

Preventing irrecoverable visual loss in CQ and HCQ therapy

Optometrists may encounter patients treated with either chloroquine (CQ) or hydroxychloroquine (HCQ). These drugs are quinolones, and have been known to cause irreversible retinal toxicity.

The first report of probable retinal toxicity to chloroquine was in 1959¹. HCQ is now more frequently used than CQ. Current treatment favours a lower dosage than employed earlier, resulting in fewer cases of retinal toxicity¹. Dosage relates to lean body weight, and is usually 400mg daily².

What is the optometrist's responsibility in examining the eyes and sight of these patients? Recent ophthalmological reviews include the definitive 1998 Royal College of Ophthalmologists' Guidelines (RCOGs)³, which mention optometrists.

Background

CQ and HCQ are both used in the treatment of malaria, systemic arthritis, systemic lupus erythematosus and immune disease. They can induce side-effects that include irreversible retinopathy, gastrointestinal disorders, headache, dizziness, non-retinal eye problems, hearing loss and rash.

A phototoxic cause may be indicated for changes in the skin pigmentation, corneal opacity, cataract formation and retinopathy³. In regions of high light intensity, as in malaria regions, the use of protection (clothing, sun-block, sunglasses or eye wraps) has been recommended³. CQ can cumulate in the body, particularly in high dosages, and with the presence of renal and hepatic insufficiency⁴. The lethal dose of CQ is 1g for children and 4g for adults, producing rapid death. During pregnancy, CQ presents the potential risk of foetal damage. CQ must be kept out of the reach of children⁴.

Occurrence of retinal toxicity

The number of retinopathies in a group receiving HCQ and CQ therapy will depend on a number of risk factors. These include dosage, length of treatment, the patient's health and their age. Easterbrook (1992)⁵ found 62 (3.76%) patients had irreversible visual field defects out of 1,650 patients treated with anti-malarial drugs. The 22 patients who presented with relative (not absolute) scotoma, and were followed for a median follow-up period of six years, did not lose VA; 75% maintained their visual fields, and 11% showed some improvement of their visual field. From these results, Easterbrook concluded that visual prognosis is excellent

if anti-malarial therapy is stopped at an early stage of the disease.

One case of bilateral maculopathy in an elderly patient was presumed secondary to HCQ with a dosing regime within therapeutic guidelines. It was suggested that special attention should be given to the elderly⁶. HCQ retinopathy has been reported in two relatively young women, who did not receive overdoses, but had been treated for six years⁷.

Wang et al (1999)⁸ found 1.3% of patients on HCQ for at least six years developed retinopathy, one patient at a dose of 6.5mg/kg/day. They stated that ophthalmological testing was essential for patients on HCQ medication as irreversible retinopathy can occur, albeit rarely. The frequency of examination may be inferred by the following:

- The Department of Ophthalmology, University Hospital of Wales, in respect of HCQ retinal toxicity, found no patients exhibiting retinal toxicity in a study of 73 patients, and no longer routinely screens for HCQ retinal toxicity⁹.
- Spalton et al¹ found no retinopathy in 82 patients, who had taken HCQ for over one year, and concluded that retinopathy was unlikely to occur with HCQ at dosages less than 6.5mg/kg body weight with less than 10 years of treatment.
- The Department of Ophthalmology, Royal Infirmary, Glasgow, on the basis of a study of 758 HCQ patients, concluded that there was no indication for regular ophthalmic screening, provided the dose was low¹⁰.
- CQ, if administered in high dosage long-term, may occasionally give rise to maculopathy; HCQ very rarely, if ever, causes retinal toxicity¹¹.

The RCOG lists:

- Six studies, between 1966 and 1996, together totalling 1,500 patients treated with HCQ, found only one patient with retinopathy and visual loss.
- In a single series of 1,207 patients, one developed retinopathy after seven years (1997).
- In a study of 973 patients, whose dosage of HCQ was kept low, no retinal toxicity was found.

The RCOGs state that if quinolones were introduced now, there would be no evidence for the cost-effectiveness of a screening programme².

Effect on the eye

Easterbrook found that 95% of patients on CQ showed corneal deposits, whilst less than 10% on HCQ showed any corneal changes, which may have indicated retinal toxicity¹². The corneal changes seen in patients treated with CQ or HCQ, also occur with amiodarone, indomethacin, tamoxifen, chlorpromazine, mepacrine or atovaquone. They appear as faint greyish or creamy or golden lines that radiate out from an area below the pupil and spare the limbus (corneal verticillata). Identical changes occur in Fabry's disease, and vortex corneal dystrophy¹³. The Hudson Stahl corneal lines are somewhat similar, due to epithelial iron deposit, more commonly seen in the older patient, and injured corneae of any age¹³.

The early macular changes are difficult to differentiate from age-related maculopathy, and there is no reliable screening test which will identify reversible toxicity before ophthalmoscopic changes². The characteristic early change is loss of the foveal reflex, with irregular and increased pigmentation, or 'granularity' of the macula. The later changes resemble a 'bull's eye' disposition of pigment, with a central foveolar hyperpigmentation surrounded by a ring of reduced pigmentation and, in turn, surrounded by an annulus of slightly increased pigmentation. The appearance can progress to a retinitis pigmentosa appearance, with vessel attenuation and peripheral pigmentary changes, if treatment is not withdrawn¹¹. Retinitis pigmentosa inversa was diagnosed in one patient who had a medical history of CQ and HCQ¹⁴. Rynes et al (1993)¹⁵ differentiated between a true retinopathy, and a pre-maculopathy. The former may involve visual loss, the latter subtle field and fundus changes that are reversible with drug discontinuation.

Two cases of HCQ retinopathy, and cumulative doses of 1,788g and 2,920g respectively, were analysed by Weiner et al (1991)¹⁶. They found that one patient presented bilateral bull's eye maculopathy, whilst the other a perifoveal

depigmentation. One complained of glare and difficulty in adjusting to changes of illumination; both had pericentral scotomata, bilateral VA of 6/7.5, abnormal dark-adaptation, and electroretinograms.

Screening

Easterbrook (1999)¹⁷ recommended the screening test should include VA, colour vision, Amsler grid, and corneal assessment; routine automated perimetry was not necessary. Grierson (1997) used the red Amsler grid¹⁰. Neither of the two cases of HCQ retinopathy, reported by Mavrikakis et al (1996), had abnormal colour vision, and their binocular VAs were 6/6 and 6/7.5 respectively⁷. Self-administered Amsler testing between reviews may add safety¹⁸. Evidently, experience in binocular viewing of the fundus, including the fovea, is desirable.

The RCOGs state the ophthalmologist should include assessment of:

- Distance and near VA
- Colour vision
- Visual field – red target and red Amsler grid
- Biomicroscopy of the cornea
- Retinal examination

Obligations

The RCOGs' baseline recommendations, to rheumatology and dermatology clinics, in respect of eye examinations before HCQ treatment is commenced, are:

- Ask about visual impairment (which is not corrected by spectacles).
- Record near VA of each eye (with spectacles where appropriate).
- "If visual impairment is present, an assessment by an optician is advised...any relevant abnormality detected would be referred to an ophthalmologist in the usual way".

The RCOGs recommend (to rheumatology and dermatology clinics) annual evaluation, when visual symptomology should be enquired after, rechecking acuity and assessing for blurred vision with the reading chart. Hence, optometrists can be involved before treatment commences, requiring a report to be sent to the referring physician (and GP). Where age-related macular changes are present with pigmentary changes and/or corneal verticillata, a referral to an ophthalmologist is indicated since these are relevant abnormalities. An ophthalmologist may wish to have them photographed. There is no requirement for an optometrist to put such patients on early review.

The RCOGs state that patients under long-term treatment (>5 years) should make an arrangement with an ophthalmologist. Children receiving quinolones in specialist clinics will, from early on, be checked by an ophthalmologist. An optometrist examining a child receiving quinolones, or an adult on long-term treatment, would be prudent to question (and note the answers) whether an ophthalmologist has been, or is to be consulted. Should such an arrangement not have been made, the patient should be referred to their GP, with a note of the RCOG requirement. It is important not to worry the patient.

The RCOGs state that referral to an ophthalmologist is appropriate, should there be a change in acuity or blurred vision (as assessed by reading chart) whilst on treatment. Patients should be warned to stop treatment and seek advice from the prescribing doctor. This is a warning and advice that optometrists may need to make, and they might be found wanting if they did not.

Where a patient has a potential of eye disease, an optometrist has an obligation to make such tests to detect that eye disease, as is relevant and reasonable. Once a patient is under an ophthalmologist's care, there is evidently no need for an optometrist to employ tests for the sole reason of detecting the condition that is being screened for by the ophthalmologist, save in exceptional circumstances. The same arguably applies to patients screened by optometrists. Thus, there is no need to instil a mydriatic for the only reason that the patient is diabetic, provided that:

- the next review is not imminent or overdue;
- attendance for diabetic screening reviews has been on schedule;
- blood sugar levels have not changed or varied as indicated by deterioration in health, or adverse report from a medical review, or refractive error change; and
- compliance with treatment has been good.

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About the author

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