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Research Article

EVALUATION OF THERAPEUTIC RESPONSE OF MULTIDRUG THERAPY REGIMENS IN CASES OF LEPROSY

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ABSTRACT

Introduction: Leprosy is a chronic infectious disease of skin and nerves. Multidrug therapy (MDT) has been backbone of leprosy elimination strategy for last 20 years and this therapy is extremely well accepted all over the world. Failure of MDT is also reported from various parts of the world as low as 0.77% to as high as 20%. ***Aim & Objective:*** To evaluate the therapeutic response of multidrug therapy regimens in cases of leprosy and to observe the clinical, histopathological and microbiological evidence of disease after completion of therapy. ***Material & Method:*** The study group comprised of 50 leprosy patients in which 22 patients received WHO recommended MDT – PB regimen and 28 patients received MDT – MB regimen. The workiup of 50 patients before starting MDT and after completion of MDT was done through history, clinical examination of patients and histopathological examination of skin biopsies and slit skin smear for AFB. The PCR study for detection of M. Leprae DNA was performed in each patient who completed the MDT. ***Observation and Discussion:*** Study group comprised of 50 cases, among these 22 cases were of pancibacillary (TT 6, BT 16) and 28 cases were of multibacillary (BT 8, BB 2, BL 6, LL 12) leprosy. All the cases were treated according to WHO guidelines. After completion of therapy clinical evidence of disease was present in 14 patients (5 and 9 patients of PB & MB Leprosy each) whereas histopathological evidence of disease was present in 24 patients and Slit skin smear and PCR was found positive in 24 and 30 patients respectively. ***Summary & Conclusion:*** The response of MDT in leprosy patients vary with type and duration of MDT given in both PB & MB treatment groups as well as it also depends on initial bacterial loads of the patients.

Keywords: *MDT – PB Regimen*; *Leprosy*

INTRODUCTION

Leprosy is a chronic infections disease caused by mycobacterium leprae. The organism has a predilection for the nerves and skin. The infection may be evident by any or all of its cardinal features.

Hypopigmented patches 2. Partial or total loss of temperatures, touch and pain in the affected areas 3. Thickening, tenderness or both, of the peripheral nerves and 4. Presence of acid fast bacilli. Therapy of leprosy has undergone many changes in last 2 decades. Earlier treatment of leprosy was restricted to Dapsone mono therapy. It predisposed to emergence of secondary and subsequent primary Dapsone resistant mutants. To check the spread of drug resistant bacilli, WHO in 1982 introduced multidrug therapy (MDT).

MDT has been back bone of leprosy elimination strategy for last 20 years. It is effective in curing the disease and rendering the patient non infectious after a treatment of relatively short duration. MDT has been extremely well accepted all over the world resulting millions of patients became free from their disease, another millions escaped from troublesome deformities and many other from acquiring new infection due to a effective check on transmission of disease. Though effectiveness of MDT is extremely high, reports from various parts of world have raised the question on effectiveness of WHO- MDT. The ultimate significant test for effectiveness of MDT is and will be relapse rate. Therefore, the diagnosis of relapse in patients who have completed MDT is very important. Failure of MDT is reported from various parts of world as low as 077% to as high as 20% (Shetty *et al.*, 2001).

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Aims & Objective

Aim: To evaluate the therapeutic response of multidrug therapy regimens in cases of leprosy.

Objective: To study the effect of type and length of MDT on various clinical groups of leprosy and after completion of MDT, PCR assay targeting 36 KDa gene of *M. leprae* DNA was done to evaluate effectiveness of MDT.

MATERIALS & METHODS

The study was carried out in the department of skin, STD & leprosy, SMS Medical College & Hospitals, Jaipur which is tertiary care referral center for skin, STD & Leprosy patients. The study group comprised of 50 leprosy patients, 22 patients received WHO recommended MDT Paucibacllary regimen (WHO – MDT – PB) and 28 patients received multidrug therapy multibacillary regimen (WHO-MDT-MB). The work up of 50 patients before starting MDT & after completion of MDT was done via detailed history regarding age, sex, place of residence native place, marital status, occupation and socio economic status etc.

History of intra/extra familiar contact with leprosy patients was taken, details of treatment was noted. Clinical examination of all the 50 patients was done before starting MDT & after completion of MDT. Bacteriological examinations of slit skin smears was done after completion of MDT and histopathological examinations of skin biopsies were performed before starting and after completion of MDT. The PCR Study for detection of M. leprae DNA was performed in each patient who completed the MDT. The PCR study was done with the help of Central Institute of JALMA for Leprosy, Agra.

RESULTS AND DISCUSSION

Observations

50 patients of leprosy attending the outpatient department of dermatology, STD & leprosy of SMS Medical College Jaipur constituted the subject material of this study. The following observations were made –

The majority of the patients presented in between the age of 21-60 year. The peak incidence was observed in 31-40 year age groups. The males were predominantly affected than the females with a male: Female ratio of 2:1;1. More than 80% of patients were Hindus and less than 20% of patients were Muslims. The disease was most prevalent in poor socio- economic group. The source of infection could not be elicited in majority (82%) of the case studied. The duration of illness prior to attending the leprosy clinic was less than 1 year, Labourers (62%) constituted the major part of study.

Of 50 cases majority (48%) of patients had borderline tuberculoid leprosy while 24% patients were suffering from lepromalous leprosy 12% of the patients were suffering from tuberculoid and borderline lepromalous leprosy each and only 4%were suffering from borderline borderline leprosy (as shown in Table 1). Out of 50 cases 22 (44%) were treated with WHO- MDT-PB regimen and rest 28 (56%) cases were treated with the WHO- MDT- MB regimen.

In 22 patients who were put on WHO- MDT- PB regimen 27.7% cases had persisting disease activity on clinical examination after completion of MDT, most (80%) of these patients were those cases of BT leprosy who were treated with WHO- MDT-MB for 6 months. Clinical examination of 28 patients after completion of MDT who were put on WHO- MDT- MD regime revealed that 9 (28.12%) patients showed persisting disease activity after complete therapy.

Histopthological examination of 50 patients treated with MDT PB or MB regimen revealed that 24 (48%) of patients showed evidence of disease even after completion of therapy whereas slit skin smear was found positive in 4 (18.1%) out of 22 patients treated with MDT – PB regimen either for 6 months to 1 year and all these 4 cases were of BT leprosy.

Slit skin smear was found positive in 8 patients out of 28 who received MDT – MB regimen majority of these patients were those who had a high bacterial load and were treated for 1-2 years.

All the 50 patients after completion of therapy were subjected for PCR study and 30 (60%) patients had given positive PCR signals which was targeted for 36 K Da gene of M. Leprae. Majority of the PCR

positive patients in MDT- PB regimen group belonged to BT leprosy treated for a duration of 6 months or 1 year.

Table 1: Response of Two Types of MDT in Various Clinical Groups of Leprosy

Type of MDT Given	Clinical Type of Leprosy	No. of Cases	Active Lesion or Now Lesion Present		Positive Histo-Pathology of Skin		Smear Positivity in No. of Cases		PCR POS in No. of Cases	
			No. of Cases	%	No. of Cases	%	No. of Cases	%	No of Cases	%
PB	TT	6	1	16.66	2	33.33	-	-	3	50.00
	BT	16	4	25.00	8	50.50	4	25.00	10	62.50
MB	BT	8	1	12.50	5	62.50	1	12.50	4	50.00
	BB	2	1	50.00	1	50.00	-	-	2	100.00
	BL	6	2	33.33	2	33.33	2	33.33	4	66.66
	LL	12	5	41.66	6	50.00	5	41.66	7	58.33
TOTAL		**50**	**14**	**28.00**	**24**	**48.40**	**12**	**24.00**	**30**	**60.00**

Discussion

We studied 50 patients of leprosy who had undergone MDT. Among these the majority of the patients who had clinically active lesions after MDT were either the patients of BT leprosy treated with MDT PB regimen or the patients of BB, BL or LL Leprosy with MDT MB regimen for a short duration (i.e. 12 months). In lepromatous leprosy group, majority of the patients with persisting clinical activity were those, who had a high bacterial load (BI 4 + or more) before starting treatment.

After completion of MDT, biopsies were found positive in histopathological examination in 24 patients and smear positivity was found in 12 patients whereas PCR positivity was quite high in 30 patients. Vijay Vijayakumaran *et al.*, (1995) studied 360 MB leprosy, patients treated with 2 years MDT- MB regimen. The bacterial index (BI) was up to 2 + in 60.7% of them. They reported that majority (71.60%) of patients with an initial BI of up to 2 + become smear negative within 3 years after starting therapy (MDT), for those with a BI of > 2 + only 26.2% become smear negative within 3 years after starting therapy. In our study it was observed that in LL patients skin smears tend to be positive in all (100%) patients treated with MDT-MB for 1 year and (60%) patients treated with 2 years MDT-MB but after 3 years of MDT none of them was found smear positive. Similar findings were observed by Janet and Ji (1995) and Katoch *et al.*, (1997).

The PCR study targeting 36 K Da gene of M. Leprae DNA revealed that out of 50 patients treated with MDT 30 (60%) patients were PCR positive.

If we consider the PCR assay as a marker of viability of M. leprae than the result of PCR are contradictory with the WHO report of relapse rate of 0.77% (WHO, 1994) in MB patients. Further it is against the findings of very low relapse rate reported by many workers (Chen *et al.*, 1999 and Chopra *et al*., 1996).

In MB patients treated with MDT-MB, Santosh *et al.*, (1999) evaluated the patients and reported 50% PCR positivity. This finding roughly correlates with our study whereas Rafi *et al.*, (1995) reported PCR positivity in 25% cases which is quite low in comparison to our study.

The probable reason of higher percentage of PCR positivity in our study may be due to the fact that Majority of the patients in our study were with higher bacterial load before starting MDT hence they were found positive for PCR for M. Leprae DNA. After completion of MDT, Jamil *et al.*, (1993) also reported that there is a positive relation between initial higher bacterial load and PCR positivity after completion of the treatment.

Summary and Conclusion

1. The response of MDT in leprosy patients vary with type and duration of MDT given in both PB & MB treatment groups as well as it also depends on the initial bacterial load of the patients in MB leprosy treated with MDT MB regimen.

2. MDT for more than 2 years has a definite advantage over fixed duration treatment (i.e. MDT for 1 or 2 years); though many studies proved that the bacterial clearance tends to continue even after stopping of MDT, hence, it was concluded that in patients with initial higher bacterial load it is better to continue MDT for longer duration or up to smear negativity.

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