI of \geq 4 showed a decline in BI, they did not become smear negative at the end of 1 year of FD-MDT. These findings are comparable to study by Daming J.²¹

SUMMARY

100 MB leprosy patients (all smear positive) who have taken FD-MDT of 12 months were taken for the study to find out the effectiveness of FD-MDT in terms of clinical improvement, change in bacillary index at the end of treatment. Evaluation of clinical improvement was done by observing the reduction in Ramu's clinical score. The score at the end of treatment was compared with the score at the time of presentation. The mean clinical score of 100 patients before treatment was 14.69 and after treatment, it was 7.25. Hence, the average reduction in clinical score at the completion of treatment was 7.44 which was found to be statistically significant ($p=0.005$). Bacteriological clearance was evaluated by slit skin smear, which was done at the base line and then repeated at the end of treatment. The mean BI of 100 patients before treatment was 3.29 and after treatment, it was 2.28. Hence the average reduction in BI at the completion of treatment was 1.01 units which was found to be statistically significant ($p=0.005$). However, the decline in BI in highly bacilliferous cases (BI \geq 4) was less than the decline in BI in low bacilliferous cases (BI \leq 3), indicating that high bacilliferous cases (BI \geq 4) at the time of presentation is a risk factor for relapse.

Smear negativity after 12 months of MDT was seen in 21% patients, all having initial BI less than 4. Patients with initial BI more than 3 did not become smear negative after therapy. The results of our study indicate that shortened FD-MDT of 12 months for multibacillary patients is effective and safe and seemingly it has tremendous operational advantage and we should be prepared to treat few relapses in post elimination period as they occur. However, a long term follow up in large number of patients especially highly bacilliferous cases is the best option to settle the issue of safety and efficacy of shortened FD-MDT of 12 months.

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