Chloroquine Retinopathy
Dr. Shrinkhal1 & Dr. M.K. Singh2
1Junior Resident, Department of Ophthalmology
2Professor and HOD, Department of Ophthalmology
Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005, Uttar Pradesh.

INTRODUCTION:
Chloroquine Retinopathy refers to the changes seen in the retina of patients due to long term use of chloroquine. The late presentation, classically described as bull’s eye maculopathy, is preceded by a number of subtle changes. With the advent of new investigation modalities and regular screening, it is possible to prevent irreversible retinal damage due to this important and widely used drug. In this article we aim to highlight the ocular manifestations and recommended screening protocols.

DISCUSSION:
Both chloroquine and hydroxychloroquine are alkylated 4-aminoquinolone (4AQs) derivitives of quinine.

Chloroquine metabolism:
The concentration of 4AQs in different tissues after ingestion varies. In pigmented rats, the concentration of the drug after a single dose is greatest in uvea followed by liver, lung, kidney, vitreous, heart, skin, hair, brain, blood, serum in descending order [1]. The results seen are similar in humans [2].

For the same dose of hydroxychloroquine and chloroquine, levels of chloroquine are 2.5 times those of hydroxychloroquine in the body tissues [3]. The 4AQs remain in tissues for many years and are mainly excreted by the liver and the kidney.

Side effects of chloroquine toxicity:
Chloroquine can have a variety of ocular and systemic side effects.

Symptoms of Chloroquine toxicity
First symptom is difficulty in near work due to loss of accommodation. This phenomenon is reversible on discontinuation of the drug and is caused by the effect of the drug on the ciliary body.

Signs of chloroquine toxicity
Corneal signs: Punctuate or whorls like corneal epithelial deposits (cornea verticillata), transient corneal edema, and decreased corneal sensitivity. The patient may complain of blurring of vision, haloes around light and photophobia. These changes are reversible.

Early retinal changes: Fine pigmentary stippling of the macula and loss of the foveal light reflex.

Late retinal changes: Prolonged use can cause development of an annular zone of depigmentation of the retinal pigment epithelium surrounding the fovea, classically known as “Bull’s eye maculopathy” (Figure 1).
Visual field: The earliest sign of HCQ retinopathy on a central visual field is a cluster of paracentral points with decreased sensitivity.

Progressive HCQ retinopathy leads to a semi bull’s eye like scotoma that may resemble an arcuate defect, and in later stages may form a complete bull’s eye scotoma, with a complete ring defect and relative sparing of fovea.

Optical coherence tomography: High resolution cross-sectional scans of the retina using SD-OCT (Spectral Domain Optical Coherence Tomography) may detect changes in the retinal architecture before the onset of clinically apparent HCQ retinopathy. On SD-OCT, HCQ retinopathy manifests as disruption, or complete loss, of the outer nuclear layer (ONL), external limiting membrane (ELM), inner/outer segment junction (IS/OS), and retinal pigment epithelium (RPE) in the parafoveal region [4] with foveal sparing. This foveal sparing gives the “flying-saucer sign” of HCQ retinopathy.

Recent studies conducted on the effects of HCQ on the inner retinal layers showed a selective thinning of the ganglion cell layer (GCL) and inner plexiform layer (IPL) without any structural changes to the outer retinal layers and RPE [5]. Thus, developing screening methods to measure the inner layers of the retina

Multifocal electroretinography: Multifocal Electroretinography (mfERG) may be the most sensitive test for early HCQ retinopathy. Unlike full-field ERG, mfERG localizes deficiencies at the central macula, thereby detecting the subtle changes characteristic of early HCQ retinopathy. Specifically, paracentral reductions in amplitude, indicative of depressed retinal function, are the most specific waveform patterns for HCQ retinopathy [6].

Major Risk Factors for Toxic Retinopathy:

Daily Dosage: HCQ >5.0 mg/kg real weight
CQ >2.3 mg/kg real weight
Duration of use: > 5 years, provided no other risk factors associated.
Renal disease: Subnormal glomerular filtration rate
Concomitant use of drugs: Tamoxifen
Associated Macular disease: It affects screening and susceptibility to HCQ/CQ.

2016 guidelines for prevention of chloroquine retinopathy:

The most critical risk factor for chloroquine retinopathy is the daily dose by weight.

Screening Frequency – If the patient is not being overdosed and does not have co-existing risk factors, AAO recommends that annual screening can be deferred till there has been 5 years of exposure to the drug.

Recommended Screening Tests – AAO recommends Automated Visual Fields and SD-OCT be done in all cases being screened for hydroxychloroquine retinopathy.

Examination Techniques:

Primary Tests: Ideally do both Automated visual fields (adjusted to race) SD OCT

Other Objective Tests (as needed or available): mf-ERG, FAF

Newer Tests: Microperimetry, Adaptive Optics Retinal Imaging


REFERENCES:

5. Pasadhika S, Fishman GA. Effects of chronic exposure to hydroxychloroquine or chloroquine on inner retinal structures. Eye (Lond) 2010; 24:340-6.