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Original Article

Study of 35 Cases of Hansen's Disease, which Required Treatment beyond Fixed Duration – Multi Drug Therapy

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Multi Drug Therapy (MDT) is the main weapon against leprosy since its inception in 1981. India achieved the level of elimination (<1 case/10,000) on 31st December 2005. It has been proved in few studies that despite 2 years of regular therapy10% of the patients continue to harbour viable persisters. There are many problems related with FD-MDT. Many cases have residual disease activity after completion of treatment. Aims of the present study was to study the profile of RFT cases in leprosy treated with FD-MDT, who required extended MDT, duration between completion of FD -MDT and clinical presentation, Acid Fast Bacilli (AFB) status, histopathology and type of leprosy at the time of presentation. A prospective study of 35 RFT (Released From Treatment) cases with signs of activity were recruited in period between May 2007 to November 2008. All cases were diagnosed clinically and investigations were done for AFB smear, histopathological examination and Fite Faraco staining. We found that all the 35 cases, which required extended MDT, age group ranged from 10 to 65 years. Majority (71.4%) had taken previous Multi-Bacillary (MB) treatment for 1 year duration. Eleven (31.42%) of cases came within one year, 17(48.57%) between one to two years and 7(20%) cases after two years of stopping FD-MDT. AFB smear was positive in 36.84% of cases in which done. Majority of previously diagnosed MB cases presented as BT/TT in histopathology. Thus there is need to search for reliable prognostic markers for therapeutic purposes.

Keywords : Leprosy, Multi Drug Therapy, Histopathological Examination

Introduction

Multi Drug Therapy (MDT) is the main weapon against leprosy since its inception in 1981. India achieved the level of elimination (<1 case/10,000) on 31st December 2005. Fifty nine percentage of new leprosy cases in the world were detected in India (WHO 2014). In 2013-14, a total of 1.27 new leprosy cases were detected in India (NLEP 2014). Chhattisgarh and Dadra & Nagar Haveli have still not achieved elimination (NLEP 2014).

It has been proved in a few studies that despite 2 years of regular therapy 10% of the patients continue to harbor viable persisters. Patients can be bacteriologically positive or negative, and bacteriologically negative patients can still be clinically active. New lesions after completion of

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Fixed drug - Multi Drug Therapy (FD-MDT) may be due to late reactions or relapse. Higher rates of relapse of almost 39% have been reported in a subgroup of patients with a large bacterial load [Bacillary Index (BI) ≥4+] treated with 24 months of standard MDT. It has been observed that higher the BI or shorter the duration of therapy, higher the risk of relapse (Malathi and Thappa 2013) .

There are many problems related with FD-MDT. Many cases have residual disease activity even after completion of treatment. In highly bacilliferous cases, fall of BI is slow and stopping treatment at a fixed point of time may not be desirable. In FD-MDT leprosy treatment is stopped without objective evidence of remission, for majority of cases this strategy works, but in a small number of cases disease activity may be continued even after stopping treatment. With FD -MDT bacteriological cure may be achieved but neurological and cutaneous symptoms may persist.

According to World Health Organization (WHO) relapse in leprosy is "the occurrence of new signs and symptoms of the disease during the period of surveillance or thereafter in a patient who successfully completes an adequate course of multidrug therapy (Ramu 1995). Relapse can be defined as an"increase in BI of 1+ or more at any site seen on two consecutive skin smear at a 6 month interval with or without evidence of clinical activity" (Shaw et al 2000).

Relapse of treated leprosy cases has recently emerged as a challenge after almost one and half decades of MDT implementation and release of more than 4 million patients from treatment. Now it has become necessary to review the risk of relapse following the recommended FD-MDT regimes. The reason for relapse in most cases was miscategorization of MB cases as PB cases due to poor techniques, resulting in inadequate treatment (Jacobson 1994). Chaudhari et al (1998) suggested that relapse is likely to be due to genetically predetermined impairment of bacteria clearing capacity of the macrophages.

Aims of the present study were to study the profile of RFT cases in leprosy treated with FD-MDT who required extended MDT, duration between completion of FD-MDT and clinical presentation suggestive of disease activity, Acid Fast Bacilli (AFB) status, histopathology and type of leprosy at the time of presentation.

Materials and Methods

A prospective study of 35 RFT (Released From Treatment) cases with signs of activity was carried out in the department of Skin-V.D of a tertiary care hospital between period May 2007 to November 2008.

Any case who completed an adequate course of FD- MDT and coming with new signs and symptoms of the disease either during surveillance period (5 years) or thereafter, due to persistence of disease activity at the end of 12 months was included in study. Criteria for inclusion were: clinically active lesions or development of new lesions, no falls in BI from initial on starting therapy or increase in BI and all cases having BI ≥2 on completion of FD-MDT.

All cases were diagnosed clinically on the basis of cardinal features of leprosy. AFB smear was done from eyebrows, earlobes and 2 active skin lesions. Biopsy was taken in cases having clinically active skin lesions or those who developed new lesions. Material was subjected to histopathological (HP) examination and Fite Faraco staining. Other investigations like routine hemogram, urine examination and X-ray chest were done before starting treatment.

All cases having sign of disease activity (not reaction) were restarted MDT and followed at regular interval of one month for six months.

Any change in size and number of skin lesions and sensory or motor dysfunction were noted and skin smear was taken at the end of six month. Physiotherapy was advised to all cases on preventive and curative basis.

Results

The study population consisted of 35 cases, which required extended MDT, age group ranged from 10 to 65 years.

Maximum number of patients were in 31-40 years of age group (Table 1) and there were 28 (80%) males and 7 (20%) females. Majority (71.4%) had taken previous Multi-Bacillary (MB) treatment for 1 year duration (Table 2 & 3).

Eleven (31.42%) cases came within one year, 17 (48.57%) between one to two year and 7 (20%)

Table 1 : Age - wise distribution in RFT cases, who required extended treatment

Age (In years)	Total (n=35)
0-10	01(2.86%)
11-20	03(8.57%)
21-30	06(17.14%)
31-40	11(31.42%)
41-50	08(22.85%)
51-60	05(14.28%)
61-70	01(2.86%)
Total	**35**

Table 2 : Details of treatment taken

Previous Treatment taken	RFT cases n=35
MB	25(71.4%)
PB	07(20%)
ROM +MB	-
MB+ IMMUVAC	
PB f/b MB	01(2.8%)
Only Dapsone	02(5.71%)
Total	**35**

Table 3 : Duration of previous treatment

Treatment taken	Duration	Total n = 35
MB	1 year	23
	2 year	01
	13 month	01
PB	6 month	07
PB f/by MB	1.5 year	01
Only Dapsone	2 year	02

Table 4 : Presenting complaint of RFT cases, who required extended treatment

Presenting complaint		No. of cases	Total No. of cases
Skin lesions	Active patches	22	25(71.42%)
	Erythematous papules & nodules	03	
Sensory			
	New comlaint of Tingling and numbness	01	03(8.57%)
	New loss of sensation with ulcers	02	
Motor (recent onset)			
	Claw hands	03	
	Foot drop	02	07(20)
	Eye problems	02	

Table 5 : Histopathological finding

Previous treatment taken	Type of leprosy in RFT cases, who required extended treatment				
	TT	BT	BB	BL	LL
MB(20/25)	09	10	0	01	0
PB(3/7)	01	01	01	0	0
Total	10	11	01	01	00

cases after two years of stopping FD-MDT. Out of 35, 25 cases (71.4%) presented with complaint of new skin lesions in form of active patches or erythematosus papules and nodules (Table 4).

AFB smear was taken in 19 out of 35 RFT cases. AFB smear was positive in 36.84% cases out of 19. Histopathology was done in 23 out of 35 cases, majority of previously diagnosed MB cases presented as BT/TT (Table 5). Family history was positive in only 2 cases.

All cases continued or restarted MDT treatment, leprosy vaccine (Immuvac) was given in two cases with BI>4. There were no new complaints on monthly follow up.

Discussion

FD-MDT works in majority of cases, but may be inadequate in small number of highly bacilliferous cases.

Kar and Sharma (2008) reported 28 cases of relapse, out of which, 11 were MB [1 Lepromatous Leprosy (LL), 6 Borderlin Leprosy (BL) and 4 Borderline Borderline leprosy (BB)] and 17 were PB (Pauci-Bacillari) [12 Borderline Tuberculoid (BT), 4 Tuberculoid (TT) and 1 Neuritic] at their first treatment.

According to Ramu (1995) 55 to 57% relapse occurred within 3 years in non-lepromatous, 5 years in borderline, 6 years in lepromatous after stopping MDT.

As compared to PB cases, more MB cases presented with new signs and symptoms of the disease in present study. Cases having initial high bacillary load or active lesions at end of therapy must be subjected to clinical, bacteriological and histopathological examination before stopping MDT.

Relapse rate is closely related with bacteriological index of patients, occurring more frequently among patients with BI $\geq$ 4 before MDT (Girdhar 2000). Waters et al reported 6 LL patients after long period of RFT and smear negativity were found to be relapse to BT leprosy (Waters and Ridley 1990).

Relapse among paucibacillary patients is difficult to diagnose because *Mycobacterium leprae* cannot be detected in these cases by AFB. Among multibacillary patients diagnostic confirmation is possible by means of slit-skin smear examination. Histopathological examination is useful for diagnosis and confirmation of relapse in both MB and PB cases. Ideally biopsies should be done once every 6 months from the same lesions (Job 1995).

Policy of stopping MDT without objective evaluation in all cases needs to be thoroughly debated. FD-MDT must be restarted only if there is clinical activity (in skin lesion or nerve) supplemented by bacteriological (BI >2+) or HP finding (active granuloma).

Inadequately treated cases can be the cause of further neurological deficit, with potential for emergence of drug resistance and resurgence of epidemic and by addition of immunotherapy reactions and relapses can be minimized. Tailoring of regimen and/or immunotherapy

may be helpful for cases with initial high bacillary load or active lesions at the completion of FD-MDT. Katoch et al (2004) reported that by the addition of immunotherapy duration of reactions reduced by 33% and there were no relapses in the 10-12 years follow-up period.

Rigorous annual follow-up for at least 3 years and even more for PB cases and 9 years and even more for MB cases must be strongly recommended (Ramu 1995).

References

1. Chaudhuri S, Hajra SK, Mukherjee A et al (1998). Why Relapse Occurs in PB leprosy Patients after Adequate MDT despite they are Mitsuda Reactive: Lessons form Convit's Experiment on Bacteria Clearing Capacity of Lepromin induced granuloma. *Int J Lepr Other Mycobact Dis*. **66**: 182-189.
2. Girdhar BK (2000). Relapse in MB leprosy patients, effect of length of therapy. *Lepr Rev.* **71**: 144-153.
3. Jacobson RR (1994). Treatment of Leprosy. In Robert C Hastings, Diltor VA Opromolla, editors Leprosy, Singapore, p332.
4. Job CK (1995). Histopathological features of relapsed leprosy. *Indian J Lepr*. **67**: 67-69.
5. Kar HK and Sharma P (2008). New lesions after MDT in PB and MB leprosy: A report of 28 cases. *Indian J Lepr*. **80**: 247-255.
6. Katoch KK, Katoch VM, Natrajan M et al (2004). 10-12 years follow-up of highly bacillated BL/LL leprosy patients on combined chemotherapy and immunotherapy. *Vaccine*. **22**: 3649-3657.
7. Malathi M and Thappa D (2013). Fixed-duration therapy in leprosy: Limitations and Opportunities. *Indian J Dermatol*. **58**: 93-100.
8. NLEP (2014). 'Progress Report for the year 2013-14 ending on 31st March 2014', Central Leprosy Division, Directorate General of Health Services, New Delhi.
9. Ramu G (1995). Clinical Features and Diagnosis of Relapses in Leprosy. *Indian J Lepr*. **67**: 45-59.
10. Shaw IN, Natrajan MM, Rao GS, et al (2000). Long-term follow up of multibacillary leprosy patients with high BI treated with WHO/MDT regimen for a fixed duration of two years. *Int J Lepr Other Mycobact Dis.* **68**: 405-409.
11. Waters MFR and Ridley DS (1990). Tuberculoid relapse in lepromatous leprosy. *Lepr Rev*. **14**: 353-365.
12. World Health Organization (2014). Weekly Epidemiological Record. **89**: 389-400.

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