The efficacy and tolerability of rifampicin in Burmese patients with lepromatous leprosy(*)

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SUMMARY — Seventy-one Burmese adult patients with lepromatous leprosy were treated with various regimens of rifampicin monotherapy, 450 mg. daily for 60 days or 900 mg. once weekly for 12 weeks or 450 mg. daily for six months. Of the patients, 18 had relapsed after stopping DDS therapy, 20 were intolerant of DDS, 18 were DDS resistant and 15 had received no previous treatment.

Rifampicin produced a 75% reduction in the size of skin nodules in two thirds of the patients and a complete disappearance of nodules in the others. After one month drug treatment the MI fell to zero but the BI remained unchanged. The once weekly regimen was as effective as the daily treatment. Four patients had to be withdrawn due to ENL reactions.

Key words: Virchowian hanseniasis. Therapy. Rifampicin.

INTRODUCTION

Clinical relapse in patients with lepromatous leprosy (LL) has only recently been recognised as being a problem. Studies on Fagets original 22 LL patients showed that of the 13 who were still living, 10 cases had clinically relapsed after thirty years of DDS therapy. In Burma an unpublished study in 1974 at the Htaukkyant Leprosy Hospital showed that as many as 3.6% of the LL patients relapsed in one year after discontinuation of DDS.

Relapses can be due to resistance development, drug failure or discontinuation of drug therapy because of intolerance or non-compliance.

Rifampicin has been shown to be active against *M. leprae* in mice and in man (Rees *et al.* (5) Shepard *et al.* (7) Levy *et al.* (2) and so it was decided to investigate the effect of this drug in Burmese patients with LL, both previously untreated and in relapsed cases.

PATIENTS AND METHODS

Beginning in 1975, we treated 75 consecutive patients who presented with LL

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at the Leprosy Hospital Htaukkyant in Rangoon. On admission a case history was taken and a clinical examination made including routine blood tests (ESR, haemoglobin, total and differential WBC). In cases of doubt these blood tests were repeated after drug therapy. Six skin smears were taken from each patient and the bacteriological index (B.I.) and the morphological index (M.I.) were established and checked at monthly intervals subsequently.

On admission, stool samples were routinely examined and any intestinal parasitic infestation treated before antilepromatous therapy was instituted. Patients were examined at fortnightly intervals and a clinical evaluation of lesions was made.

Four patients did not complete the course of drug treatment but data are presented on all 71 patients. Patients were treated with various treatment regimens (see Table I).

Group A included 34 patients who received 450 mg rifampicin daily for 60 days. Of this group 8 were patients who had relapsed after stopping previous DDS therapy and 9 were patients intolerant to DDS, a further 9 were probably DDS resistant having shown no clinical response to a minimum of 3 years therapy, and the other 8 had not been previously treated.

Group B contained 36 patients, each of whom received 900 mg rifampicin once weekly for a period of 12 weeks. Ten of these patients were intolerant of DDS and 10 had relapsed after previous DDS therapy, 9 had not responded to a minimum of 3 years DDS therapy and 7 had received no previous treatment.

Group C contained only one patient, a woman with histoid leprosy who could not tolerate DDS and who was treated with 450 mg rifampicin daily for six months.

Once the patients had completed their course of rifampicin treatment they were given DDS 50 mg/day and followed up for at least 6 months.

RESULTS

Details of the initial and final stages of the individual patients in groups A and B are given in Tables 1-8.

In the patient in Group C the skin nodules diminished to about one quarter of their initial size within two months, after which no further clinical improvement occurred.

The four patients who could not complete the course of drug treatment all developed an ENL reaction (one in Group A and 3 in Group B) and all had histories of such reactions before rifampicin therapy was instituted. No unwanted effects of the drug were noted clinically or in laboratory examinations.

Our findings are that in Burmese patients with LL, rifampicin was effective in reducing the size of skin nodules by 75% in two thirds of our patients and in bringing about their complete disappearance in the others. After the first month of treatment the MI fell to zero but the BI remained at the same level. The most striking finding was that rifampicin produces clinical improvement more quickly than DDS or clofazimine.

DISCUSSIONS AND CONCLUSIONS

Rees *et al.* (6) have published data on the long term therapy of LL with rifampicin and showed that even after long term treatment viable organisms can still be detected. Hense the drug cannot be regarded as being the complete curative agent for LL. However, in view of the rapidity of clinical improvement (4) and the epidemiological implications of any diminution of transmission, (5, 7) it seems worthwhile to start treatment with rifampicin, in order to diminish the bacterial load and then to continue with another drug, if possible dapsone. There is a place for the continued use of rifampicin in patients who do not respond to dapsone or who have problems of drug intolerance.

In our study a 12 week treatment with 900 mg once weekly was as effective as 450 mg daily for 60 days. Recently Levy *et al.* (1) have shown that a single dose of 1200 mg is as effective as a single dose of 1500 mg or a 600 mg daily dose. Such dosage schemes would have a considerable impact on the economics of anti-leprosy chemotherapy.

Rifampicin cannot prevent the development of lepra reactions and since the BI showed no significant decline over a six month period, although the MI fell to zero within the first month, our data agree with those of Pattyn *et al.* (3) who studied M. leprae "persisters" after treatment with dapsone and rifampicin and concluded that these drugs are not capable of completely eliminating micro organisms after drug therapy of multibacillary forms of the disease.

Previously clofazimine was our drug of choice for patients who were intolerant of DDS or who were probably unresponsive to DDS therapy but in view of the darkish grey skin discolouration which developed and the slow Onset of action we now regard rifampicin as being the agent of choice for such cases.

TABLE 1

Dosage regimens employed

Patients	Rifampicin dosage	Patient chemotherapy history				
		Relapsed after stopping DDS therapy	Intolerant of DDS therapy	Resistant to DDS therapy	Previously untreated	TOTAL
Group A	450 mg/day for 60 days	8	9	9	8	34
Group B	900 mg/once weekly for 12 weeks	10	10	9	7	36
Group C	450 mg/day for 6 months	—	1	—	—	1
	Total	18	20	18	15	71

TABLE 2

The effect of Rimactane (Rifampicin) 450 mg x 60 days on lepromatous leprosy patients with clinical relapse following stoppage of D.D.S. therapy

Serial N.°	Sex	Age	N.° of years with leprosy	N.° of years with previous treatment	N.° of years with no treatment	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
							B.I.	M.I.	B.I.	M.I.	
1.	M	32	16	9	2	Histoid nodules all over the body	5.6	40%	5.2	0%	All nodules reduced in size to less than ¼ original size
2.	M	40	20	15	1	Fresh lesions as plaques all over body	5.2	35%	5.0	0%	
3.	M	35	11	10	1	Histoid nodules all over the body	3.3	40%	3.6	0%	—
4.	F	34	9	7	1	Histoid nodules all over body	4.5	45%	3.9	0%	—
5.	M	44	9	7	1	Nodules on ears and buttocks	4.9	40%	4.9	0%	—
6.	F	49	13	11	1	Nodules on buttocks	5.5	35%	5.4	0%	All nodules completely disappeared
7.	M	55	22	18	2	Fresh nodules on elbow & buttocks	5.6	40%	5.2	0%	—
8.	M	49	18	14	2	Fresh nodules on elbows	3.5	20%	3.2	0%	—

BI = Bacteriological index (Ridley's scale)
MI = approximate morphological index

TABLE 3

The effect of Rimactane (Rifampicin) 450 mg x 60 days on le promatous leprosy patients who cannot tolerate D.D.S. therapy

Serial N.°	Sex	Age	N.° of years with leprosy	N.° of years with treatment	N.° of years that cannot tolerate D.D.S. therapy	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
							B.I.	M.I.	B.I.	M.I.	
1.	M	37	20	18	3	ENL off and on	4.2	30%	4.0	0%	Skin lesions disappeared completely
2.	M	30	16	15	2	Fresh lesions on face and hands	4.4	25%	4.4	0%	—
3.	F	40	15	14	3	Fresh lesions on face & buttocks	4.5	25%	4.0	0%	—
4.	M	44	14	12	2	Lionine face	6	40%	6.0	0%	—
5.	M	59	17	15	3	Histoid nodules all over the body	5.5	35%	5.4	0%	Nodules reduced size to less than ¼ original size
6.	F	60	33	30	7	Infiltration all over the body	5.8	30%	5.4	0%	
7.	M	59	20	19	5	ENL off and on	5.4	30%	5.4	0%	
8.	M	58	16	13	3	ENL off and on	3.2	20%	3.2	0%	
9.	M	37	12	10	2	ENL off and on	4.2	5%	—	—	Cannot complete the courses as ENL was developed after 2 week therapy

ENL = Erythema Nodosum Leprosum

TABLE 4

The effect of Rimactane (Rifampicin) 450 mg x 60 days in lepromatous leprosy patients who showed no response to D.D.S. therapy (D.D.S. resistent cases).

Serial N.°	Sex	Age	N.° of years with disease	N.° of years with treatment	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
						B.I.	M.I.	B.I.	M.I.	
1.	M	33	12	10	Histoid like nodules all over body	5.2	40%	5.0	0%	All nodules get reduced in size to less than ¼ original size
2.	M	40	13	10	Histoid like nodules all over body	4.8	35%	4.5	0%	——
3.	M	44	12	11	Lionine faces	6.0	40%	6.0	0%	Clinically improved but lesions persist
4.	M	35	8	8	Nodules on face months duration	4.0	20%	4.0	0%	All nodules disappeared
5.	M	68	15	7	Nodules all over the body	5.5	30%	5.5	0%	Nodules reduced to half original size
6.	F	56	10	7	Histoid like nodules all over body	3.8	30%	3.5	0%	Nodule reduced to less than ¼ original size
7.	M	55	18	16	Lionine faces	5.8	35%	5.4	0%	Clinically improved
8.	M	55	13	6	Nodules all over the body	4.8	30%	4.4	0%	Nodules reduced in size to less than ½ original size
9.	F	60	14	13	Nodules all over the body	5.6	30%	5.4	0%	All nodules disappeared

TABLE 5

The effects of Rimactane (Rifampicin) 450 mg x 60 days on patients with untreated lepromatous leprosy

Serial N.°	Sex	Age	N.° of years with symptoms of leprosy	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
					B.I.	M.I.	B.I.	M.I.	
1.	M	33	2	Red raised lesions all over the body	3.8	40%	3.2	0%	All lesions get flattened
2.	M	38	2	Red nodules all over both ears	4.0	25%	4.0	0%	Nodules reduced to less than ¼ original size
3.	F	22	1	Raised erythematous patches all over the body	4.5	20%	4.2	0%	All lesions get subsided
4.	M	30	1	Red raised nodules all over the body	4.4	20%	4.0	0%	Nodules reduced to less than ½ original size
5.	F	34	1	Red raised nodules all over the body	3.5	10%	3.0	0%	All lesions get flattened and changed to normal skin colour
6.	M	22	2	Few small nodules all over the body	4.0	15%	4.0	0%	All nodules disappeared
7.	M	35	2	Raised red lesions especially in ears	3.3	15%	3.0	0%	All lesions changed to normal skin colour
8.	F	20	1	Raised erythematous patches all over the body	4.0	15%	4.0	0%	All lesions changed to normal skin colour

TABLE 6

The effect of Rimactane (Rifampicin) 900 mg weekly x 12 weeks on lepromatous leprosy patients with clinical relapse following stoppage of D.D.S. therapy

Serial N.°	Sex	Age	N.° of years with leprosy	N.° of years with previous treatment	N.° of years with no treatment	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
							B.I.	M.I.	B.I.	M.I.	
1.	M	47	16	10	4	Nodules all over the body 1 year	5.4	20%	5.6	0%	Skin nodules totally disappeared
2.	F	40	12	8	3	Histoid nodules all over body 6 months	4.6	20%	5.0	0%	— ditto —
3.	M	32	14	10	2	Small nodules in arms 3 months	2.2	10%	2.0	0%	— ditto —
4.	M	49	16	14	2	Small nodules on buttocks 4 months	3.6	20%	3.0	0%	— ditto —
5.	F	50	17	10	6	Nodules all over body 2 years	5.2	20%	5.0	0%	Nodules reduced to less than ½ original size
6.	M	44	19	10	4	Nodules all over body 1½ year	4.4	20%	4.2	0%	— ditto —
7.	M	36	15	9	4	Nodules all over body 3 years	4.0	20%	4.3	0%	— ditto —
8.	F	40	13	6	3	Histoid nodules all over body 2 years	3.8	25%	4.0	0%	— ditto —
9.	M	37	14	10	2	Histoid nodules all over body 1 year	4.4	20%	4.0	0%	— ditto —
10.	M	49	11	8	2	Small nodules all over body 1 year	5.2	20%	5.0	0%	— ditto —

TABLE 7

The effect of Rimactane (Rifampicin) 900 mg per week x 12 weeks on lepromatous leprosy patients who cannot tolerate D.D.S. therapy

Serial N.°	Sex	Age	N.° of years with leprosy	N.° of years with tr.	N.° of years that cannot tolerate D.D.S. therapy	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
							B.I.	M.I.	B.I.	M.I.	
1.	M	50	6	4	2	ENL reaction off and on	3.5	10%	3.5	0%	Developed ENL and cannot complete the course
2.	F	69	7	4	2	ENL off and on	4.4	5%	4.2	0%	— ditto —
3.	M	49	6	4	2	Small fresh nodules in ears	4.8	10%	4.3	0%	Small nodules disappeared completely
4.	M	29	9	5	1	Small nodules in body 6 months	5.2	10%	5.0	0%	— ditto —
5.	M	48	9	7	1	Histoid nodules all over the body 1 year	5.0	15%	5.0	0%	Nodules reduced to less than ½ original size
6.	F	44	10	9	2	Histoid nodules all over the body 1 year	5.2	20%	5.0	0%	— ditto —
7.	M	39	9	5	2	ENL off and on nodules all over body 1 year	4.4	10%	4.4	0%	— ditto — no more ENL
8.	F	50	10	8	2	Nodules all over both arms 1 year	3.4	10%	3.0	0%	— ditto —
9.	M	30	10	7	2	Nodules all over buttocks 1 year	3.6	10%	3.4	0%	— ditto —
10.	M	43	10	7	1	ENL off and on with nodules all over buttocks 2 years	4.6	10%	4.4	0%	— ditto — no more ENL

TABLE 8

The effect of Rimactane (Rifampicin) 900 mg per week x 12 weeks on lepromatous leprosy patients who showed no response to D.D.S. therapy (? D.D.S. resistant cases).

Serial N.°	Sex	Age	N.° of years with disease	N.° of years with treatment	Clinical status of the patient before therapy	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
						B.I.	M.I.	B.I.	M.I.	
1.	M	49	20	18	Nodules all over the body with ENL off and on	4.4	10%	4.0	0%	Cannot complete the course as the patient developed severe ENL
2.	M	44	27	12	Histoid nodules all over buttocks 2 years	4.2	30%	4.0	0%	All nodules reduced to less than ¼ original size
3.	M	36	20	13	Nodules all over both elbows 1 year	3.8	25%	4.0	0%	— ditto —
4.	F	38	16	10	Small nodules all over body 2 years	5.2	20%	5.0	0%	— ditto —
5.	F	59	20	13	Nodules all over ears 6 months	4.0	20%	3.8	0%	— ditto —
6.	M	60	22	18	Histoid nodules all over body 3 years	5.0	25%	5.0	0%	— ditto —
7.	M	55	13	10	Fresh nodules on elbows 1 year	3.6	20%	3.0	0%	— ditto —
8.	M	45	13	11	Histoid nodules on buttocks 6 months	4.4	25%	4.4	0%	— ditto —
9.	M	39	10	10	Nodules all over the body 2 years	5.0	20%	5.2	0%	— ditto —

TABLE 9

The effect of Rimactane (Rifampicin) 900 mg per week x 12 weeks on patients with untreated lepromatous leprosy

Serial N.°	Sex	Age	N.° of years with signs & symptoms of leprosy	Clinical status of the patient	Bacteriological status of the patient before therapy		Bacteriological status of the patient after therapy		Clinical remarks
					B.I.	M.I.	B.I.	M.I.	
1.	M	22	1	Raised erythematous plaques all over the body	2.8	25%	2.8	0%	All skin lesions get flattened and smooth
2.	F	25	1½	Nodules in both ears	4.0	5%	4.0	0%	— ditto —
3.	M	37	3	Nodules on arms and ears	5.2	10%	5.0	0%	Nodules reduced to less than ¼ the original size
4.	M	50	2	Nodules all over the body	4.3	10%	4.6	0%	— ditto —
5.	F	44	1	Nodules in ears and hands	3.8	10%	4.0	0%	— ditto —
6.	M	28	1½	Plaques all over the body	4.4	10%	4.6	0%	— ditto —
7.	M	53	2	Nodules all over the body	5.4	10%	5.0	0%	— ditto —

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