

TREATMENT OF LEPROSY WITH 'SULFON-CILAG'

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In this short paper the results of 19 months therapy of cases of lepromatous leprosy with 'Sulfon-Cilag,' administered parenterally is presented.

The Drug: Sulfon-Cilag is a derivative of the parent substance, diamino diphenyl sulphone (DDS) with the structural formula,



The sulphone -N-acetate molecule contains 75.6% of DDS. This substance is water soluble and the Ph of the injectible solution of Sulfon-Cilag is 7.3 to 7.7.

The special advantage of this new sulphone derivative appears to be the utilisation of the bactericidal properties of the active substance under favourable conditions of toxicity. The glucose-bisulphite complex for bacteriological agents is considered unsuitable since relatively energy-rich substances like sugar, alcohol, etc., by promoting oxidative processes in bacterial cells may oppose the inhibitory action of the chemotherapeutic agent on the proliferative apparatus of the bacteria. On the other hand, with Sulfon-Cilag, it is claimed, that by virtue of the low energy grade of its carrier substance, its ability to release the reductive processes and thereby have an inhibitory action on bacterial proliferation will be more pronounced.

THE MATERIAL

Fourteen cases, all adults, of lepromatous leprosy of varying severity were chosen for the investigation. All these cases, except one, had been treated previously either with hydnocarpus remedies, or one or other of the sulphone group of drugs.

THE METHOD

The 14 patients chosen for this investigation were divided into three groups, A, B, and C. Group A, consisting of 6 patients, was treated with daily injections of Sulfon-Cilag, 5cc intravenously leaving out Sundays. Group B, comprising 4 patients, was given 10cc of Sulfon-Cilag subcutaneously twice a week. Group C, with 4 patients, was treated with 5cc of Sulfon-Cilag subcutaneously every day for 6 days in the week.

THE DOSAGE

Sulfon-Cilag was supplied in ampoules of 5cc containing 0.5G of the active substance. Even though the manufacturers of this drug suggested a daily dose of 1G intravenously, slowly increasing it to 2.5G daily, it was considered advisable to plan out the investigation with groups of patients who received the drug by two different routes and in three different dosages. Taking into consideration the very high DDS content of this drug (75.6%), a dose of 0.5G Sulfon-Cilag intravenously or subcutaneously every day was considered suitable and safe. In addition a third group was added wherein the patients were given 10cc of Sulfon-Cilag (1G) subcutaneously twice a week. The drug was administered continuously without rest periods so long as supplies were available.

THE RESULTS

Clinical trials with the drug were commenced in March 1949 and patients were treated for periods varying from 1.0 to 18.5 months. The treatment has to be discontinued for two months for groups A and C owing to lack of supply of the drug. It should be mentioned here that in spite of the break of two months in treatment, there was no deterioration in the patients' clinical condition during that period nor was there any untoward effect when treatment was recommenced.

(a) *Clinical*

It was the general impression that the drug produced perceptible clinical improvement in most of the cases. There was subsidence of infiltration in the lesions, and nodules showed considerable shrinking, leaving behind loose, redundant skin. It was such favourable results which kept the patients so regular in attendance.

(b) *Bacteriological*

It was obvious that the improvement in the bacteriological status of the patient was not commensurate with the clinical improvement. Secondly, while four cases were 'much improved' bacteriologically, only one became 'negative.'

INCIDENCE OF COMPLICATIONS

The general impression about Sulfon-Cilag was that it was very well tolerated by most of the patients. Out of the 14 cases treated for periods varying from 1.0 month to 18.5 months, (a) severe and intractable neuritis was seen in one patient (A3); (b) severe lepra reaction in two cases (A4 and B3); and (c) anaemia of moderate severity developed in one case (C4). In case (A3), the neuritis affecting the right ulnar was so very severe that the patient stopped away from treatment.

CASE HISTORIES.

GROUP A—5cc Sulfon-Cilag intravenously every day for 6 days in the week.

Patient A1. Hindu, male, 29 years. A case of moderate leproma of 9 years' duration. Had previous treatment with Hydnocarpus remedies, indigenous drugs, Promin, Soluthoizole and Diasone.

Commenced treatment with Sulfon-Cilag on 14-3-1949 with a bacteriological index of 1.06. Continued treatment regularly except for a break of two months when supplies of the drug ran out. Total dosage of the drug administered: 215.0G. Did not show any untoward sign during the treatment. At the end of the therapy, patient appeared 'much improved' clinically, though the bacteriological index registered an increase (1.56).

Patient A2. Muslim, male, 24 years. A case of moderate leproma with a few nodules here and there, the duration of the disease being 11 years. Patient was treated with hydnocarpus remedies. Got better. Relapsed later; took to Unani treatment and got steadily worse.

Commenced treatment with Sulfon-Cilag on 15-3-1949 with a bacteriological index of 2.25. Continued treatment regularly without any untoward sign but had to stop treatment in November 1949 due to development of 'infective jaundice.' Restarted treatment in February 1950 and continued till the drug ran out of stock in November 1950. Total amount of the drug given: 217.0G. The patient had an uneventful course of treatment. The nodules shrank in size; the infiltration cleared up leaving behind areas of mottled hypo-pigmentation. The bacteriological index came down to 1.25.

Patient A3. Hindu, male, 21 years. A case of macular leproma of 6 years' duration. Had routine hydnocarpus treatment haphazardly for six years.

Commenced treatment with Sulfon-Cilag on 10-3-1949 with a bacteriological index of 0.12. On 9-6-1949, patient complained of fever in the evenings, indicative of possible onset of lepra reaction. Symptomatic treatment was given and the drug was continued. On 20-6-1949, patient complained of severe pain on the course of the right ulnar. On palpation the nerve was found swollen and tender. The patient was started on a course of antimony injections (potassium antimony tartrate) 00.2G intravenously on alternate days for 3 injections and 00.4G intravenously for the next three injections. On 22-6-1949, the neuritis became very severe and hence Sulfon-Cilag was withheld. The patient completed a course of potassium antimony tartrate without any relief from the neuritis. Thereafter, the patient did not attend the Clinic and on 14-9-1949, he was reported to be suffering from 'fever' for a week. On

17-10-1949 the patient was coaxed into restarting the treatment on a smaller dose of the drug; but after the injection on that day, he disappeared. Total quantity of the drug administered: 41.5G.

Patient A4. Hindu, male, 18 years. A case of advanced nodular leproma of 12 years' duration. Had irregular hydnocarpus treatment on and off.

Commenced treatment with Sulfon-Cilag on 18-4-1949 with a bacteriological index of 2.68. Continued treatment till 17th December 1949, when he was given rest due to lack of supply of the drug. On 9-1-1950, 22 days after the treatment was temporarily stopped, he reported with severe lepra reaction. On that day he was given another injection of Sulfon-Cilag to augment the reaction and then put on dihydrostreptomycin, 1G intramuscularly once a day, in order to study, incidentally, the effect of this anti-biotic on lepra reaction and the disease. On 20-1-50, the temperature touched normal but streptomycin was continued till 21-2-50; in all 40G of streptomycin being given. The bacteriological index at commencement of streptomycin treatment was 1.65 and at the end of the therapy, it was 1.44. Treatment with Sulfon-Cilag was recommenced on 21-3-50 and continued regularly till 22-7-50 and then discontinued since the patient went out of town. Total dosage of Sulfon-Cilag administered: 139.5G. At the time the treatment was discontinued (July '50) the patient appeared 'much improved' clinically, even though bacteriologically he was only slightly improved. (B.I. 2.00.)

Patient A5. Hindu, female, 25 years. A case of moderate leproma of 12 years' duration. Had regular treatment with hydnocarpus remedies from 1937 to 1944. Became 'negative' in June 1941, but relapsed in January 1944. Prior to starting of Sulfon-Cilag she had 200 tablets of Diasone which brought on a lepra reaction.

Commenced treatment with Sulfon-Cilag on 25-4-1949 with a bacteriological index of 1.43. Continued treatment regularly till 22nd November '50 except for a break of treatment in January and February 1950, due to lack of supply of the drug. The total dosage of the drug taken was 213.5G. During the course of treatment she had very mild activity in the lesions twice but this cleared up spontaneously. At the end of the therapy, she looked 'much improved' clinically and her bacteriological index registered a drop to 0.12.

Patient A6. Hindu, male, 34 years. A case of atypical leproma of 10 years' duration. Had routine hydnocarpus treatment irregularly and before starting on Sulfon-Cilag had treatment with Diasone.

Commenced treatment with Sulfon-Cilag on 14-3-1949 with a bacteriological index of 1.56. Continued treatment regularly till

7-7-49 and later stopped away from the treatment. The total amount of the drug administered: 11.0G.

GROUP B:—10cc of Sulfon-Cilag subcutaneously twice a week.

Patient B1. Hindu, male, 20 years. A case of macular leproma of 12 years' duration. Had hydnocarpus treatment irregularly for 12 years.

Commenced treatment with Sulfon-Cilag on 14-3-49 with a bacteriological index of 0.38. Continued treatment regularly till July 1950, when he developed mild lepra reaction. He was given treatment for the reaction and the drug was withheld for two weeks. Restarted treatment on 29-8-50 and continued till 20-11-50. The total amount of the drug administered: 145.5G. At the end of the therapy, the patient appeared 'stationary,' clinically and bacteriological index was 1.25.

Patient B2. Hindu, male, 25 years. A case of moderately advanced leproma of 10 years' standing. Poor vision in both eyes as a result of previous keratitis. Had treatment irregularly with hydnocarpus remedies for 12 years.

Commenced treatment with Sulfon-Cilag on 21-3-49 with a bacteriological index of 2.50. Continued treatment regularly without any untoward sign or symptom till 20-11-50, except for a break of two months in January and February 1950 when the drug ran out of stock. Total amount of the drug administered 149G. At the time the drug was discontinued (November 1950) he appeared 'much improved' clinically, the infiltration on the face and elsewhere having reduced considerably. The bacteriological index also registered a fall to 0.94.

Patient B3. Hindu, male, 53 years. A case of moderate leproma of over 10 years' duration. Had hydnocarpus treatment regularly for 3 years before starting on Sulfon-Cilag.

Commenced treatment with Sulfon-Cilag on 15-3-1949 with a bacteriological index of 1.75. Continued regularly till 25-3-1949 when he developed lepra reaction. He was given a course of potassium antimony tartrate injections. Improved, but did not turn up for further treatment. He was visited in his house on 19-6-1949 and found to be in a state of severe lepra reaction. It was learnt that he was taking sulphetrone tablets as treatment for the reaction on the advice of a local physician. He was advised to stop the tablets and was given appropriate treatment for his reaction. The reaction later subsided and he was restarted on the same dose of Sulfon-Cilag on 13-10-1949. He went into another mild reaction on 8-12-1949. The drug was then withheld and the patient was treated for the reaction. After the subsidence of reaction he recommenced treatment on 2-3-1950 and continued till 20-11-1950 when the treatment was finally stopped. The total amount of the

SUMMARY OF RESULTS

Case No.	Duration of treatment in months	Total Dosage in Grms.	Complications			Final Assessment	
			L.R.	N	A	Clinical	Bacteriological
A1	18.25	215.0	Nil	Nil	Nil	M.I.	W.
A2	16.75	217.0	Nil	Nil	Nil	M.I.	I.
A3	3.50	41.5	Nil	Severe once	Nil	Not	assessed
A4	12.75	139.5	Severe once	Nil	Nil	M.I.	I.
A5	16.50	213.5	Mild Twice	Nil	Nil	M.I.	M.I.
A6	1.00	11.0	Nil	Nil	Nil	Not	assessed
B1	18.00	145.5	Mild once	Nil	Nil	S.	W.
B2	18.50	149.0	Nil	Nil	Nil	M.I.	M.I.
B3	12.25	95.0	Severe twice, Mild once	Nil	Nil	I.	I.
B4	16.50	132.5	Nil	Nil	Nil	I.	M.I.
C1	14.00	181.5	Nil	Nil	Nil	I.	M.I.
C2	17.25	189.0	Nil	Nil	Nil	I.	N.
C3	16.75	196.0	Nil	Nil	Nil	M.I.	I.
C4	16.75	199.0	Nil	Nil	Mild once	I.	I.

L.R.: Lepra reaction.

N.: Neuritis.

A.: Anaemia.

I.: Improved.

M.I.: Much improved.

S.: Stationary.

W.: Worse.

N.: Negative.

drug administered: 95G. During the period 2-3-1950 to 20-11-1950, the patient once showed mild activity in the lesions. At the end of the therapy the patient appeared slightly 'improved' clinically the infiltration on the face having subsided somewhat. Bacteriological index came down from 1.75 to 1.5.

Patient B4. Hindu, male, 49 years. A case of early macular leproma of one year duration. Did not have any previous treatment.

Started treatment with Sulfon-Cilag on 25-4-1949 with a bacteriological index of 2.25. Continued treatment regularly till 21-10-1950, except for a period of one month's rest in December 1949. The total quantity of the drug administered: 132.5G. The course of the treatment was uneventful. At the end of the therapy, the patient appeared 'improved' clinically and the bacteriological index was 0.43.

GROUP C—5cc subcutaneously every day for 6 days in the week.

Patient C1. Indian christian, male, 20 years. A case of moderate diffuse leproma of 7 years' standing. Had hydnocarpus treatment for a year and later resorted to indigenous treatment under which he is said to have had some benefit. Lesions reappeared in November 1948.

Commenced treatment with Sulfon-Cilag on 16-3-1949 with a bacteriological index of 1.5. Continued treatment regularly till July 1950 when he stopped away from treatment for 3 months due to fracture of his forearm. Recommenced treatment on 6-11-1950 and stopped on 22-11-1950 due to lack of supply of the drug. The total amount of the drug administered: 181.5G. The patient did not develop any untoward symptom during the course of treatment. At the end of the therapy the patient appeared clinically 'improved' and the bacteriological index came down to 0.50.

Patient C2. Hindu, male, 22 years. A case of early leproma of 12 years' duration. Had hydnocarpus treatment irregularly for about 1½ years.

Commenced treatment with Sulfon-Cilag on 17-3-1949 with a bacteriological index of 0.18. Continued treatment regularly up to 22-11-1950 except for a rest period of two months. Total quantity of the drug taken: 189G. The course of treatment was uneventful. At the end of the therapy there was slight clinical improvement: but bacteriologically he became 'negative' (B.I: 0.00).

Patient C3. Hindu, male, 40 years. A case of advanced nodular leprosy of 10 years' duration. Had very irregular hydnocarpus therapy.

Commenced treatment with Sulfon-Cilag on 18-4-1949. The bacteriological index being 2.06. Continued treatment regularly till 22-11-1950 except for a rest period of 2 months. The total



Patient C.3. Before treatment.



Patient C.3. After 10 months' treatment.



Patient A.4. Before treatment.



Patient A.4. After 6 months' treatment.

quantity of the drug taken: 196G. Had an uneventful course of treatment at the end of which he appeared 'much improved' clinically. The bacteriological index at the end of the therapy was 1.62.

Patient C4. Hindu, male, 46 years. A case of moderate leproma of 14 years' duration. Had irregular hydnocarpus treatment.

Commenced therapy with Sulfon-Cilag on 18-4-1949 with a bacteriological index of 2.5. Continued regularly up to 22-11-1950 except for a period of rest for 2 months and an absence of 3 weeks. was uneventful except for the occurrence of mild anaemia in November 1950. At the end of the therapy, the lesions appeared November 1950. At the end of the Therapy, the lesions appeared partly subsided and the bacteriological index was 2.00.

CONCLUSIONS:

1. Sulfon-Cilag appears to be an effective drug in the treatment of leprosy.
2. Administered in appropriate doses it appears to be relatively non-toxic.
3. The intravenous route of therapy does not appear to have any special therapeutic advantage over the subcutaneous route.
4. The subcutaneous route on the other hand, appears to be more effective, considering the results obtained in groups B and C.
5. In group B and C getting the drug bi-weekly and daily, subcutaneously, it is observed that there does not appear to be any appreciable difference in the results. Both appear to be equally effective and hence bi-weekly subcutaneous injections of the drug in doses of 10cc appears to be the method of choice.

SUMMARY

The details of treatment of 14 cases of lepromatous leprosy with Sulfon-Cilag administered parenterally are presented. The results, both clinical and bacteriological, with the complications are recorded.

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