ORIGINAL RESEARCH PAPER

Medical Science

KEY WORDS:

ROLE OF MULTIFOCAL ERG IN DETECTING EARLY HCQ TOXICITY

Dr M. Sri Rama Chandra Murthy Associate Professor designate Andhra Medical College Visakhapatnam AP India

Dr P. Syam Sundar* Associate professor designate Andhra Medical College Visakhapatnam AP India *Corresponding Author

Dr Vishnu Deepthi Narayanam Fellow Shankar Foundation Eye Hospital Visakhapatnam.

INTRODUCTION:

The electroretinogram (ERG) is a recording of the bioelectric potential, which is the summed activity of the retinal cells located at the back of the eye, when stimulated by light. When bioelectrical changes occur within the retina, the change is propagated to the surface of the cornea. These small (and often very fast) signals can be captured by an electrode placed on the surface of the cornea.

The mfERG has been used widely to diagnose and study retinal diseases Multifocal ERG (mfERG) is most useful in the diagnosis of unknown visual loss,distinguishin between optic nerve and retinal disease and determination of hydroxychloroquine toxicity (Plaquenil toxicity).

In general, an abnormal mfERG indicates that the foveal cones and/or bipolar cell layers are dysfunctional and the source of vision loss

Hydroxychloroquine sulfate is a colorless crystalline solid, soluble in water to at least 20 percent; chemically the drug is 2-[[4-[(7-Chloro-4-quinolyl) amino]pentyl] ethylamino] ethanol sulfate (1:1).PLAQUENIL (hydroxychloroquine sulfate) tablets contain 200 mg hydroxychloroquine sulfate, equivalent to 155 mg base, and are for oral administration.

Mostly used in the prophylaxis and treatment of acute attacks of malaria and treatment of chronic discoid and systemic lupus erythematosus (SLE) and acute or chronic rheumatoid arthritis in patients not responding to other therapies.

Ocular side effects have included disturbances of accommodation with symptoms of blurred vision (dose-related and reversible with treatment cessation). Corneal side effects have included transient edema, punctate to lineal opacities, decreased corneal sensitivity, corneal changes (with or without accompanying symptoms, including blurred vision, halos around lights, photophobia), and corneal deposits.

Retinal (macular) side effects have included edema, atrophy, abnormal pigmentation (mild pigment stippling to a "bullseye" appearance), loss of foveal reflex, increased macular recovery time following exposure to a bright light (photostress test), and elevated retinal threshold to red light in macular, paramacular, and peripheral retinal areas. Other fundus changes have included optic disc pallor and atrophy, attenuation of retinal arterioles, fine granular pigmentary disturbances in the peripheral retina, and prominent choroidal patterns in advanced stage.

Retinopathy appears to be dose related and has occurred within several months (rarely) to several years of daily therapy. In an early form, retinopathy is reversible with cessation of hydroxychloroquine treatment. If retinopathy is conserved, then there is a risk of irreversible retinal lesions, even after withdrawal of treatment.

Multifocal ERGs therefore help us better identify patients who are more likely to develop retinal toxicity. Almost as important, mfERGs provide psychophysical evidence to continue drug in those patients who have small changes in visual field testing.

AIM OF THE STUDY

- The study aims at seeking the role of mfERG in the detection of early Hydroxychloroquine toxicity.
- Along with this the study also aims at the understanding the effects of Hydroxychloroquine usage on Lens, Retina and Cornea.

MATERIALS AND METHODS

Patients are randomly chosen in a Tertiary Teaching Hospital who are on long term hydroxychloroquine therapy for rheumatoid arthritis & other diseases from July 2017 to August 2018.

Patients requiring long term hydroxychloroquine therapy at first visit and patients already on hydroxychloroquine were included in the study. Patients with pre existing retinal disorders including Diabetic or Hypertensive retinopathy, ARMD, CME, Macular hole, epiretinal membrane, prior intraocular surgery & any other drug intake.

20 patients who were referred to ophthalmology department from rheumatology department who were on hydroxychlo roquine were recruited for the study.

11 patients who fulfilled the inclusion criteria were included in the study. Of which 4 were males & 7 were females with age ranging between from 30 to 60years. All the patients underwent a through ocular examination including visual acuity, refraction, IOP. colour vision, Amslers grid, perimetry(10-2), dry eye evaluation , dilated fundus examination, fundus photography, OCT & Multifocal ERG.

If all tests are normal, patient is enrolled in study and patients are followed up every 3 months 6 months.

RESULTS-

4 out of the 11 patients in the setting of normal BCVA, normal fundus, colour vision, Amslers grid , perimtery and OCT showed reduced foveal and parafoveal ring responses and minimally reduced perifoveal ring responses with mf ERG.

Number of patients recruited	20
Patients eligible for study	11
Sex male 4 & female 7	

Indication for treatment Rh.arthritis
Duration of treatment -3months to 2years
Chloroquine dose 200mgm twice daily

- Mf ERG positive for retinal toxicity 4 cases

Normal

DISCUSSION:

The onset of retinotoxicity might occur well before clinically visible changes were seen, and antecedent to documentation of ring-scotomata on perimtetry. This represents a preclinical stage of retinotoxicity that occurs prior to the onset of symptoms. This demonstrates that a patient on appropriate dosing and no systemic risk factors can develop retinotoxicity way before the 'safety limit' of 10 years in contrast to recommendations by Bernstein[1] and Mackenzie.

To date, the most significant risk factor for retinotoxicity accepted widely by ophthalmologists has been the dose per kg body weight per day, rather than cumulative dosage. Alt the risk of retinotoxicity is low at dosages of <6.5 mg/kg/day[2] It is well known that by the time symptoms appear, clinical macular retinotoxicity is irreversible. Visual acuity, colour acuity, field defects, and clinical bull's-eye maculopathy is permanent once it occurs and may continue to deteriorate for several years after even upon cessation of therapy[3] These parameters currently form the basis of most recommended screening strategies.[4] However, even in the presence of high-risk factors, the recommendations generally suggest clinical follow-up with visual field assessment. Marmor *et al*[5] reserved mfERG only as an optional tool during follow-up *after* macular toxicity has occurred. Recent studies have reported cases that, like our patient, had mfERG abnormalities despite being asymptomatic with normal or clinical findings[6] Typically, the mfERG will demonstrate a paracentral ring depression of signals around the fovea as was seen in our patient.[7] Moschos *et al*[8] reported that early cessation of hydroxychloroquine in patients resulted in improvement of mfERG patterns and reversible of toxicity over a period of 6 months. This suggests that early toxicity detectable only on mfERG is possibly reversible. There is thus a need to identify this subclinical stage of macular toxicity to prevent irreversible retinal changes.

In our study all the 11 patients had normal visual function including visual acuity, Colour vision, fundus, perimetry,Amsler grid, OCT etc. there was no symptom of visual disturbances. But on mf ERG 4 patients changes suggestive of retinal toxicity.

Early screening devices such as fundus examinations, color vision testing, automated perimetry,and Amsler grid testing are currently recommended to detect the changes of hydroxychloroquine toxicity.Results of these tests have been normal unless the patient has a visual complaint, at which point the damage appears to be irreversible despite discontinuation of therapy. The early pigment stippling of the macula in an asymptomatic patient is often reversible following discontinuation of the drug. There is thus a need to identify this subclinical stage of macular toxicity to prevent irreversible retinal changes.

CONCLUSION

We believe that multifocal ERG is a more definitive test for demonstrating retinal dysfunction from hydroxychloroquine toxicity in the setting of a normal-appearing fundus without changes on Amsler grid and perimetry and with relatively normal visual acuity and normal OCT. Multifocal ERG has the potential to be used as an early screening device for patients taking high doses of hydroxychloroquine before they become symptomatic or show clinical signs of toxicity.

REFERENCES:

1. Bernstein HN. Ophthalmologic considerations and testing in patients receiving long-term anti-malarial therapy. Am J Med 1983; 75:
2. Easterbrook M. Editorial: Current concepts in monitoring patients on antimalarials. Aust NZ J Ophthalmol 1998; 26: 101–103
3. Easterbrook M. Long-term course of anti-malarial maculopathy after cessation of treatment. Can J Ophthalmol 1992;27: 237–239. | PubMed | ISI | ChemPort |
4. Fielder A, Graham E, Tullo A. Royal college of ophthalmologists guidelines: ocular toxicity and hydroxychloroquine. Eye 1998; 12: 907–909. | PubMed | ISI
5. Marmor MF, Carr RE, Easterbrook M, Farjo AA, Mieler WF, American Academy of Ophthalmology. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy: a report by the AAO. Ophthalmology 2002; 109: 1377–1382. | Article | PubMed | ISI |
6. .Maturi RK, Yu M, Weleber RG. Multifocal electroretinographic evaluation of long-term hydroxychloroquine users. Arch Ophthalmol 2004; 122: 973–981. | Article | PubMed | ISI | ChemPort
7. Moschos MN, Moschos MM, Apostolopoulous M, Mallias JA, Bouros C, Theodossiadis GP. Assessing hydroxychloroquine toxicity by the multifocal ERG. Doc Ophthalmol 2004; 108: 47–53. | Article | PubMed | ISI |
8. Moschos MN, Moschos MM, Apostolopoulous M, Mallias JA, Bouros C, Theodossiadis GP. Assessing hydroxychloroquine toxicity by the multifocal ERG. Doc Ophthalmol 2004; 108: 47–53. | Article | PubMed | ISI |