

OCULAR TOXICITY AND HYDROXYCHLOROQUINE: GUIDELINES FOR SCREENING 2004 (REPLACING THE ROYAL COLLEGE OF OPHTHALMOLOGISTS GUIDELINES 1998)

BACKGROUND

Hydroxychloroquine is used primarily by rheumatologists for rheumatoid arthritis and systemic lupus erythematosus, and by dermatologists for cutaneous lupus. It binds to melanin and interacts with nucleic acids. Although irreversible retinopathy has been described with its use, this has occurred at total doses in excess of those currently recommended. The literature¹ and contemporary practice² favour the use of low dose hydroxychloroquine which confers minimal risk, or the unrelated antimalarial mepacrine (which has negligible ocular toxicity³). In eight case series with a total of 2500 patients treated with hydroxychloroquine, only two cases of retinopathy with visual loss were observed^{4,12}. In the largest single series one patient out of 1207 developed retinopathy after seven years¹³. In another study where doses of hydroxychloroquine were kept below 6.5mg/kg lean body weight/day only 2 cases of toxicity were reported in both of which the drug had been used for > 6 years¹⁴.

Chloroquine is also used for similar indications but should only be considered if other agents have failed, the safe daily dose, cumulative dose and frequency of ocular screening being much less clear. In view of these concerns it is recommended that ALL patients on chloroquine should have regular ocular examination and a protocol for this should be arranged locally between the prescribing physician and the ophthalmologist¹⁵.

CLINICAL FEATURES

Reversible	Corneal epithelial changes (verticillata) - these rarely cause symptoms
	Loss of normal foveal reflex
Irreversible	Fine granular appearance to macula
	"Bull's eye" maculopathy - only this sign is associated with impaired visual acuity and central visual field disturbance

IS THERE A CASE FOR SCREENING FOR OCULAR TOXICITY?

Despite two editorials^{16,17} which recommended baseline ophthalmological examination, the working party believes that were hydroxychloroquine to be introduced now, no evidence based case for the cost effectiveness of a screening programme would be justified.^{1,18,19} Screening programmes are costly and may generate needless anxiety, work for clinicians and unnecessary appointments. More importantly, screening may not enable ophthalmologists to pick up reversible toxicity as (a) there is no reliable screening test which will identify this before ophthalmoscopic changes develop and (b) it is difficult to distinguish toxicity from age-related macular degeneration.²⁰

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RECOMMENDATIONS FOR GOOD PRACTICE IN RHEUMATOLOGY AND DERMATOLOGY CLINICS

Maximum Daily Dosage Recommendations

Hydroxychloroquine 6.5mg/kg lean body weight daily (usually 200-400mg); if patient overweight check lean body weight with body mass index calculator available in endocrine clinics.

Baseline assessment

- Establish renal and liver function
- Ask about visual impairment (which is not corrected by glasses)
- Record near visual acuity of each eye (with glasses where appropriate) using a test type* - or the reading chart in this document.

If no abnormality is detected, treatment with hydroxychloroquine can be commenced.

If visual impairment is present an assessment by an optometrist is advised. Any relevant abnormality detected would be referred to an ophthalmologist in the usual way.

Annual evaluation

Patients should be monitored yearly, enquiring about visual symptoms, rechecking acuity and assessing for blurred vision using the reading chart. (Amsler Charts have not yet been validated beyond their use in ophthalmology clinics)²¹

Referral to the Ophthalmologist

This is appropriate if any patient:

- has visual impairment or eye disease detected at baseline assessment (confirmed by an optometrist). It should be noted that in elderly patients there is often coincidental ocular morbidity from cataract, glaucoma and age-related maculopathy.
- develops change in acuity or blurred vision (as assessed by reading chart) whilst on treatment Patients should be warned to stop treatment, have their eyes checked by an optometrist, and seek advice from the prescribing doctor.

Although quinolones are not licensed for children, they are used in specialist units particularly in the management of juvenile chronic arthritis, SLE, and fibrosing alveolitis. Some of these children are already attending an ophthalmologist for slit-lamp examination to check for the development of uveitis. In the absence of evidence to the contrary it would be sensible to establish a locally agreed protocol between prescribing doctor and ophthalmologist to monitor the vision in such children.

EXAMINATION BY THE OPHTHALMOLOGIST

Examination should include assessment of:

- distance and near acuity
- colour vision
- visual field - use a red pin to detect central scotoma or colour desaturation
- macular function - use an Amsler grid
- the cornea, using the slit-lamp
- the retina

Evaluation may need to be extended according to signs and symptoms, e.g. macular threshold fields, retinal photography. Subsequent examinations should be at the discretion of the ophthalmologist, but indefinite follow up is not likely to be required. For the patient who ultimately requires long term treatment (>5 years) an individual arrangement should be agreed with the local ophthalmologist.

READING CHART

Use the texts below to test each eye separately with glasses when appropriate. Record the smallest text that can be read at a distance most comfortable to the patient

N.8

He moved forward a few steps: the house was so dark behind him, the world so dim and uncertain in front of him, that for a moment his heart failed him. He might have to search the whole garden for the dog.

N.10

The camp stood where, until quite lately, had been pasture and ploughland; the farm house still stood in a fold of the hill and had served us for battalion offices; ivy still supported part of what had once been the walls of a fruit garden;

N.12

And another image came to me, of an arctic hut and a trapper alone with his furs and oil lamp and log fire; the remains of supper on the table, a few books, skis in the corner;

*Available from: - Keeler Limited, Clewer Hill Road, Windsor, Berkshire SL4 4AA
Telephone: 01753 857177 Facsimile: 01753 857817

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