



## DETECTION OF HYDROXYCHLOROQUINE TOXICITY ON HUMAN RETINA USING ELECTRORETINOGRAPHY

**Mobasserian A**

Tehran Medical Sciences Branch , Islamic Azad University Tehran – Iran

**Shushtarian S.M\***

Tehran Medical Sciences Branch , Islamic Azad University Tehran – Iran  
\*Corresponding Author

### ABSTRACT

**Aim:** Rheumatoid arthritis (RA) is an autoimmune disease marked by symptoms of inflammation and pain in the joints. Early diagnosis of this disease is important as far as better treatment is concerned. There is no cure for RA, but there are treatment that can help you to manage it. Hydroxychloroquine (HCQ) is a drug that can decrease the pain and swelling caused by RA. This drug has toxic effect on the retina, mainly on macula. Electroretinography (ERG) which measures the electrical response of various cell types in the retina is an electrophysiological technique which may be used for diagnosis of adverse effect of HCQ on retina. The aim of present work is to search for ERG changes in RA patients consuming HCQ for a quite a long period.

**Method:** Twenty five RA patients selected for the purpose of present research work. They were all female patients in age range of 30-40 years and under HCQ treatment for at least two years. ERG was tested in total patient group. b peak of ERG pattern was selected and amplitude ( $\mu\text{V}$ ) and latency (msec) of the peak were measured in total population. The same procedure was followed for twenty five subjects with healthy visual system, mainly retina. The control group matched with case one as for as the sex and age were concerned. The results obtained in two groups were compared together for possible ERG b peak changes in two groups.

**Results:** It was observed in case group that mean amplitude / S.D. was 128 / 13.68 and the same calculation was 85 / 11.25 ( $\mu\text{V}$ ) in control group. As for as latency was concerned the mean latency / S.D. was 53 / 4.28 and 42 / 2 (msec) in case and control groups respectively.

It was observed that the differences in two groups i.e. case and control were statistically significant as far as latency and amplitude were concerned.

**Conclusion :** From the results of present work one can conclude that HCQ may affect retina in RA patients which will be discussed in detail in full paper.

**KEYWORDS :** Rheumatoid Arthritis , Hydroxychloroquine, Electroretinography

### Introduction

Early diagnosis of Hydroxychloroquine (HCQ) toxicity on human retina is an important task.

The primary screening tests are automated visual fields plus spectral-domain optical coherence tomography (SD OCT). The multifocal electroretinogram (mfERG) can provide objective corroboration for visual fields, and fundus auto fluorescence (FAF) can show damage topographically. Modern screening should detect retinopathy before it is visible in the fundus. [1].

Beside recommendations on screening for Chloroquine and Hydroxychloroquine retinopathy introduced by American academy of ophthalmology there are quite a large research work on chloroquine and HCQ toxicity on retina using different electrophysiological techniques which will be pointed briefly as follow.

Neubar AS and his colleagues worked on detection of chloroquine retinopathy using Electrooculography and colour vision tests.

They came to conclusion that screening for chloroquine retinopathy can be improved by using a sensitive color test and on other hand they came to conclusion that EOG is of little diagnostic value in this regard [2]

The literature review in this connection is very interesting. In previous work little diagnostic value of EOG was reported where as on the other hand Fatmeh Alahdady et al on 2016 reported the usefulness of EOG. In early detection of chloroquine and HCQ toxicity on human retina [3]

In an attempt Heravian j et al in 2011 worked on usefulness of color vision photostress recovery time and visual evoked potential tests in early detection of ocular toxicity from HCQ consumption. They came to know that in the early stages of maculopathy P100 latencies of VEP and photostress recovery time (PSRT) are useful predictors of HCQ ocular toxicity [4]

Beside two routine electrophysiological techniques i.e. EOG and VEP, electroretinography (ERG) was also taken into consideration by quite a large scientists, hereby we will take into consideration one of this research.

Cavagna L and his team reported early electroretinographical changes in elderly RA patients treated with HCQ [5]

The above mention literature survies is a proof for importance of electrophysiological techniques related with HCQ toxicity, therefore we try to consider ERG and its changes due to HCQ uptake in RA patients.

### Material and Method

Twenty five RA female patients with age range of 30-40 were taken randomly for the purpose of present work. They were all under HCQ prescription for at least two years. The patients did not have apparent change in retina. The visual acuity of the patients were 10/10 or other wise could be corrected to normal one by suitable lenses. ERG was tested in total population. Mangoni, an electrophysiological machine capable of recording conventional VEP, ERG and EOG was used to record ERG in these patients.

Three electrodes active, reference and ground were used to connect the patients to recording machine. Active was a hard contact lens fixed on cornea. Reference was an earring electrode placed on pinna and finally ground was a cup shaped electrode attached to forehead.

b peak of ERG was taken into consideration and amplitude ( $\mu\text{V}$ ) and latency (msec) of b wave were measured for each subjects. finally mean and S.D. of amplitude and latency of b peak of ERG were calculated. The same procedure was repeated for 25 subjects with normal visual system mainly retina. The normal subject were matched with patients one as for as sex and age were concerned. The results obtained by two groups were compared together for possible significant changes, which will be explained in result section.

### Results

ERG was examined in 25 patients under HCQ prescription. Beside that 25 healthy subjects with normal visual system, mainly retina were tested for ERG examination.

The results indicate the mean amplitude / S.D. of b peak of ERG were 128 / 13.68 and 85 / 11.25 ( $\mu\text{V}$ ) in control and case groups respectively

In case of mean latency / S.D. of ERG b peak the results were 53  $\pm$  4.28 and 42 / 2 msec in patients and normal population groups.

Comparing the value obtained in two group, the differences are significant as for as amplitude and latency of ERG, b peak were concerned ( $P < 0.05$ )

## Discussion

Hydroxychloroquine (HCQ) is a drug to prevent or treat malaria infections caused by mosquito bites. This medication is also used usually with other medication to treat certain auto-immune diseases like rheumatoid arthritis (RA) and lupus.

This drug has certain side effects. Retina is a part of visual system which may be affected in RA patients due to HCQ consumption. The purpose of present work is to search on toxic effect of HCQ on retina using electroretinography (ERG) which will be discussed as follow.

It is a fact that electrophysiological tests are reliable techniques to look for side effects of different drug on visual system mainly retina and visual pathway [6-8]. In this connection ERG also may be considered to detect the toxic effect of HCQ on retina.

The result of present work indicates the reduction of ERG b peak amplitude and increase of latency of the same peak in case and control groups. These finding can be supported by following references.

Nair AA et al worked on different types of ERG techniques to check for the effectiveness of the techniques to detect the toxicity of HCQ on retina and he reported reduced amplitude of full-field ERG which supports the result of reduction of ERG amplitude obtained in present work[9].

Kakanova M et al worked on ERG contribution in early diagnosis of chloroquine and hydroxychloroquine maculopathy and he could observed the value of b wave latency was changed in HCQ consuming patients[10]. This reference also supports the result of present research work as for as latency of ERG, b peak is concerned.

From these two above references and other work one can conclude that ERG is a suitable technique to indicate the early toxic effect of HCQ on human retina[11].

Finally it is to mention that there are some references to report the inefficiency of ERG in detection of HCQ toxicity on retina but this document has considered only one patients that cannot be generalized in this regard[12].

## Conclusion

From the result of present work one can conclude that ERG and mainly the changes in amplitude and latency of b peak can be taken as proper parameters to detect the early toxic effect of HCQ on human retina.

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