Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/apme

Short survey

Screening for hydroxychloroquine retinal toxicity: Current recommendations

Nikunjkumar Dadhaniya [a,*], *Isha Sood* [a], *Abhishek Patil* [a], *Himanshu Aggarwal* [a], *Sundeep Kumar Upadhyaya* [b], *Rohini Handa* [b], *Sirinder Jit Gupta* [b]

[a] *DNB Trainee, Department of Rheumatology, Indraprastha Apollo Hospitals, Delhi, India*
[b] *Senior Consultant, Department of Rheumatology, Indraprastha Apollo Hospitals, Delhi, India*

ARTICLE INFO

Article history:
Received 5 January 2017
Accepted 12 January 2017
Available online xxx

Keywords:
Hydroxychloroquine
Retinal toxicity
Screening recommendation
Optical coherence tomography
Visual field

ABSTRACT

Hydroxychloroquine (HCQ) is a commonly used drug for the treatment of various autoimmune diseases including systemic lupus erythematosus and rheumatoid arthritis. Though HCQ may be associated infrequently with systemic side effects, its long-term use is associated with retinal toxicity in some patients. Most patients with HCQ associated retinal toxicity are asymptomatic initially. Retinal toxicity if allowed to persist is usually associated with irreversible damage. Therefore, screening is needed to detect retinal toxicity at an early stage to prevent visual loss. Various methods have been utilized for the screening of HCQ associated retinal toxicity, but until recently, no test(s) had been established as the gold standard. Current recommendation is to screen for HCQ associated retinal toxicity with both automated visual field and spectral domain optical coherence tomography after 5 years of use, provided baseline ocular examination is normal and there are no associated high risk factors.

1. Introduction

Hydroxychloroquine (HCQ) is an effective drug used commonly in the treatment of rheumatoid arthritis (RA) and other connective tissue diseases (CTDs). HCQ lacks systemic toxicity usually seen with other conventional disease modifying antirheumatic drugs (DMARDs) like – bone marrow suppression, secondary infection and malignancy. However retinal toxicity is a major concern with long-term use of HCQ. Conventional methods of screening over the years, have included – clinical ocular examination with testing of visual acuity, fundus examination with a dilated pupil, color vision, Amsler's Grid and visual field testing (perimetry). Once abnormalities are detected using these conventional methods of screening, retinal toxicity has already occurred and this toxicity may not be completely reversible.[1] Continuing visual loss even after discontinuation of the drug is reported.[1] It is therefore critical to detect retinal toxicity as early as possible to limit the extent of retinal toxicity. Newer methods of screening for HCQ related retinal toxicity include optical coherence tomography (OCT), fundus auto fluorescence (FAF) and

* *Corresponding author*. Tel.: +91 9712999726.
E-mail address: nikunjvdadhaniya@gmail.com (N. Dadhaniya).
http://dx.doi.org/10.1016/j.apme.2017.01.012

multifocal electroretinography (mfERG). These newer modalities are more sensitive for detection of HCQ associated retinal toxicity. Regular and effective screening can recognize toxicity at earlier stages before there is significant and irreversible visual loss.[2]

2. Mechanism of HCQ retinal toxicity

The mechanism of HCQ associated retinal toxicity has been extensively studied but not well understood. HCQ toxicity appears to first affect retinal ganglion cells and photoreceptors, particularly in the perifoveal region.[3] Accumulation of lipid complexes in ganglion cells, bipolar cells and glial cells in the retina is proposed as the triggering event in HCQ associated retinal toxicity.[4] The primary damage involves photoreceptors, and as the outer nuclear layer degenerates, there is secondarily disruption of the retinal pigment epithelium (RPE).[5] Anatomic features of retina that correlate specifically with the parafoveal or extra macular patterns of damage are not identified.[1]

3. Clinical features of HCQ retinal toxicity

Most patients with HCQ associated retinal toxicity have no visual symptoms.[1] A few patients may notice scotoma while reading. In advanced cases symptoms of HCQ associated retinal toxicity includes decreased vision, visual glare, night blindness, impaired color vision and visual field defects.[6]

4. Methods of screening for HCQ retinal toxicity

Screening tests can be classified into those looking at morphological changes [fundus examination, FAF and spectral domain optical coherence tomography (SD-OCT)] and those looking at functional changes [mfERG and Humphrey visual field]. Although all tests have a value in identifying the retinal toxicity none is considered as 100% sensitive and specific and they usually complement each other.[7]

Fundus examination is usually normal in early toxicity but it is vital for baseline screening. Earliest changes on fundus examination are fine pigmentary stippling of macula, some irregular pigmentation and loss of foveal light reflex.[8] Progressive changes of toxicity show irregular central pigmentation surrounded by a zone of depigmentation – the classical 'Bull's Eye' maculopathy.

Automated visual field (perimetry) is very useful for screening HCQ toxicity. Visual field testing may show abnormalities before abnormal findings in other parameters including visual acuity or abnormalities on fundus examination.[9] Visual field testing will reveal partial or complete ring defect in 2°–6° with central foveal sparing on 10-2 white tests (Fig. 1) whereas on 24-2 or 30-2 testing it will reveal central scotoma affecting one or more of the 4 points around fixation (more evident on pattern deviation plots). Unfortunately patients frequently have nonspecific abnormalities on field examination, these findings should be interpreted with caution taking in account other test results and reproducibility of defects.[10]

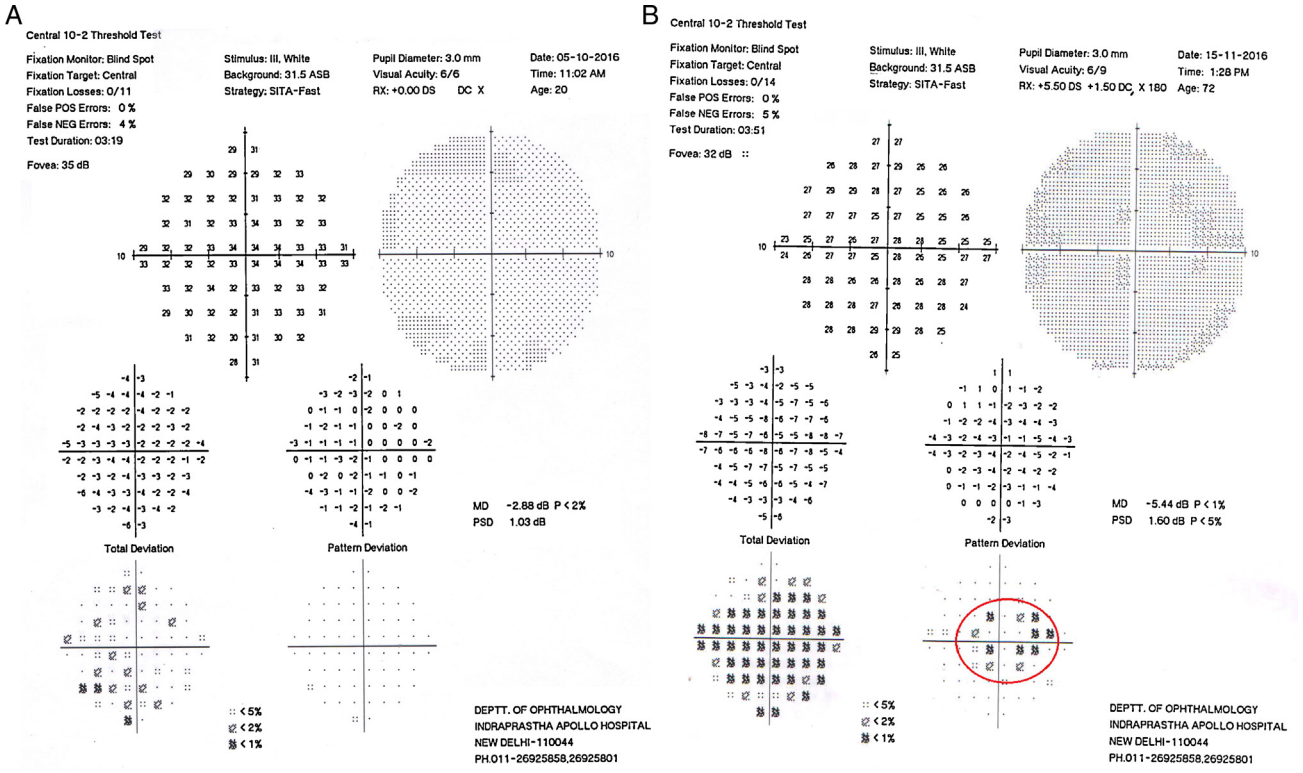

Fig. 1 – (A) Normal 10-2 visual field. (B) 10-2 visual field showing paracentral ring scotoma.

Please cite this article in press as: Dadhaniya N, et al. Screening for hydroxychloroquine retinal toxicity: Current recommendations, *Apollo Med.* (2017), http://dx.doi.org/10.1016/j.apme.2017.01.012