

Clofazimine (Lamprene, B663) in the Treatment of Lepromatous Leprosy in the United Kingdom. A 12 Year Review of 31 Cases, 1966–1978¹

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Clofazimine (Lamprene, B663) was synthesized by Barry and his colleagues in Dublin in 1957⁽¹⁾ and first used in the treatment of leprosy patients by Browne and Hogerzeil (1962) in Eastern Nigeria⁽⁴⁾. Since that date it has been used increasingly in all countries where leprosy is endemic, mainly as an anti-leprotic but also for the prevention and suppression of immune complex reactions in lepromatous leprosy, including erythema nodosum leprosum (ENL) in the skin. The literature contains numerous reports of its value in the management of patients with multi-bacillary leprosy, with increasing emphasis on its role in the treatment of those with dapsone-resistant infections^(26,28). Hastings, *et al.*⁽⁹⁾ reviewed most of the important publications on clofazimine in a paper that drew attention to its remarkable freedom from serious side effects despite accumulation of crystals in the tissues over long periods of time. The value of clofazimine in the treatment of erythema nodosum leprosum (ENL) in patients with lepromatous leprosy is also well documented^(2,8,10), and some observers^(9,14,18,20) have reported its beneficial effect in the treatment of reversal (upgrading) reactions and of neuritis in patients with borderline (dimorphous) forms of leprosy.

In this paper we describe the clinical and histopathological findings in a group of 31

patients with lepromatous or borderline-lepromatous leprosy, treated in the United Kingdom with clofazimine as the only drug for periods varying between 1½ and 12 years, and who received it for either proven or suspected dapsone-resistance or for the suppression of reactions.

PATIENTS AND METHODS

There were 22 male and 9 female patients in this racially diverse group, most of them being immigrants. Sex, age on first registration, racial origin, classification of leprosy, year of starting anti-leprosy drugs, drug intake prior to clofazimine treatment, and the year of starting clofazimine are given in Table 1. Without exception, the six subjects of British origin had all been abroad, in areas where leprosy is endemic. All the patients in this study had acquired the disease outside the United Kingdom. Some patients were seen as outpatients in London and treated as such from the outset, but others received the drug as hospital inpatients for periods varying from a few months to several years and then continued treatment as outpatients. The diagnosis and classification were established by clinical examination and histopathological examination of skin biopsies, the system of classification being essentially that of Ridley and Jopling⁽¹⁷⁾. In most cases, the Bacteriological Index (BI) and Morphological Index (MI) from slit-skin smears were recorded at the outset or on relapse, but both for confirmation of classification and subsequent monitoring of the patients' progress, greater reliance was placed on the examination of skin biopsies as described below.

Histopathological examination of skin biopsies. Using techniques already described by Harman⁽⁷⁾, skin biopsies were taken before starting clofazimine treatment and thereafter at approximately 6-monthly

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TABLE 1. *Thirty-one patients treated with clofazimine in the United Kingdom, 1966–1978.*

Patient no.	Sex	Age on first presentation	Racial origin	Classification	Year first treated with antileprosy drugs ^a	Drug intake prior to clofazimine treatment ^b	Year first treated with dapsone (or Sulphetrone)	Year clofazimine treatment started
1	F	28	Anglo-Indian	LL	1965	Thiambutosine solapsone (Sulphetrone), dapsone	1965	1971
2	M	32	Anglo-Indian	LL	1947	Bayer FBA 2457, Sulphetrone, isoniazid, thiambutosine, Etisul, Lederkyn, dapsone	1947	1971
3	M	38	Armenian	LL	1956	Mainly low-dose irregular dapsone	1956	1966
4	F	48	Guyanese	LL	pre-1947	Chaulmoogra oil, dapsone	1947	1972
5	M	19	British	LL	pre-1959	Thiambutosine, Etisul, Lederkyn, dapsone	?1950	1966
6	M	23	British	LL	1947	Sulphetrone, PAS, thiacetazone, dapsone	1948	1971
7	M	36	Irish	LL	pre-1949	Chaulmoogra oil, sulfonamides, Vadrine, Lederkyn, dapsone	1947	1967
8	M	73	Anglo-Indian	LL from BL	1969	Dapsone	1969	1970
9	F	46	Vietnamese	LL from BL	1965	Mainly low-dose irregular dapsone	1965	1970
10	M	49	British	LL	1946	Sulphetrone, thiambutosine	1946	1966
11	M	27	Guyanese	LL	1946	Palmicel, Drazone, Sulphetrone, dapsone	1951	1970
12	F	23	British "Eurasian"	LL with BL features	1941	Chaulmoogra oil	not recorded	1969
13	F	32	British Guyanese	LL	?1947	Mainly low-dose irregular dapsone	1949	1968
14	M	31	Portuguese/Guyanese	LL	pre-1950	Thiambutosine, Lederkyn, Vadrine	1948	1966
15	M	31	West Indian	LL	1963	Thiambutosine, dapsone	1964	1971
16	M	13	Anglo-Indian	LL from BL	1962	Mainly low-dose irregular dapsone	1962	1976
17	F	8	Anglo-Burmese	LL with BL features	1969	Low-dose dapsone	1969	1971
18	M	22	Sri Lanka	LL	pre-1968	Low-dose dapsone	pre-1968	1970

TABLE 1. *Continued.*

Patient no.	Sex	Age on first presentation	Racial origin	Classification	Year first treated with antileprosy drugs ^a	Drug intake prior to clofazimine treatment ^b	Year first treated with dapsone (or Sulphetrone)	Year clofazimine treatment started
19	M	?	Moroccan	BL	1970	None (dapsone not used) ^c	—	1970
20	M	35	Maltese-English	LL from BL	1954	Chaulmoogra oil, Promin, dapsone	1954	1968
21	F	37	British	LL from BL	1950	Sulphetrone, thiace-tazone, thiambutosine, Etisul, Lederkyn, Vadrine, dapsone	1950	1968
22	M	44	West Indian	LL	1964	Mainly low-dose irregular dapsone	1964	1970
23	F	22	British	LL	1950	Chaulmoogra oil, thiambutosine, Lederkyn, streptomycin and isoniazid, dapsone	1955	1969
24	M	29	Sri Lanka	BL	1956	Mainly low-dose irregular dapsone	1956	1966
25	M	27	Pakistani	LL from BL	1974	Thiambutosine, dapsone, rifampin	1975	1975
26	M	39	Anglo-Indian	LL	1953	Sulphetrone, ? also dapsone	1953	1967
27	M	37	West Indian	LL from BL	1964	Thiambutosine, low-dose dapsone	1967	1968
28	M	28	Indian	LL	1969	Dapsone	1969	1972
29	M	29	Indian	LL with BL features	1949	Sulphetrone, sulfonamides, thiacetazone, dapsone	1949	1971
30	M	10	British	LL	1958	Etisul, thiambutosine, Sulphetrone, dapsone	not recorded	1966
31	F	12	Pakistani	LL	1970	Low-dose dapsone	1970	1972

^a In most instances this is also the year of first diagnosis of leprosy.

^b It should be noted that in virtually all cases the intake of dapsone was irregular in this period; in some, no dapsone was taken at all for 1 or more years. Palmicel and Drazone = anti-leprotics used in Guyana in the 1940s; composition unknown. Lederkyn = sulfamethoxypyridazine; Vadrine = the p-aminosalicylate of 2-pyridyl-(4)-1,3,4,-oxydiazoline-(5). Bayer FB 2457 = 2-mercapto-5-(4-pyridyl)-1-ox-3,4-diazole; Etisul = Ditophal; diethyldithiolisophthalate. Promin = glucosulfone sodium; solapsone (Sulphetrone) = tetra sodium 4: 4'-di(3-phenyl-1:3 disulfopropylamino-) diphenyl sulfone.

^c See text: clofazimine was used from the outset in this case because of the belief that dapsone might "precipitate" neuritis.

intervals during the first 1–2 years, reducing to yearly or longer intervals after clinical inactivity had been achieved. In most patients many previous biopsies had been taken and examined at the Leprosy Study

Centre, London, sometimes over several years before the start of clofazimine treatment. Fixation was in formol-Zenker with transfer to 70% alcohol 15–24 hours later; staining was with a combined trichrome

TABLE 2. Eight patients with dapsone resistance proven on mouse foot pad inoculation.

Patient no.	Year first treated with anti-leprosy drug	Year first treated with dapsone (or Sulphetrone)	Year in which dapsone resistance was diagnosed	Interval in years ^a	Level of resistance to 3 concentrations of dapsone in mouse diet
1	1965	1965	1971	6	low
3	1956	1956	1965	10	high
4	pre-1947	1947	1973	25	high
11	1946	1951	1970	19	intermediate
15	1963	1964	1971	7	low
20	1954	1954	1968	14	intermediate
21	1950	1950	1968	18	intermediate
29	1949	1949	1971	22	high
Mean	1953.8	1954.5	1969.6	15.1	
Range	(1946-1965)	(1949-1965)	(1965-1973)	(6-25)	

^a In virtually all cases this included quite long periods during which dapsone was taken in low dosage, or not at all.

^b High level of dapsone in the mouse fed 0.01%; equivalent to a dose of 100 mg dapsone/day in man. Intermediate and low levels of dapsone in mice fed 0.001% and 0.0001%: equivalent to doses of 10 mg. and 1 mg/day in man, respectively.

and the Fite-Faraco modification of the Ziehl-Neelsen stains ("TRIFF")⁽²⁵⁾. Tissues were embedded in wax and cut at 5 μ .

Previous chemotherapy. With one exception (patient 19), who started and continued his treatment with clofazimine as the only drug, all the others had previously received treatment with an antileprosy drug, usually with several, over a period of many years (Table 1). All 20 who were proven or suspected to be dapsone-resistant had taken dapsone for periods of between 6 and 25 years in doses now considered to be too low, often on a weekly or twice weekly basis, and, on their own admission, with long periods of non-compliance. While some of the drugs listed in Table 1 may not have had a significant effect on the final outcome, the use of a rapidly-acting bactericidal drug such as rifampin may well have been significant, and we therefore recorded the following details of its use in 5 patients. Patient 14 relapsed in this country, having taken dapsone intermittently and at a low dose for some 15 years while abroad. He was treated with clofazimine, but after a few months he complained about the color of his skin and the drug was stopped. He received rifampin 600 mg on 2 successive days each month for 4 months. This was then stopped, clofazimine reinstated, and his subsequent progress was uneventful. Patient 15, having previously taken dap-

sone irregularly in a low dosage for a long period, was treated with rifampin 600 mg daily as the sole drug for 21 months before starting clofazimine in early 1971. Patient 16 had 4 weeks of rifampin, 600 mg daily, together with clofazimine at the outset, thereafter continuing with clofazimine alone. Patient 20 received 600 mg rifampin daily for 3 weeks, 4 years after starting clofazimine, because one of the serial biopsies suggested the presence of a few solid-staining organisms; these were not seen on subsequent biopsies, and the patient made excellent progress on clofazimine alone. Finally, Patient 24 started clofazimine therapy in 1966 and developed abdominal and epididymal tuberculosis while still taking clofazimine regularly under supervision at a dose of 100 mg twice weekly in early 1973. He was treated with ethambutol, isoniazid, and rifampin, the latter being given for 5 months at a dose of 600 mg daily.

Indications for clofazimine. Out of a total of 31, eight patients received this drug for proven dapsone resistance (Table 2) and 12 for dapsone resistance strongly suspected on clinical and histopathological grounds (Table 3), including lack of response to supervised dapsone in doses of 50-100 mg daily. Four were treated because of persistent ENL, and the remaining seven mainly because of the presence of borderline-lepromatous features, and the clinical impres-

TABLE 3. Twelve patients with dapsone resistance strongly suspected on clinical and histopathological evidence.

Patient no.	Year first treated with antileprosy drug	Year first treated with dapsone (or Sulphetrone)	Year in which dapsone resistance was diagnosed	Interval in years ^a
2	1947	1947	1971	24
5	pre-1959	?1950	1966	?16
6	1947	1948	1977	23
7	1946	1947	1967	20
9	1965	1965	1970	15
10	1946	1946	1970	24
13	?1947	1949	1968	19
14	pre-1950	1948	1966	18
16	1962	1962	1976	14
22	1964	1964	1970	6
23	1950	1955	1969	14
24	1956	1956	1966	10
Mean	1953.3	1953.0	1967.7	16.9
Range	(1946-1965)	(1946-1965)	(1966-1977)	6-24

^a In virtually all cases this included quite long periods during which dapsone was taken in low dosage, or not at all.

sion that dapsone would be more likely to precipitate reversal (upgrading) reactions, and that clofazimine might modify or even prevent them.

Dosage. In the earlier years covered by this study, and including several patients treated at other centers before referral, 11 received clofazimine at a dose of 100 mg daily for periods ranging from 3 months to 3½ years, and five at doses between 200 mg and 300 mg daily for periods which ranged from 3 to 20 months. The latter high doses were used exclusively for the treatment of immune complex reactions in lepromatous leprosy, including ENL lesions in the skin. Doses of this order have never been used by us in the treatment of the bacillary infection, the highest dose in any patient currently under care being 100 mg daily, and this only for short periods. The standard dose has been 100 mg three times weekly. However, having attained clinical and histological quiescence, 14 patients have received a lower dose than this. Ten patients have taken 100 mg twice weekly for varying periods up to 10 years, and four patients received 100 mg weekly for periods up to 8 years. With the few exceptions already noted above, referring to the use of rifampin, clofazimine has been used alone, i.e., as monotherapy.

Dapsone resistance. Fresh tissues were

submitted to Dr. R. J. W. Rees at the National Institute for Medical Research, Mill Hill, London, for mouse foot pad inoculation, according to techniques already described^(15,19) and recently reviewed in detail⁽²⁴⁾. Details of the eight patients concerned, together with the mouse foot pad results, are given in Table 2.

RESULTS

Clinical findings. All patients with proven or suspected dapsone resistance improved clinically to an extent which was recorded by different observers as either "highly satisfactory" or "remarkable." Lesions subsided at least as rapidly as in patients with dapsone-sensitive organisms treated with full doses of dapsone, and there has been no relapse in any patient of the series. Two patients who did not have ENL at the beginning of treatment developed it in an extremely mild form after a few weeks of treatment with clofazimine; it subsided on continuing routine dosages of clofazimine. The patients who were treated with this drug because of persistent ENL all responded routinely and did not have a recurrence of this form of reaction, and so also did those who received it because of the fear that dapsone might precipitate a reversal (upgrading) reaction. None of the 31 patients complained of gastro-intestinal

symptoms of any significance; even in those on large doses for the treatment of ENL, virtually no modification of dosage was necessary on this account.

Histopathology. Classical histopathological findings were recorded in the skin biopsies of four patients who received clofazimine for ENL and of seven who received it mainly because of the presence of borderline lepromatous features. In the remaining 20 patients with proven or suspected dapsone resistance, there was in all instances clear histopathological evidence of relapse with the reappearance of large numbers of solid-staining *M. leprae*. No histoid lesions were noted in this series; the histopathological features of relapse were similar to those already described by Ridley (16).

In the follow-up examination of a large number of biopsies taken from the 31 patients through the years, brown, pink, or reddish discoloration of dermal histiocytes was frequently seen. No actual crystals, as checked by the use of polarized light, were found in any tissues in this series, but this would not be expected after the transfer of formol-Zenker-fixed material to 70% alcohol, with subsequent processing through the usual range of organic solvents, before embedding. No unusual features were found in the cellular infiltrate and eosinophils were not noted, nor were foreign body reactions observed. As judged by safran staining and also by examination under polarized light, the collagen did not differ in appearance from that seen in biopsies from lepromatous patients treated with other drugs, previously examined at this center. Incontinence of pigment, with ingestion of pigment granules by dermal macrophages, was observed with a frequency again similar to that in biopsies from patients treated with other drugs.

Bacterial clearance. Although not quantified in the present study, we had the impression in some cases that the Bacteriological Index (BI) fell somewhat faster towards zero (i.e., faster than one unit per year) than in similar cases treated with dapsone, and monitored with serial biopsies at this center.

As regards the morphology of bacilli in sections, the Morphological Index (MI) fell to zero in all patients within 6 months of

starting clofazimine treatment and has not risen from zero since starting treatment with the one exception of Patient 20. This patient started clofazimine at a dose of 100 mg three times weekly in October 1968 and was found to have a few possibly solid-staining (and therefore possibly viable) bacilli in the skin biopsy of October 1974, 6 years after starting the drug. To cover the possibility of bacillary persistence, he was treated with rifampin in a dose of 600 mg daily for 3 weeks, thereafter continuing clofazimine in the above dosage. The clofazimine dose was reduced to 100 mg twice weekly in October 1976. He has remained on this dosage since then, making excellent progress, subsequent biopsies showing only non-solid-staining bacilli.

Pigmentation. Pigmentation of both the skin generally and the lesions was obvious in nine cases, but only four patients actually complained. In a fifth patient, mild pigmentation was accompanied by ichthyosis of the extensor aspects of the extremities. Patient 26 developed conspicuous black pigmentation of lesions on the face similar to that described by Browne (3) and which remained unchanged over a period of approximately 5 years, later receding, possibly aided by the use of isoniazid (5). The possible role of pigmentation, as a factor leading to death by suicide in one of the four patients noted above, is discussed later in this report.

Deaths. During the 12 years of this study, there were 5 deaths. Patient 31 was tragically killed in a car accident at the age of 13 years; Patient 23 died of broncho-pneumonia in 1970; Patient 10 of coronary thrombosis; Patient 7 of ischemic heart disease. In none of these was there any evidence for an association between the use of clofazimine and the cause of death. In a fifth patient, Patient 13, a 36 year old female, the mode of death was suicide while in the hospital. The possibility that her concern about pigmentation may have been a contributory factor must be considered. In four of these patients, the clinical and histopathological response to clofazimine, up to the time of death, was highly satisfactory. The remaining patient stopped taking clofazimine (and all other treatment) 5 years before death. During this period he did not come to London for examination,

but there is no evidence that he had any recurrence of leprosy lesions or of reaction.

DISCUSSION

The long clinical histories and complex pattern of previous drug treatment, together with the varying racial and social backgrounds of the patients in this study, make it difficult to interpret the data with clarity. The patients have, however, been observed in detail for considerable periods of time by clinicians whose experience of leprosy predates the sulfone era, and their histopathological progress, based on skin biopsies over many years, is unusually well documented. We record the data mainly in order to emphasize the excellent immediate and longer term response to regular clofazimine in a complex group of patients, almost all of whom were either deteriorating or failing to respond to other drugs.

In view of the fact that clofazimine is now being even more widely advocated in the context of dapsone resistance^(26,27) and the likelihood that this will involve patients with light colored skins, the matter of pigmentation from this drug merits careful consideration. It was noticeable and gave rise to complaint in four patients in the present series and led to interruption of treatment on this account. It must, however, be emphasized that in all of them the drug had been used in high dosage for the treatment of immune complex disease in lepromatous leprosy. We have not encountered such pigmentation, or complaints, in patients taking clofazimine in a dosage in the order of 100 mg three times weekly. On the other hand, it is possible that the level of acceptability would have been lower if the patients had had to start and continue treatment as outpatients, perhaps while continuing normal work in the company of colleagues who would remark on the change in skin color. It would also be a more obvious disadvantage in light-skinned patients not represented in the present study, such as the Chinese. Objectionable pigmentation by clofazimine in this racial group has indeed already been recorded^(13,22). Here again, however, it should be noted that this is more likely to be serious in those patients on the high dosages used for the treatment of ENL. An additional factor which "highlights" the lesions on

clofazimine treatment is the presence of a borderline-lepromatous element, the lesions often being larger and more conspicuous than those of diffuse polar or sub-polar lepromatous leprosy. It is clearly a matter for serious consideration that one of the patients in this study committed suicide while taking this drug. She had, however, a documented history of psychiatric problems, and there was no real evidence to suggest that concern about pigmentation was a major factor leading to death. Nonetheless, it may have been contributory.

A detailed study of the chemistry of pigmentation has indicated that the staining of lepromatous lesions results from selective concentrations of the dye by tissue elements present in the lesions and that the phenomenon may be essential to the therapeutic effect of the drug. It is regrettable that an analog of clofazimine, B 1912, once thought to be potentially as effective while at the same time less pigmenting, has now been shown regularly to produce abortion in mice⁽¹²⁾ and will not be manufactured. The lowest possible, yet effective and safe, dosage of clofazimine in the human being is thus of great importance. It is unfortunate that it is still impossible to determine the minimum inhibitory concentration of this drug against *M. leprae* because of its marked tissue accumulation⁽²⁹⁾. A dosage of 100 mg three times weekly has been widely used in clinical practice with good effect. One of the few publications in the literature on a dose lower than this found that 100 mg twice weekly, short term, was as effective as 300 mg daily⁽²³⁾. It is extremely important to assess the progress of patients on lower dosages of this order and to ensure that they are followed up for periods in the order of 20 years, in view of the possibility of the emergence of drug resistance. Although few in number, those in the present study who, following a period of at least one year on 100 mg three times weekly, have taken a reduced dose of 100 mg twice weekly, or 100 mg weekly, are clearly in this category.

The fact that one patient was found to have abdominal and epididymal tuberculosis while taking clofazimine is a reminder of the fact that although active against experimental infections with *M. tuberculosis* in mice⁽²¹⁾, the drug has not been shown

to be active against such infections in man. It may be relevant that the autopsy findings in a 16 year old male patient treated with high dose clofazimine in India (6) included a brain tuberculoma and tuberculous subdiaphragmatic abscesses. The use of rifampin in our patient (for the treatment of his tuberculosis) is also a reminder of the need for a complete record of the drug intake in all cases before assessing the impact of clofazimine. In this group, four patients were treated with rifampin, a bactericidal drug, already well-known to be highly effective clinically in lepromatous leprosy.

In summary, this study indicates that the clinical and histopathological response to clofazimine in a group of 31 patients, both as regards the bacillary infection and reactions, has been impressive both in the early stages and on follow-up over several years. It is our view that no other drug currently available in leprosy could have achieved comparable results in patients with such severe and long established disease.

SUMMARY

This paper records the results of treatment with clofazimine of a group of 31 patients of mixed racial origin in the United Kingdom suffering from lepromatous or borderline-lepromatous leprosy. Progress was assessed by clinical and histopathological examination for periods up to 12 years after starting treatment. Although given mainly for dapsone resistance, either proven on mouse foot pad inoculation or strongly suspected on clinical grounds, clofazimine was also used in some patients for the suppression of reactions, notably those due to the formation of immune-complexes, the manifestations of which included erythema nodosum leprosum (ENL). Four patients, all of whom had taken clofazimine in relatively high dosage for many months, usually for ENL, complained about pigmentation. In the remaining patients, on doses of the order of 100 mg three times weekly, pigmentation was not a problem. None of the 31 patients suffered from gastro-intestinal symptoms or signs of any significance during the period of study.

Many of the patients started taking dapsone in the 1940s; most had a long, complex, and unsatisfactory history of previous treatment with many drugs. This made as-

essment of response to clofazimine difficult in some cases. The general impression is that clofazimine has been outstandingly valuable both as regards treatment of the bacillary infection and the suppression of reaction. No patient relapsed during the period of study. The authors express the opinion that no other drug currently available for the treatment of leprosy could have achieved such good results in a comparable group of patients.

RESUMEN

En este trabajo se mencionan los resultados del tratamiento con clofazimina de un grupo de 31 pacientes con lepra lepromatosa o cercana ("borderline") a la lepromatosa, de diverso origen racial, en el Reino Unido. El progreso del estudio se valoró con exámenes clínicos e histopatológicos periódicos efectuados hasta por 12 años después de iniciado el tratamiento. Aunque la clofazimina se administró principalmente en los casos de resistencia a la dapsona (probada en el sistema del cojinete plantar del ratón o establecida a partir de los datos clínicos), la clofazimina también se usó en algunos pacientes para la supresión de reacciones, fundamentalmente aquellas debidas a la formación de complejos inmunes cuyas manifestaciones incluyeron al eritema nodoso leproso (ENL). Cuatro pacientes que habían tomado dosis relativamente altas de clofazimina se quejaron de la pigmentación producida. En los pacientes restantes, tratados con dosis del orden de 100 mg, 3 veces por semana, la pigmentación no fue un problema. Ninguno de los 31 pacientes presentó síntomas gastrointestinales o molestias significativas de otra índole durante el periodo de estudio. Muchos de los pacientes empezaron tomando dapsona en la década de los años 1940; la mayoría tenía una historia larga, compleja y no satisfactoria de tratamiento previo con varias drogas. Esto dificultó, en muchos casos, la valoración de la respuesta a la clofazimina. La impresión general es que la clofazimina ha sido de un inmenso valor tanto en el tratamiento de la infección bacilar como en la supresión de la reacción leprosa. Ningún paciente sufrió recaídas durante el periodo de estudio. Los autores opinan que ninguna otra de las drogas conocidas utilizadas en el tratamiento de la lepra, hubiera dado mejores resultados que la clofazimina en un grupo comparable de pacientes.

RÉSUMÉ

Cet article présente les résultats obtenus, au Royaume-Uni, par le traitement à la clofazimine d'un groupe de 31 malades d'origine ethnique mélangée, qui souffraient de lèpre lépromateuse ou borderline-lépromateuse. Les progrès ont été mesurés par l'examen clinique et histopathologique de ces malades, pendant des périodes s'étendant jusqu'à 12 ans après le début du traitement. La clofazimine a été utilisée surtout par

suite de résistance à la dapsons, celle-ci étant confirmée par l'inoculation au coussinet plantaire de la souris, ou bien suspectée fortement sur la base de l'examen clinique. Néanmoins, la clofazimine a également été étudiée chez quelques malades en vue de supprimer les réactions, en particulier les réactions dues à la formation de complexes immuns, dont les manifestations comprenaient l'érythème noueux lépreux (ENL). Quatre malades, qui tous avaient reçu de la clofazimine à doses relativement élevées, pendant plusieurs mois, et ceci généralement par suite d'ENL, se sont plaints de pigmentation. Chez les autres malades, à la suite de doses de l'ordre de 100 mg, 3 fois par semaine, la pigmentation ne s'est pas révélée être un problème. Aucun des 31 malades étudiés n'a souffert de symptômes ou de signes gastro-intestinaux significatifs, au cours de la période d'étude. La plupart des malades ont entamé leur cure à la dapsons dans les années 40. La plupart présentaient une anamnèse prolongée, complexe et fort peu satisfaisante de traitements antérieurs par de nombreux médicaments. Ceci a rendu l'évaluation de la réponse à la clofazimine malaisée dans quelques cas. L'impression générale est que la clofazimine a été remarquablement utile, tant en ce qui regarde le traitement de l'infection bacillaire que la suppression des réactions. Aucun malade n'a présenté de récurrences durant la période d'étude. Les auteurs sont de l'opinion qu'aucun autre traitement disponible à présent pour le traitement de la lèpre n'aurait pu accomplir de résultats aussi bons, dans un groupe semblable de malades.

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