REACTIONS IN LEPROSY WITH VARIOUS DOSES OF DAPSONE

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It is well known that the incidence of reactions in leprosy has increased since the advent of sulphones, the effective chemotherapy for leprosy. If the effectiveness of a drug is to be judged by its ability to render the maximum number of bacilli fragmented within a short period of time, dapsone is unrivalled in this respect. But unfortunately at a time when patients get maximum benifits of the therapy from clinical and bacteriological stand points, the reaction in leprosy occurs in a significant proportion of cases and it seriously interferes with further effective chemotherapy. It has been for a long time believed that the dose of dapsone has some relation to the incidence of reactions in leprosy.

To find out the optimum dosage schedule which would minimize the incidence of reactions, trials with varying deses of dapsone were undertaken in patients suffering from lepromatous leprosy.

The specific aims of the investigations were to find out:—

(1) Whether the incidence of reactions varies with different rates of induction of dapsone, starting with small and high doses, and

(2) Whether the onset of first reaction after the commencement of treatment has any relation to the dosage of dapsone.

MATERIALS AND METHODS

271 patients typed as leprosy (2) attending the out patient clinic of the Acworth Leprosy Hospital, Wadala, Bombay, were the subjects for the study. Patients with nodular lesions, with skin smears showing large numbers of acid fast becilli in singles and bunches and showing negative lepromin reaction were selected and started on the following dosage schedule.

TABLE No. 1.*

Dose Shedule of Dapsone.

Initial Dose	Slow Induction	Rapid Induction.
25 mgm. daily	Increased by 25 mgm. every 3 months to 100 mgm. daily.	Increased every month instead of every 3 monts. 100 mgm daily
25 mgm. alternate days.	Increased by 25 mgm. every 3 months to 200 mgm. three times a week.	-do-
10 mgm. daily	Increased by 10 mgm. every 3 months to 100 mgm daily	-do-
10 mgm. alternate days.	Increased by 10 mgm every 3 months to 200 mgm. three times a week.	-do-

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(*It should be noted that a patient on rapid induction with 25 mgm daily initial dose reaches the maximum of 600 mgm. per week in the fourth nonth, where as a patient on slow induction with a starting dose of 10 mgm. on alternate days reaches the maximum dose of 600 mgm. per week only at the end of 4 years and 9 months; the patients in the other groups falling in between these two extremes).

In all the groups the maximum dose was 600 mgm per week which was maintained during the remaining period of trial, unless the patient developed a reaction which necessitated reduction in the dose or withdrawal of dapsone altogether.

The follow-up included periodical clinical and bacterial assessments with special reference to incidence of reactions. The diagnosis of reaction was made on the clinical grounds. i.e. by the appearance of rose spot nodules (Erythema Nodosum Leprosum) associated with or without neuralgia, arthralgia, and pyrexia.

RESULTS AND COMMENTS

Table No 2 shows the incidence of reactions in the different groups of dapsone treatment encountered during the follow-up ranging from one month to 84 months.

TABLE No. 2

Incidence of Reaction in different groups.

	Slow Induction			Rapid Induction.		
	Total cases.	Reaction cases.	% Reaction cases	Total cases.	Reaction cases	% Reaction case
25 mgm. daily	30	9	30.00	26	11	42.31
25 mgm. alternate days.	45	11	24.54	28	8	28.57
10 mgm. daily	43	9	20 93	28	6	21.43
10 mgm. alternate days.	41	6	14 63	30	10	33.33
Total	159	35	21.01	112	35	31.25

The above table shows that :-

1) The over all incidence of reactions with various doses of dapsone in the slow induction group is less (21.01 per cent) than in the rapid induction group (31.25 per cent)

2) When the same does is given on alternate days, the percentage of reactions is less except in the case of 10 mgm. on alternate days with rapid induction which is higher (33.33 percent) than the daily dose (21.43). No explanation could be attributed to this increase in the percentage.

3) The incidence of reactions is less with smaller doses than with higher doses in the slow as well as in the rapid induction groups except with the dose of 10 mgm on alternate days in the rapid induction group.

4) When same dose was given in two different rates of the induction, percentages of reaction cases were less in slow inducotion than in rapid induction.

The following table shows the onset of first reactions in the different groups with reference to the period of regular treatment.

TABLE No. 3

Incidence of Reactions in relation to the period of treatment.

Period of treatment in months	Slow Induction					Rapid Induction					
	25 mgm.		10 mgm.		Total	25 mgm.		10mgm.		Total	Grand Total.
	Daily	Alter-nate days	Daily	Alter-nate days		Daily	Alter-nate days	Daily	Alter nate days		
1-6	1	7	1	1	10	3	2	2	2	9	19
7-12	6	3	2	3	14	4	3	2	4	13	27
13-18	–	1	2	2	5	2	–	1	4	7	12
19-36	2	–	4	–	6	2	3	1	–	6	12
37-84	–	–	–	–	–	–	–	–	–	–	–
Total	9	11	9	6	35	11	8	6	10	35	70

The table shows that :-

1) The maximum number of reactions occured within 6 and 12 months of treatment. (24 reactions out of 35 reactions)

2) There were no reactions after 3 years of treatment in any group.

3) The majority of reactions occured during the first year of treatment in both rapid and slow induction schedule.

4) In one patient first reaction occured within one month with the dose of 10 mgm. and in two with 25 mgm. This fact shows that irrespective of the dose of dapsone reactions may be encountered within a very short period after the commencement of treatment, if the patient is a susceptible individual.

The following table shows the number of followed up cases and follow up period in the different groups.

TABLE No. 4.

Period of Follow up Cases.

Follow up period in months.	Slow Induction (No. of Cases 112)					Rapid Induction (No. of Cases 159)					Grand.
	25 mgm.		10 mgm.			25 mgm.		10 mgm.			
	Daily	Alter-nate days	Daily	Alter-nate days	Total	Daily	Alter-nate daps	Daily	Alter-nate days	Total	
1-6	30	45	43	41	159	26	28	28	30	112	271
7-12	20	24	27	27	98	20	18	23	21	82	180
13-18	10	17	23	20	70	14	12	19	14	59	129
19 36	7	10	18	13	48	12	9	15	9	45	93
37-84	2	3	4	5	14	5	–	7	2	14	28

It is seen that as the period of follow up increases the number of cases followed up regularly declines in all the groups.

As very few reactions have occured beyond one and half years and also the number of patients followed up beyond this period is much less, a comparison of these percentage of reactions seen beyond this period of follow up in different grougs cannot be made.

It must however be noted that in certain groups namely in Slow Induction (25 mgm. alternate days, 10 mgm. daily, 10 mgm. alternate days and (In Rapid Induction 10 mgm. alternate days,) the maximum dose of 600 mgm. per week would not have been reached at the end of one and half years.

Correlation between concentration of dapsone in the blood and excretion in the urine.

In an earlier investigation (Ganapati & Naik, 1968) it was found that the urinary excretory pattern of dapsone is different in different individuals as shown by 24 hour urinary excretion test following an oral test dose of 100 mgm of dapsone. The cases of reaction investigated in that study were observed to fall in the excretion range of 30 to 55 mgm.

Fourteen patients (nine with reactions) in the present trials with Rapid and Slow Induction who were available were investigated from this point of view. The following table shows the excretion of dapsone in the urine during 24 hours and its concentration in the blood, 24 hours after a test dose of 100 mgm. orally of these cases.

TABLE No. 5.

Sr. No.	Dose & Induction	Excretion of dapsone in the urine in 24 hours in mgms	Concentration of dapsone in the blood after 24 hrs mgm/p.c.	Remark.
1	Slow 25 mgm. daily	55.72	0.5517	Reaction
2	,, ,, ,, ,,	38.71	0 2331	,,
3	,, ,, ,, ,,	45.89	0.4138	,,
4	,, ,, ,, ,,	39.23	0.2931	Reaction
5	,, 10 ,, ,,	18.00	—	No Reaction
6	,, 10 ,, alternate days	45 34	0.2241	,,
7	,, 10 ,, ,, ,,	52.17	0.3104	,,
8	Rapid 10 mgm. alternate days	44 17	0.3362	No Reaction
9	,, ,, ,, ,, ,,	65.28	0.2241	Reaction
10	,, ,, ,, ,, ,,	36.77	0.1724	No Reaction
11	,, 10 mgm. daily ,,	32.82	0.3103	Reaction
12	,, ,, ,, ,, ,,	43 96	—	No Reaction
13	,, 25 mgm. daily ,,	32.37	0.3448	Reaction
14	,, ,, ,, ,, ,,	50.06	0.4731	Reaction

From the above table it can be seen that there are reactions in cases who are fast and slow excretors of dapsone in the urine as well as those with high and low concentration of the drug in the blood in the group of the slow as well as the rapid induction of dapsone.

It seems probable, therefore, that the rate of excretion of dapsone might not be related to the occurrence of reaction.

SUMMARY

271 patients suffering from lepromatous leprosy were treated with varying doses of dapsone at various initial dosage levels and different rates of induction reaching to a maximum of 600 mgms of dapsone weekly with a view to study the relation of reaction in leprosy to the various doses of dapsone with slow and rapid induction ("slow induction" meaning increasing the dose every three months and "rapid induction" meaning raising the dose every month).

During the follow up period ranging from one month to 84 months the incidence of reactions in the group of patients under rapid induction was 31.25–percent (35 out of 112), while in the group with slow induction was 21 0 (35 out of 119).

The maximum reactions occured during 7 months to 12 months from the commencement of treatment. The majority of reactions were encountered within the first year of treatment. In none of the groups were there cases of reactions after 3 years of treatment.

The fact that small daily doses of dapsone such as 10 mgm. or even less provoke reaction within a period of one month's treatment in some patients shows that irrespective of the dosage, reactions may be encountered within a very short period after the commencement of treatment provided the patient is a susceptible individual. Yet a schedule of 10 mgm dose on alternate days with a gradual increase would appear to give much less reactions than other doses.

It was observed that in some cases, (only 14 cases were available for these tests) concentration level of dapsone in the blood and its rate of excretion in the urine had no relation to the occurence of reactions in the different groups.

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