



# Hydroxychloroquine retinopathy—less than meets the eye

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## To the Editor:

Royal College of Ophthalmologists (RCOphth) recommend that definite hydroxychloroquine (HCQ) retinal toxicity is diagnosed when both functional and anatomical tests are abnormal; and abnormality in one test alone is classified as possible retinopathy. Using these criteria, Marshall et al. report that prevalence of definite HCQ toxicity was 1.6% in 869 patients taking HCQ for  $\geq 5$  years [1].

Effect of co-morbidities like diabetes, hypertension, chronic kidney disease, etc. on ocular toxicity in patients treated long term with HCQ is important. In a cohort of 2867 rheumatic patients taking HCQ, 31 patients had a diagnosis of blindness or toxic maculopathy [2]. Majority of these were associated with co-morbidities, and only three cases had HCQ-related retinal toxicity, each without blindness or functional vision loss. In all three patients, HCQ had been used for  $>18$  years. It is important to estimate the ocular effect of co-morbidities in the cohort analysed by Marshall et al. Eyes with pathologies can also lead to increase in errors and misinterpretation of data from techniques such as SD-OCT—false-positive rates as high as 26.2% have been reported [3]. Marshall et al. also report that the visual field tests were ‘unreliable’ (fixation losses, false positives and/or false negatives) in as many as one-third of their patients. Such limitations of these techniques must be considered before deciding on toxicity causality and therapy modification.

The risk of HCQ retinal toxicity is dependent on daily dose and duration of use. At recommended doses, risk of toxicity up to 5 years is under 1%. Both, the RCOphth and

American Academy of Ophthalmology, recommend annual monitoring after 5 years of therapy with HCQ. Thus, after 5 years of use, the *incremental* annual risk of toxicity must be looked at rather than the *cumulative* risk; because it gives the actual risk for a patient who is found to be free of retinopathy at a given point in time. This risk is 1% after 10 years of use and less than 4% after 20 years of use [4]. These data should reassure physicians that HCQ can be prescribed safely for extended periods with understanding of the ocular risks and with effective screening.

## Compliance with ethical standards

**Conflict of interest** AP and RTM are employees of Ipca Laboratories Ltd, India, and are involved in clinical research on hydroxychloroquine. SC declares no relevant conflicts in relation to this manuscript.

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