Blind Trial of Weekly Doses of Sulforthomidine (Fanasil [Roche]) and Disulone in Lepromatous Leprosy

Comparison of Results after Thirty Months of Treatment

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There is agreement in the results obtained by numerous research workers in the treatment of tuberculoid leprosy with long-acting sulfonamides; clinical cure is rapidly obtained and complications and relapses are less common than with the sulfone treatment. In lepromatous leprosy the results are less clear cut. According to some, sulfonamides, such as sulfadimethoxin, sulfamethoxypyridazine and sulformethoxin are superior to Disulone (DDS), but according to others are as effective as, or less effective than, this drug.

In 1966 ([6]) and in 1967 at the Chemotherapy Congress in Vienna ([5]), we reported our first conclusions on a controlled treatment trial carried out on 25 patients (13 lepromatous and 12 tuberculoid), aged between 20 and 35, at the height of the disease, none of whom had ever received any treatment prior to their arrival at the Institut Marchoux. We wanted to obtain a necessary and sufficient sulfonamidemia of 30 mgm. per liter of the blood total, and after a number of tests carried out by Pharmacien Colonel J. Clary, we decided on *an oral dose of 1.5 gm. over a weekly cycle* (Figs. 1, 2). After 36 months of treatment, we had obtained the following clinical and bacteriologic results: *In all the tuberculoid patients the disease was rendered inactive. Of the 13 lepromatous patients, the disease was rendered inactive in 6 (i.e., 46%).*

Erythema nodosum occurred in four lepromatous patients, but the reactions were benign and rapidly checked; at no time did they warrant stopping the specific treatment. Tolerance of the drug, checked monthly, was complete. At the same time we studied a sample of 25 lepromatous patients and 25 tuberculoid patients. After the same three years' treatment, only in four lepromatous (16%) and nine tuberculoid (36%) patients had the disease been rendered inactive. We continued the treatment of the patients in our first experiment for an additional two years, and the percentage of lepromatous patients in which the disease had been rendered inactive was 59 per cent after five years' treatment.

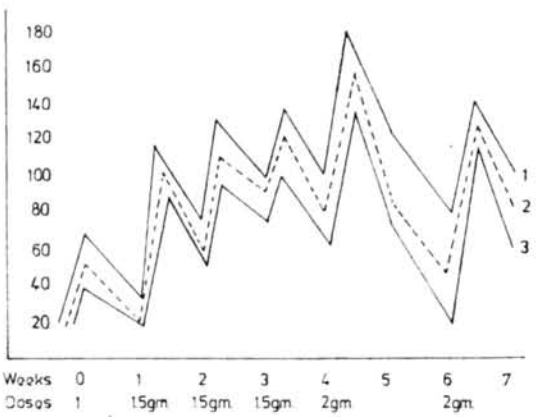

FIG. 1. Dosages of sulfonamide during seven weeks.

SULFONAMIDES: maximum 1, mean 2, minimum 3

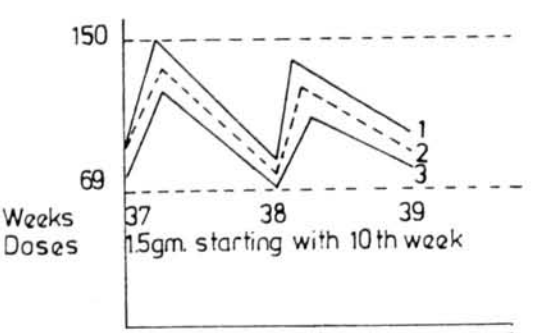

FIG. 2. Dosages of sulfonamide after tenth week.

SULFONAMIDES: maximum 1, mean 2, minimum 3

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However, no double blind trial had been carried out, except for our experiment "Ciego" published in 1967 in the Comptes Rendus Trimestriels of the Institut Marchoux. We demonstrated, after three years of treatment, the clinical and bacteriologic superiority of sulfonamides, especially Fanasil, in lepromatous leprosy (Figs. 3 and 4).

The aim of the study reported here was to make a "double blind" comparison between the therapeutic effects of 200 mgm. and 600 mgm. of DDS, and 500 mgm. and 1500 mgm. of Fanasil given once per week. We chose 40 typical lepromatous patients [diagnosis confirmed by histopathology (Form LL, Mitsuda-negative)] who had never received any treatment previously. The patients, aged between 20 and 35, were numbered 1 to 40 according to the date of their admission to the Institut Marchoux at Bamako. The drugs were placed in boxes numbered 1 to 40, each containing 200 tablets (70 mgm. or 200 mgm. of DDS; 170 mgm. or 500 mgm. of Fanasil). The patients were allocated to one of these four groups by statistical methods. During the trial, all the patients lived in the village at the Institut Marchoux. They were examined once a week when the drugs were administered (3 tablets). The criteria used were similar to those proposed by Pettit and Rees.

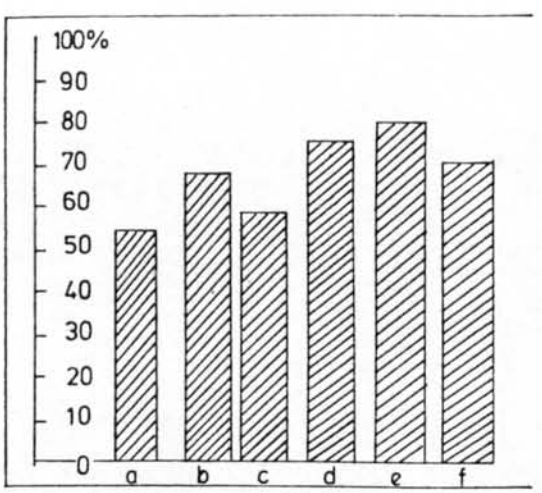

FIG. 3. Clinical improvement with several drugs in lepromatous form.[a]

[a] a, Disulone (DDS); b, Acetylazide; c, Ciba 1906; d, Sultirene; e, Fanasil; f, Madribon.

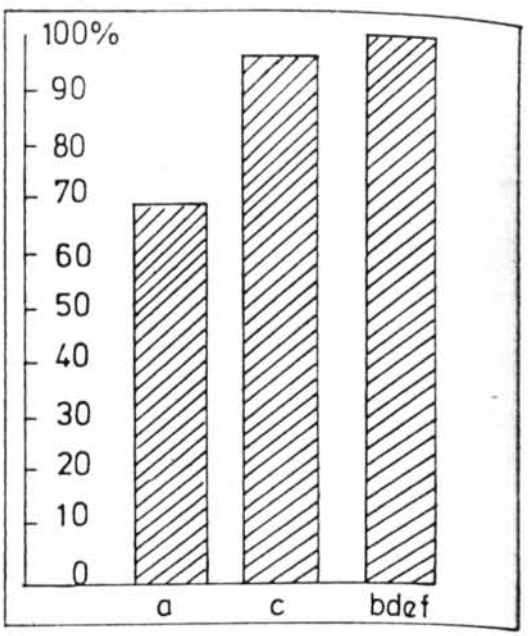

FIG. 4. Clinical improvement with several drugs in tuberculoid form.[a]

[a] a, Disulone (DDS); b, Acetylazide; c, Ciba 1906; d, Sultirene; e, Fanasil; f, Madribon.

The results obtained for the four groups after 30 months of treatment refer only to 36 typical lepromatous patients. Three of the patients were in fact paralepromatous, i.e., clinically and histologically very close to the lepromatous patients, but they improved clinically and bacteriologically very rapidly after passing through a borderline transformation, had turned white by the 16th month, and were therefore excluded. The fourth patient died of a pulmonary disorder unconnected with leprosy.

Table I shows how four groups of 10 lepromatous patients each were treated once a week for 30 months, either with 200 mgm. or 600 mgm. of DDS or with 500 mgm or 1500 mgm. of Fanasil. Table 2 shows how we established the clinical evaluation and the bacteriologic evaluation (calculation of bacillary index BI). Fig. 5 shows the clinical results obtained: viz., superiority of heavy doses over weak doses, and superiority of Fanasil over Disulone. The results were confirmed bacteriological-

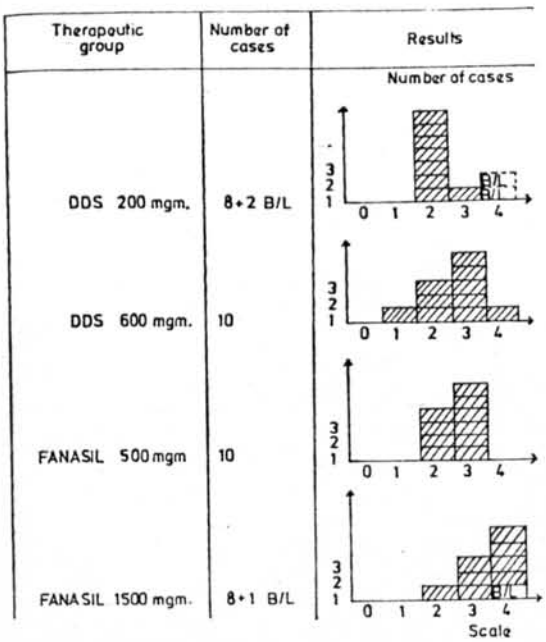

FIG. 5. Clinical results obtained in the four groups after 30 months of treatment covering 36 lepromatous and three borderline patients. Clinical improvement scaled from 0 to 4.

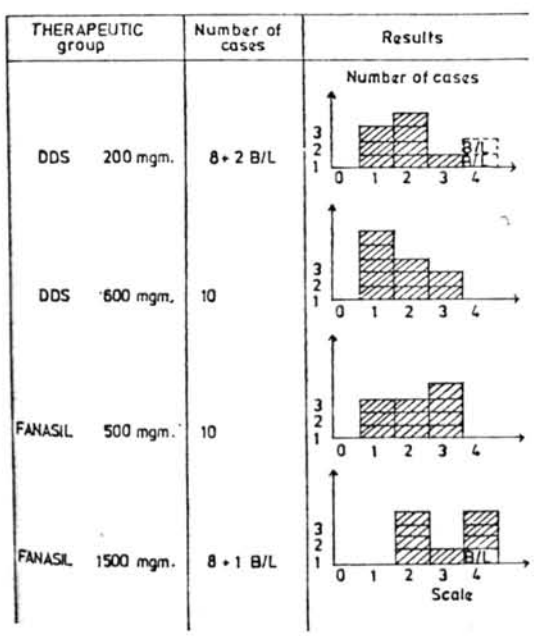

FIG. 6. Bacteriologic results obtained in the four groups after 30 months of treatment covering 36 lepromatous and three borderline patients. Improvement scaled from 0 to 4.

TABLE 1. *Double blind trial of Fanasil compared with Disulone (DDS)*

Four groups of lepromatous patients treated with:		
DDS	200 mgm.	once per week for 30 months
	600 mgm.	
FANASIL	500 mgm.	once per week for 30 months
	1500 mgm.	

ly (Fig. 6). If the individual clinical and bacteriologic rates of improvement are added together, the effect of Fanasil also is shown to be superior to that of the matrix-sulfonate (Table 3). Table 4 is a comparative table showing the frequency of lepra reaction.

There is a remarkable difference between Fanasil and DDS. Whereas a total of 13 reactions was noted with Disulone, the number of reactions with Fanasil was only seven. The same difference has been observed with other sulfonamides. Moreover, Fanasil has a particularly good tolerance; we have never come across a single case of intolerance (hematologic, hepatic or cu-

TABLE 2. *Evaluation of results of treatment as recorded in Table 1 and Fig. 5.*

A. Clinical evaluation: cutaneous lesions	Scale
Disappeared	4
Marked improvement	3
Average improvement	2
Slight improvement	1
No improvement	0
B. Bacteriologic evaluation: bacillary index	**Scale**
Negative B.I.	4
Marked reduction in B.I.	3
Moderate reduction in B.I.	2
Slight reduction in B.I.	1
No change in B.I.	0

TABLE 3. *Results for the 35 lepromatous and four borderline patients if the evaluations of clinical and bacteriologic improvement are added together.*

Cases receiving 200 mgm DDS	Cases receiving 600 mgm DDS	Cases receiving 500 mgm Fanasil	Cases receiving 1500 mgm Fanasil
(8)	7	6	(8)
(8)	6	6	8
6	5	6	8
4	4	6	8
4	4	4	7
4	4	4	5
4	4	4	5
3	3	4	5
3	3	4	4
3	3	3	—
General average 3.87	4.3	4.7	6.2

taneous) in more than 150 cases treated with Fanasil and more than 500 cases treated with other sulfonamides (sulfadimethoxin, sulfamethoxypyridazine, acetyl sulfamethoxypyrazine, etc.).

SUMMARY

On the basis of a double blind trial, comparing the therapeutic effect of Fanasil with that of the matrix-sulfonate in lepromatous leprosy, it appears that Fanasil is more effective and produces fewer leprosy reactions than Disulone. In general, Fanasil is tolerated better than DDS, which is an advantage in the treatment of leprosy. Fanasil is particularly effective with the tuberculoid forms. In less than three years, the disease was rendered inactive in 100 per cent of our patients. This is important in Africa, where 90 per cent of the patients are suffering from this allergic form.

We should also like to draw attention to the fact that Fanasil is administered once a week. This weekly method of administration is particularly attractive in French-speaking Africa, where more than 700,000 patients are scattered over vast areas.

All these points provide grounds for believing that, at the present time, Fanasil is the best drug for the mass treatment of leprosy in Africa.

TABLE 4. *Frequency of lepra reaction during the 24 months of treatment.*

Number of patients receiving:		Number of cases with leprosy reactions
DDS	200 mgm./week 10	7
	600 mgm./week 10	6
FANASIL	500 mgm./week 10	4
	1500 mgm./week 9	3

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