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Original Research Article

Comparative study of uniform-MDT and WHO-MDT in pauci and multi bacillary leprosy patients over 18 months of observation

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ABSTRACT

Background: To determine the efficacy of the current WHO-MDT and U-MDT regimen with regard to relapse rate and acceptability of the patients and to compare both regimen in pauci and multi bacillary cases.
Methods: Total of 106 leprosy patients aged between 14-60 years attending department of Dermatology, Venerology and Leprosy at RIMS, Ranchi between May 2011 and October 2012 were included in the study and they were allocated alternatively into two groups, U-MDT and WHO-MDT. Patients were followed up for 12 to 18 months for periodic clinical, bacteriological and histopathological assessment.
Results: In histopathological assessment of PB cases, after 6, 12 and 18 months, UPB group showed 91%, 100% and 100% improvement as compared to 77.5%, 86.5% and 95.2% in WPB group. Among multi bacillary cases, after 12 months 32% of UMB group of patients became smear negative whereas in WMB group 48% became smear negative. In histopathological assessment after 12 months, in UMB group, 94% patients showed good improvement whereas in WMB group only 77% patients showed good improvement. After 18 months, in UMB group, 50% patients deteriorated and showed poor improvement whereas almost 100% patients showed good improvements in WMB group.
Conclusions: In conclusion, U-MDT was observed to be an effective and useful regimen to treat PB patients of leprosy, but in MB patients it was not found to be very effective regimen when compared to WHO-MDT of 12 months duration. Mere acceptability factor of the U-MDT regimen cannot be sufficient for its routine implementation in the general health service.

Keywords: Pauci and multibacillary leprosy, U- MDT, WHO- MDT

INTRODUCTION

Leprosy is a chronic disease caused by *Mycobacterium Leprae* affecting peripheral nervous system, skin and certain other tissues like respiratory and reticulo-endothelial system, testes and eyes and transmitted by nasal droplets. The Ridley-Jopling classification is based on clinical, histological, bacteriological and immunological parameters.[1] For treatment purposes, the WHO study group, in 1982, classified leprosy into two types: paucibacillary (PB) and multibacillary (MB) on the basis of number of patches on the skin and number of nerves involved.

PB patients have five or less than five patches and up to one nerve trunk involvement. WHO recommended a MDT regimen of two drugs and a MDT regimen of three drugs for PB and MB patients respectively.[2] The WHO

technical advisory group (TAG), in its third meeting in 2002 proposed that a uniform MDT regimen (U-MDT) containing three drugs (dapsone, clofazimine and rifampicin) should be considered for six months to treat all types of leprosy.[3]

The group felt that with WHO MDT being widely implemented with very low relapse rates and complete absence of emergence of M. leprae resistance, further shortening of and simplification of the MDT regimen by introducing Uniform MDT would lead to better sustainability of services after integration. To overcome the classification process in the field setup at times, Uniform MDT has been advocated.

Present study has assessed the efficacy of U-MDT regimen based on clinical parameters and compared it with existing MDT-PB and MDT-MB regimen. clofazimine containing regimen has an added advantage that the same drugs may be given for varying durations depending upon the clinical classification. Benefits of the regimen are simpler information system, reduced training needs and better sustainability and compliance of the patient. This study also helped to evaluate the clinical and histological advantage of adding clofazimine in PB patients. The TAG in 2003 came out with the basic protocol and proposed that it be implemented for all cases of leprosy.

METHODS

A total of 106 leprosy patients (77 male and 29 female) aged between 14-60 years attending department of Dermatology, Venerology and Leprosy Department at RIMS between May 2011 and October 2012 were included in the study.

Patients of PB and MB leprosy were allocated alternatively into two groups, Group U and Group W. Both PB and MB patients of group U were given U-MDT drug regimen for six months. Whereas patients of WPB group were given WHO MDT-PB for 6 months and patients of WMB group were given WHO MDT-MB for 12 months.

Patient information and details of clinical examination were recorded, and body charting done at initial registration and at the end of the study. Patients were followed up for a minimum period of 12 months and maximum period of 18 months after enrolment and periodic clinical assessment for changes in disease activity were made at specific intervals. Skin smears were taken from all three sites in all patients at entry, 6 and 12 months and stained with Zeihl Nelson's stain.

AFB were looked for and bacterial index (BI) were graded by Ridley's scale. Patients with lepra reaction (I and II) were hospitalized whenever necessary and treated appropriately.

Statistical analysis

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 20.0.1 and GraphPad Prism version 5.

Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests.

A chi-squared test (χ^2 test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by hi-square test or Fischer's exact test, as appropriate. Univariate analysis was performed by logistic regression method for calculation of risk factors.

Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

RESULTS

Incidence of leprosy in the present was 0.7%. Maximum numbers (40.05%) of patients were found in age group 31-40 years and most of them were males. At the time of entry, total 106 numbers of patients were included out of which 62 were in MB and 44 were in PB group. These patients were then alternatively divided in W and U group in both categories. When patients under study were clinically typed based on Ridley -Joplin's classification, BT patients were 12 out of 22 and 15 out of 22 in UPB and WPB groups respectively.

At each interval, the number of patients with higher scores went on decreasing in each group and number of patients with lower scores was more in UPB group than in WPB group. At all intervals, histopathological improvement was found to be more in UPB group as compared to WPB group (Table 1).

In UMB group, 48% patients were of BL type whereas in WMB group only 36% belonged to BL type. In both group, BL and LL type constituted the maximum number of patients.

At entry, total 42 patients were smear positive, all in MB group, with 19 in UMB group (61.2%) and 23 in WMB group (74%). All PB group patients were AFB negative.

The difference in the number of patients with AFB positive in BL group was statistically significant.

The BI ranged from 1+ to 6+ with maximum patients with BI 3+ in both UMB (31.6%) and WMB group (34.8%). none of the patients with negative smears at entry showed positive smears subsequently. As shown in Table 2, during clinical assessment after 6 months none of the patients showed good improvement in UMDT group as compared to 38% patients in WMDT group.

After 12 months, 4.5% patients in UMB group showed good improvement as compared to 45% in WMB group, whereas 64% of patients of WMB group showed poor improvement as compared to 16% in WMB group. These differences were statistically significant.

Table 1: Clinical, bacteriological and histopathological assessment of pauci-bacillary cases of leprosy patients who were treated with U-MDT and WHO-MDT regimen.

		UPB	WPB
Clinical assessment	**Clinical score**		
At admission	0-3	2	1
	4-6	3	4
	7-9	6	6
	10-12	8	7
	13-15	3	4
At 3 months	0-3	5	1
	4-6	6	4
	7-9	10	6
	10-12	1	7
	13-15	0	4
At 6 months	0-3	6	5
	4-6	9	7
	7-9	7	8
	10-12	0	2
	13-15	0	0
At 12 months	0-3	8	7
	4-6	11	10
	7-9	3	5
	10-12	0	0
	13-15	0	0
At 18 months	0-3	12	10
	4-6	8	10
	7-9	1	2
	10-12	0	0
	13-15	0	0
Histopathological assessment			
At entry	Cellularity	Lymphocytes++ Epitheloid cells+++ Giant cell+ BI 2+, >1+	Lymphocytes++ Epitheloid cells+++ Giant cell+ BI 2+, >1+
At 6 months (improvements)	Good	20/22	17/22
	No change	1/22	4/22
	Poor	1/22	1/22
At 12 months (improvements)	good	22/22	19/22
	No change	0	1/22
	Poor	0	2/22
At 18 months (improvements)	Good	22/22	20/21
	No change	0	1/21
	Poor	0	0

Table 2: Clinical, bacteriological and histopathological assessment of multi bacillary cases of leprosy patients who were treated with U-MDT and WHO-MDT regimen.

		UMB	WMB
Clinical assessment			
At entry	**No. of skin lesion**	**20 to numerous**	**20 to numerous**
	Infiltration	+	++
	Size of lesion	variable	variable
At 6 months (improvement)	Good	none	12/31
	Moderate	16/31	14/31
	Poor	17/31	6/31
At 12 months (improvement)	Good	2/31	14/31
	Moderate	10/31	12/31
	Poor	19/31	5/31
At 18 months (improvement)	Good	3/30	23/29
	Moderate	7/30	4/29
	Poor	20/30	2/29
Bacteriological assessment (AFB+)			
At admission		19/31	23/31
At 6 months		16/31	17/31
At 12 months		9/31	8/31
At 18 months		14/30	4/29
Histopathological assessment			
At entry	Cellularity	Lymphocytes +, macrophages++, epitheloid cells+++, giant cell-	Lymphocytes+, macrophages++, epitheloid cells+++, giant cell-
At 12 months	Good	29/31	24/31
	No change	1/31	1/31
	Poor	1/31	6/31
At 18 months	Good	15/30	29/29
	No change	-	-
	Poor	15/30	-

After 18 months, only 10% patients of UMB group showed good improvement as compared to 79% in WMB group. This difference was statistically significant. 67% of patients in UMB group showed poor improvement as compared to only 7% in WMB group which was statistically significant. At the time of bacteriological assessment, after 12 months, UMB group showed 32% improvement whereas WMB group showed 48% improvement. But after 18 months, in UMB group, 5 more patients became AFB positive whereas in WMB group, 65% patients showed improvement in their bacillary index. At histopathological assessment, after 12 months, in UMB group, 94% patients showed good improvement as compared to only 77% in WMB group. But at 18 months, in WMB group, 50% patients showed poor improvement which showed an increase in poor grading after 12months (3%). in WMB group, 100% patients showed good improvement after 18 months.

DISCUSSION

Number of patients attending RIMS dermatology OPD in 18 months span was 50445, out of which new leprosy cases were 363. As leprosy is a chronic illness and initially symptoms are less marked, leprosy patients present before clinician very late. Low incidence in Jharkhand was due to lack of conveyance, seasonal variation, low socio-economic status and unawareness about the diseases. It was consistent with studies done by Arora M et al.[4] Most of the patients were male. It may be due to high chances of contact among male due to social gathering and they are more active in reporting to health facility for seeking treatment.

In the present study it was found that the number of cases were maximum (58.5%) in multibacillary group and BT patients were more than TT group of patients. It was consistent with Mahajan VK, et al.[5] It was observed that at the time of admission maximum number of patients in UPB (36.3%) and WPB (32%) had scores in the range of 10-12.

After 3 months, in score range 0-3 and 4-6, there was 14% increase in number of patients in UPB as compared to only 9% in WPB group. In score range 7-9, there was 18% increase in number of patients in UPB as compared

to only 5% in WPB group. After 6, 12 and 18 months of follow up, it was seen that the number of patients with higher scores went on decreasing in each group and number of patients with lower score was continuously increasing.

Among multibacillary cases 90% patients belonged to BL and LL type. After 12 months 32% of UMB group of patients became smear negative whereas in WMB group 48% became smear negative. After 18 months, there was 65% improvement in WMB group but in UMB group, 5 patients deteriorated and AFB positive at the end of the study. Kaur I, et al, reported that at the end of 2 years, 39.7% patients became smear negative with bacillary index 4+ or more and 84.8% patients became smear negative with bacillary index 3+ or less.[6] Vara N et al, reported that at the end of 2 years of MDT, 61.8% patients with bacillary index <3+ before treatment, became smear negative.[7]

A comparison of clinical grades of response between the two groups showed that the percentages of good grades were consistently higher in the WMB group in 6, 12 and 18 months of the study (38%, 45% and 79%) whereas the UMB group did not have a single good grade at 6 months. More importantly, the percentage of poor grades in the study group was 49%, 64% and 67% at 6, 12 and 18 months respectively. Rao PN et al, showed that the numbers of moderate and good responses were 78% and 61% at 6 months, 86% and 94% at 18 months and 82% and 100% at 24 months in WPB and UPB respectively.[7] In histopathological assessment after 6, 12 and 18 months, UPB group showed 91%, 100% and 100% improvement as compared to 77.5%, 86.5% and 95.2% in WPB group. This showed better improvement in UPB group as compared to WHO-MDT group.[8]

In MB group, in clinical improvements grades, good responses in WMB group was 36%, 45% and 77% at 12, 18 and 24 months of the study, whereas in UMB group did not have a single good response at 12 and 18 months with poor response being 50%, 67% and 75% at 12, 18 and 24 months.[9] In histopathological assessment after 12 months, in UMB group, 94% patients showed good improvement whereas in WMB group only 77% patients showed good improvement.[10] After 18 months, in UMB group, 50% patients deteriorated and showed poor improvement whereas almost 100% patients showed good improvements in WMB group.

CONCLUSION

PB patients on U-MDT in the present study showed marginally better clinical grades compared to PB patients on WHO MDT, although the differences were not very much significant. The addition of clofazimine to the PB treatment regimen is an improvement over the available treatment schedule and it has the added advantage of being operationally more easily administered in the field. With the PB study group on U-MDT containing clofazimine showing better grades overall and continued higher response at 12 and 18 months compared to PB study group who were on WHO MDT-PB. This continued favourable response could be attributed to the depot action of clofazimine in the tissues. In the present study, it was observed that MB patients on U-MDT, showed a significantly poor response at all period of clinical assessment at 12 and 18 months in follow up compared to the patients on WHO-MDT. It was concluded that U-MDT was not adequate for these patients. Clearly there are grounds for concern regarding the reduction of the duration of treatment for MB patients from 24 to 12 months. As there are several reports of relapses in MB patients on MDT-MB of 12 and 24 months duration, further shortening of duration to 6 months should be considered with great caution and only if it is found to as effective as the present regimen of 12 months.

In conclusion, U-MDT was observed to be an effective and useful regimen to treat PB patients of leprosy, but in MB patients it was not found to be very effective regimen when compared to WHO-MDT of 12 months duration. Mere acceptability factor of the U-MDT regimen cannot be sufficient for its routine implementation in the general health service.

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