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## Original article

# Evaluation of a follow-up protocol for patients on chloroquine and hydroxychloroquine treatment<sup>☆</sup>



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## ABSTRACT

**Objective:** To review the problems found after a new follow-up protocol for patients on chloroquine and hydroxychloroquine treatment.

**Method:** Retrospective study was conducted between May 2012 and January 2013 on the clinical files, retinographies, fundus auto-fluorescence (FAF) images, and central-10 degree visual fields (VF) of patients who were referred to the Ophthalmology Department as they had started treatment with hydroxychloroquine.

**Results:** One hundred twenty-six patients were included; 94.4% were referred from the Rheumatology Department and 5.6% from Dermatology. Mean age was 59.7 years, and 73.8% were women. All of them were on hydroxychloroquine treatment, and 300 mg was the most frequent daily dose. Rheumatoid arthritis was the most common diagnosis (40.5%), followed by systemic lupus erythematosus (15.9%). The mean Snellen visual acuity was 0.76, and 26 patients had lens opacities. The VF were normal in 97 patients, 8 had mild to moderate defects with no definite pattern, and in 9 the results were unreliable. Of the 51 patients older than 65 years, 16 (31.4%) had altered or unreliable VF. The FAF was normal in 104 patients (82.5%), and abnormal, but consistent with ophthalmoscopic features, in 12 patients (pathological myopia, age related changes, early, middle or late age-related macular degeneration).

**Conclusions:** Visual fields as a reference test for the diagnosis of AP toxicity are not quite reliable for patients over 65. Therefore, the FAF is recommended as primary test, perhaps combined with another objective test, such as SD-OCT instead of VF.

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## Evaluación de un protocolo de seguimiento de pacientes en tratamiento con antipalúdicos

### RESUMEN

#### Palabras clave:

Cloroquina  
Hidroxicloroquina  
Toxicidad retiniana  
Examen ocular  
Efectos secundarios  
Reacción adversa  
Campos visuales  
Fotos de autofluorescencia

**Objetivo:** Evaluar el protocolo implantado en nuestro hospital para el cribado de toxicidad ocular por antipalúdicos (AP) revisando las características de los pacientes estudiados y los problemas encontrados tras su implantación.

**Método:** Estudio retrospectivo de las historias clínicas, retinografías, fotos de autofluorescencia (FAF) y campos visuales (CV) centrales 10-2 de los pacientes que iban a iniciar tratamiento con AP, desde el momento de la implantación del protocolo en mayo de 2012 hasta enero de 2014.

**Resultados:** Se han revisado 126 pacientes. El 94,4% procedían del servicio de reumatología y el 5,6%, del de dermatología. La edad media fue de 59,7 años, y el 73,8% fueron mujeres. Todos estaban en tratamiento con hidroxicloroquina, siendo la dosis más frecuente 300 mg diarios. La artritis reumatoide fue el diagnóstico más frecuente (40,5%), seguido del lupus eritematoso (15,9%). La agudeza visual media fue de 0,76; 26 pacientes presentaban opacidades de cristalino. En 97 pacientes los CV resultaron normales, 8 presentaron defectos leves o moderados sin patrón definido, y en 9 los resultados fueron poco fiables. De los 51 pacientes mayores de 65 años, 16 (31,4%) presentaron CV alterados o no valorables. La FAF resultó normal en 104 pacientes (82,5%) y anormal, aunque congruente con los hallazgos oftalmoscópicos, en 12 pacientes.

**Conclusiones:** El rendimiento de los CV como test de referencia para el diagnóstico de toxicidad por AP es relativamente bajo en pacientes mayores de 65 años. Por ello creemos recomendable usar la FAF como test primordial y asociarlo quizás a otro test objetivo, como el SD-OCT, en detrimento de los CV.

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## Introduction

Chloroquine and hydroxychloroquine comprise a group of drugs traditionally used for treating malaria. Some antimalarial drugs (chloroquine [ClQ] and hydroxychloroquine [hydroxyClQ]) have demonstrated their usefulness for treating some rheumatic and dermatological diseases.<sup>1,2</sup> The two main indications are rheumatoid arthritis and lupus erythematosus, although said drugs have also been used for other rheumatic<sup>1</sup> and dermatological<sup>2</sup> diseases (Table 1). Antimalarial drugs are well tolerated and safe. Ocular side effects include retinal toxicity (which could produce irreversible loss of vision) and drug deposits in the cornea (cornea verticillata).<sup>2</sup> Retinal toxicity due to ClQ and hydroxyClQ has been known for many years but its action mechanism is not clear. Even so, it is believed to induce some changes in the cytoplasm of ganglion cells and photoreceptors which subsequently involve the retinal pigment epithelium (RPE), where it joins with melanine.<sup>3</sup>

The appearance of retinal toxicity is related to the daily and aggregate dosage of antimalarial drugs. Latest estimates reveal that toxicity increases suddenly from 1% as from 5 to 7 years of continued use or with an aggregate dose of 1000 g of hydroxyClQ.<sup>4</sup>

As there is no treatment for reverting the retinal toxicity of said drugs, it is crucial for patients and physicians to be vigilant to minimize the risks of said toxicity. For early identification of antimalarial drug toxicity, the American Academy of Ophthalmology (AAO) published in 2011 recommendations

**Table 1 – Rheumatologic and dermatological diseases which utilize antimalarial drugs for treatment.<sup>1,2</sup>**

- Rheumatoid arthritis
- Systemic lupus erythematosus
- Chronic juvenile arthritis
- Ankylosing spondylitis
- Psoriatic arthritis
- Palindromic rheumatism
- Eosinophilic Fascitis
- Juvenile dermatomyositis
- Sjögren syndrome
- Erosive osteoarthritis of hands
- Calcium pyrophosphate deposition disease
- Porphyria cutanea tarda
- Chronic ulcerative stomatitis
- Dermatomyositis
- Sarcoidosis
- Polymorphic light eruption
- Generalized granuloma annulare

for following-up patients in treatment with said drugs.<sup>5</sup> The AAO recommended a baseline exploration during the first year of treatment to discard any maculopathy (which would make the use of said drugs unadvisable) and as a benchmark for comparing subsequent findings. Annual examinations should be made as of the fifth year of treatment (or earlier in the presence of risk factors). The final objective of these examinations is to identify at an early stage any paracentral retinal damages or visual field (VF) defects. The ophthalmological examination recommended by the AAO consists in a standard

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