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Clofazimine and the eye: preliminary communication

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Summary Fifty-seven patients, admitted to the Marchoux Institute in Bamako, Mali, were treated with clofazimine for periods varying from between 3 and 26 months. Detailed ophthalmological examination was carried out in all cases, including visual acuity; conjunctival smears for crystals; corneal sensation; the ocular fundus after pupillary dilatation. In addition, slit-lamp examination was carried out in all cases. In this preliminary study, apart from brown–red sub-epithelial pigmentation in the cornea, no untoward effects on the eye were recorded.

Introduction

Clofazimine is of acknowledged value in leprosy, not only for the treatment of the bacillary infection, but also for the suppression of adverse immunological reaction in lepromatous leprosy, including erythema nodosum leprosum on the skin. Hastings *et al*[1] have reviewed the publications on its value in clinical leprosy and Yawalkar & Vischer have published a monograph[2] covering its chemical composition, dosage, clinical use, complications and toxicity. In recent years, WHO have recommended it for the treatment of patients with both dapsone-sensitive and dapsone-resistant lepromatous leprosy.[3]

The fact that this drug accumulates, partly in crystalline form, in the tissues of patients, has given rise in a small number of cases to intestinal and other complications and these have been reviewed by Jopling.[4] Although some of these have been serious and even fatal, the number of recorded complications from this drug since it was first introduced by Browne & Hogerzeil in 1962[5] is not large. Despite initial fears from some clinicians that its ingestion might be associated with damage to the foetus in the pregnant mother, this has not been reported—nor has any evidence so far come to light suggesting that its use may be associated with cancer in any organ. Eye damage of any significance has not been

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reported, though Oehman & Wahlberg[6] noted brown corneal deposits, which disappeared after stopping treatment. Karat[7] described a symptomatic bluish discolouration of the lens which cleared 6–12 months after treatment was stopped, and the finding of crystals of clofazimine in the iris, conjunctiva, sclera and cornea, on slit-lamp examination, 6 months after starting treatment.

In June 1980 we had the opportunity to examine a patient on long-term clofazimine in the Department of Ophthalmology of the Centre Hospitalier Universitaire, Lille, France (Director, Professor P Francois). Apart from corneal pigmentation, no significant findings were noted, but the case prompted us to review the literature and to embark on the examination of a small series of patients treated with clofazimine in Mali.

Patients and methods

The study included 57 patients with leprosy, hospitalized in the Institut Marchoux at Bamako (OCCGE; Director Professor P St-André). There were 41 men and 16 women. Ages ranged from 14 to 60 years with a mean of 32·5. Using the Ridley–Jopling classification, 42 were LL; 7 BL; 3 BB; 4 BT and 1 TT. The total dose of clofazimine ingested by the patient varied from 13 to 170 g, covering periods of 3–26 months; the standard dose being between 100 and 300 mg daily. In each case we examined the following—visual acuity; conjunctival smears for crystals; corneal sensation; the ocular fundus after pupillary dilatation. In addition, routine slit-lamp examination was carried out in all cases. Stools and urine specimens were collected for examination for crystals in 44 cases out of the total of 57 in the study.

Results

These are summarized in Table 1. The microcrystals of clofazimine in tears were identified from filter paper specimens smeared on microscope slides, and then examined under normal and polarized light. They had shape, dimensions and colour identical with those of the drug from capsules; their final identity is currently being studied by thin layer chromotography in Lille. In 1 case, a female of 40 years, we noted macular degeneration in 1 eye only, but without other significant abnormality; her previous ingestion of other drugs, including chloroquine, could not be established and we are therefore reluctant to associate this abnormality to clofazimine treatment. Apart from brown–red pigmentation, no significant abnormalities were noted in the cornea. No discolouration or other change, attributable to drug treatment, was recorded in the lens. (One patient previously had an operation for cataract: in 2 others there were pre-senile lens opacities.)

Table 1.

Part of the eye examined	Findings	No.
Tears	Red microcrystals	47
Conjunctiva	Brown–red pigmentation of the bulbar conjunctiva	29
Cornea	Hudson-Stahli lines	7
	Sub-epithelial brown–red pigmentation in the form of a 'comet's tail'	3
	White–yellow deposits scattered in the stroma	2

Discussion

The pigmentary changes recorded here confirm those of previous observers and may be of some value in checking that a patient is taking the drug, or has taken it in the recent past, though it should be emphasized that pigmentation both in the cornea and elsewhere may take many months to recede after cessation of treatment. Of perhaps greater interest was the finding of red crystals in the tears in over 82% of cases in this study. Whether this occurs only during active daily or thrice weekly ingestion of the drug and ceases after treatment is stopped, we do not know; this is one of the several points which will be investigated further in an on-going study, which will include detailed observations on the retina and optic nerve. At this stage, we can record that our preliminary observations on this group of patients do not suggest any significant, untoward effect on the eyes, directly attributable to clofazimine, except corneal sub-epithelial brown–red pigmentation.

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