LIMITATIONS OF CLOFAZIMINE IN REACTIONS IN LEPROSY

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Summary

Exacerbation or precipitation of reaction in leprosy due to clofazimine treatment are described in 7 of 24 patients, highlighting its limitations in such cases and hence warranting its judicious use.

Leprosy, a chronic disease, is at times punctuated by acute episodes, described as reactions[1,2]. They are well recognised entities. The precise pathogenesis of these reactions is largely speculative[3]. Various factors, namely anti-leprosy drugs, concomitant infections and malnutrition, have all been incriminated as perpetuating and/or precipitating factors. In a sizeable number of patients no known factor may be revealed[1,2,4].

Clofazimine, a riminophenazine derivative, possesses both antibacterial activity against **Myco leprae**[5,6,7,8,9] as well as anti-inflammatory effect[10,11,12]. It has been used for the treatment of reactions in leprosy by several investigators[13,14,15,16] and reported to give successful results. At times however clofazimine may fail to control or reverse reactions and instead cause exacerbations[16,17,18]. The latter phenomenon is interesting and warrants careful review. The present report highlights such situations in 7 of the 24 reaction cases under our observation.

Material and Methods

Twenty four patients with leprosy in reaction comprising 12 lepromatous, 7 borderline, 4 tuberculoid and one neuritic type were treated with clofazimine in the dosage of 100–300 mg. per day for varying periods. The primary diagnoses in all cases were based on clinical, bacteriological and histopathological examinations.

There were 19 males and 5 females, the youngest patient being 17 years old and oldest 55. In the course of therapy each patient was closely monitored for change in the symptoms and signs of reactions. Whenever the reactions were progressive, clofazimine was withdrawn, while it was continued in other patients.

Observations

Among the 24 patients, 7 had their reaction aggravated or unchanged while on clofazimine treatment. In the remaining regression of the lesions was noted. The clinical response of clofazimine therapy is shown in the table.

Type of Leprosy	Improved	Aggravated / No improvement	Total
Lepromatous	8	4	12
Borderline	5	2	7
Tuberculoid	3	1	4
Neuritic	1	—	1
Total	17	7	24

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The following case histories illustrate the exacerbation/no response of reactions to clofazimine therapy.

Case 1 :— A 35 year old male with lepromatous leprosy has been on treatment for 9 years, with anti-leprosy drugs such as dapsone, isoniazid, long-acting sulphonamides, and streptomycin. With most drugs, patient used to get ENL reactions at times severe to form ulcers. He used to be reaction free when without drugs. He reported to us with severe reaction characterized by fever, bodyache and multiple tender necrotic ulcerations all over the body. He was given broad-spectrum antibiotics, prednisolone 15 mg. per day and clofazimine (lamprene) 200 mg. per day for 30 days. The symptoms and signs of reactions continued unabated. Clofazimine was withdrawn and reaction subsided.

Case 2 :— A 20 year old girl with lepromatous leprosy of 5 years' duration has been on irregular treatment with D. D. S., sulphetrone and isoniazid. She has been getting frequent reactions (ENL) during this period. She reported to us with an ENL episode. At that time she had constitutional symptoms like fever, joint pains and multiple, tender, noduloulcerative eruptions all over the body. She was considerably emaciated. She was treated with wide-spectrum antibiotics, clofazimine (200–300 mg. daily) and supportive therapy for a period of 6 weeks. Inspite of this treatement her condition continued to deteriorate. She developed anorexia, extensive ulcerations, and ultimately died of cachexia.

Case 3 :— A 21 year old male had been suffering from lepromatous leprosy for 6 years. He has been on irregular dapsone treatment and started getting repeated episodes of ENL with which he reported to us. He was given clofazimine in the dosage of 100–300 mg. per day for 6 weeks. Initially he showed some improvement with this therapy but later exacerbation was noticed. The drug was withdrawn and patient was treated with analgesics, chloroquine and supportive therapy.

The reaction was controlled. Subsequently clofazimine was reinstituted. 12 days later he had another ENL.

Case 4 :— A 17 year old male with lepromatous leprosy for 2 years had been getting recurrent episodes of ENL while taking small dosages of dapsone. During one of the reactions, clofazimine was administered in the dosage of 200 mg. per day for 15 days. At this time further deterioration of the condition was noticed. The drug was withdrawn and patient was treated with analgesics and chloroquine.

Case 5 :— A 48 year old male, reported with tuberculoid leprosy in reaction of 4 days' duration. Clofazimine 100 mg. per day was instituted for 3 months, at the end of which further exacerbation of the lesions was observed. This was characterized by enhanced erythema, induration and ulceration (Fig. Page 175) of the skin lesions and excruciatingly tender regional nerves. The drug was withdrawn and the reaction treated in the fashion outlined above.

Case 6 :— A 53 year old male with borderline leprosy of 2 years' duration had ENL reaction while on dapsone therapy. Clofazimine was used in daily dosage of 100–300 mg. for 3 months. Patient continued to get episodes of ENL during this period.

Case 7 :— A 24 year old male with borderline leprosy developed ENL while on dapsone. In this case too, clofazimine exacerbated the reaction. After withdrawal of the drug and subsequent institution of analgesics, antipyretics, antibiotics and antimalarials the reaction was controlled.

Discussion

Although clofazimine has been widely acclaimed[10,11,12] to be an anti-inflammatory agent and specially used for treating reactions in leprosy, the response to this therapy have been equivocal according to reports[16,17,18] and as illustrated by the results of our study. In seventeen (71 per cent) patients, the drug was well tolerated and the results of treatment favourable. In 7 (29 percent) patients the response to therapy was poor. Not only that the reaction did not subside, but severe exacerbation of the reaction was observed in 4 cases. The latter was characterized by extensive nodule/ noduloulcerative lesions and constitutional symptoms. That clofazimine was responsible for exacerbation and/ or triggering of the reactions in the different types of leprosy was evident when considerable clinical improvement in the symptoms and signs of the reaction followed on the withdrawal of the drug. Reinstitution of the drug was responsible for further reactions. The present observations thus point out the limitations of clofazimine therapy in leprosy reactions and warrants its judicious use in such cases.

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