

Multifocal ERG Recording In Patient On Hydroxychloroquine Therapy

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Abstract: Introduction: Multifocal electroretinography (mfERG) is a new technique that allows analysis of local function of Retina. Hydroxychloroquine is a drug which has dose dependent systemic toxicity including significant visual disturbances & loss of vision. The use of mfERG for evaluating Hydroxychloroquine retinopathy appeared to detect retinal physiological changes earlier than other testing modalities and may enable documentation of preclinical stage of Hydroxychloroquine retinopathy. **Method:** 80 patients taking HCQS therapy are randomly selected. **Result:** Out of these asymptomatic patients electrophysiological abnormalities in two and three dimensional study were seen in 13 patients. Para central depression was found in 17 eyes while generalized depression was found in 8 eyes. In one eye normal recording was found. The study has got external validity or generalizability because the effect of drug on retina will be same in all parts of the country though affect of confounder bias i.e. the other cause associated with defect in mfERG may be there, so it is applicable in prevention of further effect on retina. **Conclusion:** mfERG has got high sensitivity & specificity in diagnosing early retinal defect.

Key words – mfERG , Hydroxychloroquine, Para central depression, generalized depression

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Introduction: Multifocal electroretinography (mfERG) is an investigation that can simultaneously measure multiple electroretinographic responses at different retinal locations of the posterior retina.¹ mfERG was developed by Sutter and Tran in 1992 and has revolutionized the objective functional assessment of retinal diseases.² In contrast to full-field electroretinography (ERG),mfERG allows simultaneous measurement of multiple retinal responses at different locations. Compared to visual field perimetry exams ,they allow the identification of the levels (retina,optic nerve) where the visual system is affected. Furthermore ,they do not require the voluntary participation of the patient.³ Hydroxychloroquine is a drug which has dose dependent systemic toxicity including significant visual disturbances & loss of vision. Irreversible retinal toxicity may be associated with long-term use of the drugs ,causing the development of bull's eye maculopathy in the late stage.⁴ Long-term hydroxychloroquine use may be associated with mfERG abnormalities.⁵

Regular ophthalmologic examinations should be performed for patients on hydroxychloroquine regimens because there is no satisfactory treatment for hydroxychloroquine retinal toxicity.⁶

Ophthalmologists, dermatologists and rheumatologists should monitor for ocular toxicity of hydroxychloroquine carefully.

mfERG is most useful in the diagnosis of:

- unknown visual loss
- distinguishing between optic nerve and retinal disease;
- determination of hydroxychloroquine toxicity (Plaquenil toxicity)⁸.

There are some specifies guidelines for performance of the test. It also provides detailed guidance on technical and practical issues, as well as on reporting test results. The main objective of the guidelines is to promote consistent quality of mfERG testing and reporting within and among centers. These 2007 guidelines, from the International Society for Clinical Electrophysiology of Vision (ISCEV: <http://www.iscev.org>), replace the ISCEV guidelines for the mfERG published in 2003.⁷ In general, an abnormal mfERG indicates that the foveal cones and/or bipolar cell layers are dysfunctional and the source of vision loss. Unlike the focal ERG, mfERG also indicates the precise distribution of the retinal dysfunction. This precision helps to correlate electrophysiologic findings with visual field testing.

Material and Method: It was a cross sectional study conducted in the Regional Institute of Ophthalmology ,Gauhati Medical College and Hospital, during the period of April 2012 to September 2012,after obtaining ethical clearance from the Institutional Ethical Committee. For recording mfERG revised Guidelines of ISCEV (International Society for

Clinical Electrophysiology of Vision) is considered.⁷

Cases: The cases were referred to the Ophthalmology department from the Dermatology and Medicine Immunology Department of Gauhati Medical College and Hospital in routine eye check up without any ophthalmological problem. The procedure of examination performed was explained to all the cases and written consent was taken prior to the examination.

Inclusion criteria:

1. Patient on Hydroxy chloroquine therapy.
2. Age group of the patient was 20-60 yrs.
3. Both male and female were taken.
4. Without any problem related to eye.

Exclusion criteria:

1. Patient with diabetic and hypertensive retinopathy.
2. Smoker and alcoholics.
3. Patient with current or past treatment with drugs causes retinal toxicity.
4. History of blunt or penetrating ocular injury.

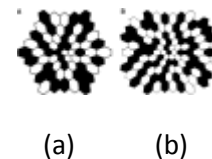
Ocular examinations were performed for visual acuity, visual field, intraocular pressure, colour vision and ophthalmoscopy.

Multifocal ERG testing was performed by Monpack 2, Metrovision in the following way:-

Proper ocular examination was done prior to examination including acuity of vision and corrective lens were given for the test proper where acuity was less. Patient eyes were dilated and kept in dark room half an hour prior to examination for adaptation which is necessary for action of the stimulus more efficiently. Then patient was brought to the examination room which was illuminated with dim red light. Topical anaesthesia was given and contact lens or jet electrode was applied over the cornea. The References and ground electrode were placed on the temple and forehead after cleaning the skin with abrasive gel. Electro conductive gel was used below the electrode. Patient chin was placed on the chin rest of the machine in such a way so that eye to be tested is only 30 cm away from the LCD monitor where stimulus were present and the patient should fix their eye at the centre. The subject viewed a black and white

pattern of hexagonal elements each of which flashes on and off with its own pseudo-random binary sequence, known as an M sequence. Cross correlation are then used to calculate the individual responses to each of the stimulus hexagons, and these resembles real ERGs. The screen is isoluminant over the whole time of the recording. The display is adjusted at 61 hexagons which provide a suitable compromise between the degree of spatial resolution and the time taken for testing.⁸ One eye to be tested at a time and the other eye is occluded. The room was now completely cut off from the light and 5000 stimuli were applied on LCD monitor in the form of black and white hexagons, flash alternatively in per fixed manner. In case of invalid or reject response the procedure was repeated from the beginning.

Analysis: The recorded were in the form of three types recording: One trace array chart showed the individual responses, 2 and 3 dimensional charts were made on the basis of the trace charts.

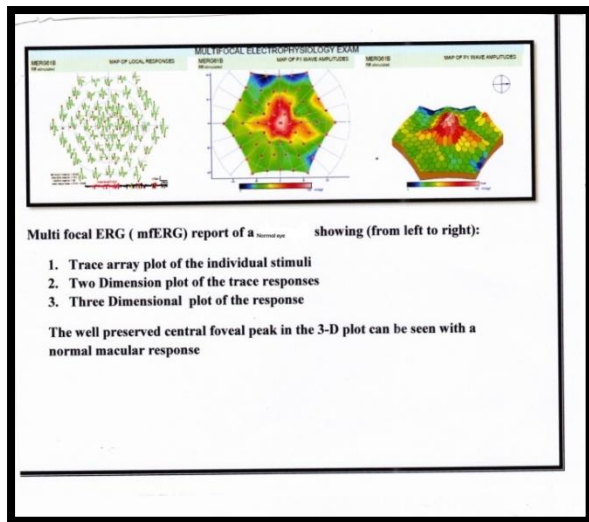


(a) Representative hexagonal mfERG stimulus array with 61 elements scaled with eccentricity. Roughly half of the elements are illuminated at any one time. (b) Same as in panel A for an array with 103 elements

The overall stimulus pattern should subtend a visual angle of 20–30° on either side of the fixation point. The stimulus region can be divided into different numbers of hexagons. The most frequently used patterns have 61 or 103 hexagons, with 241 hexagons occasionally used. The choice depends on balancing the need for good spatial resolution and a high signal-to-noise ratio, while minimizing the recording time. The typical mfERG setup includes a contact lens electrode on the cornea connected to an electrically isolated amplifier. The patient views a monitor displaying a rapidly changing sequence of hexagons. Using a cross-correlation technique, the software determines the electrical response of each of 61 segments in the posterior pole.⁹ For ease of pattern recognition, the software

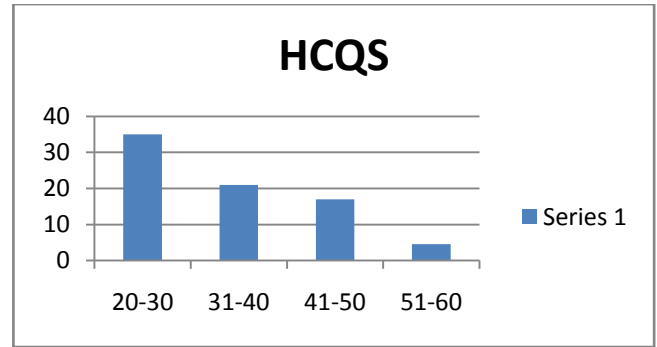
then generates a 3-D waveform of the response density reflecting a much higher response in the normal foveal center.

Results: 80 patient of Hydroxychloroquine therapy examined with mfERG, abnormalities were found in 13 patient (25 eyes, one eye showed normal recording). Paracentral depression of the central macular function was seen in 9 right and 8 left eyes and generalized depression of central macular function was seen in 4 right and 4 left eyes. Of the cases that showed abnormalities the diagnosis was SLE in 7 cases followed by Rheumatoid arthritis in 4 cases and Discoid Lupus Erythematosus in 2 cases.



Age distribution: Eye abnormalities were detected in age of 39 -60 yrs. The mean age group was 49.69+/-7.5yrs.

Age group in years	Hydroxychloroquine Cases Number of cases (n= 80)
20-30	35(43.75%)
31-40	21(26.25%)
41-50	17(21.25%)
51-60	7(8.75%)



Vertical line: Shows number of cases, Series 1: Shows number of patient fall under this group.

Sex: distribution: Out of 13 cases, 11 female (84.6%) and 2 male (15.4%).

Weight: The weight range of 13 patients was 46-60 kg; mean weight was 52.15 +/-5 kg.

Weight in kg	No. of patient
40-50	49(61.25%)
51-60	26(32.5%)
More than 60	5(6.25%)

Dose per kg body weight: Ranging from 3 to 8 mg /kg body weight with the mean was 4.41 ±1.409 mg/kg.

HCQS (mg/Kg)	Number of cases(n= 80)
<4.4	37(46.25%)
4.5-6.6	21(26.26%)
>6.6	22(27.5%)

Duration of therapy: Range was 24 month to 120 months; average duration was 53.54 ±25.7 month.

Cases	Duration of therapy(months)			Dose/body weight(mg/kg)		
	<24	24-60	>60	<4.4	4.4-6.6	>6.6
13 cases	0	10	3	11	0	2

Discussion: Multifocal ERG demonstrate the central macular cone function¹⁰. It has a consistent topographic distribution in the normal population. However, the summed amplitude of multifocal ERG can vary significantly among normal subjects. Therefore, topographic abnormalities (via a three-dimensional distribution map) are useful for the interpretation of multifocal ERG in diseased

patients. The latencies of the waveforms appear to be most consistent in the normal population. In the present study abnormalities in mfERG was found in 25 eyes out of 160 tested eyes. Most of the cases showed paracentral depression and few cases showed generalised depression. Most of the patient were on treatment for more than 5 yrs, and the doses were less than 6.5mg/kg per day.

Conclusion: The use of mfERG for evaluating Hydroxychloroquine retinopathy appeared to detect retinal physiological changes than other testing modalities and may enable documentation of preclinical stage of Hydroxy chloroquine retinopathy.¹¹ It is an analytic study or prevalence study because proportion of the patient taking the treatment has the particular defect on mfERG, other had no abnormality, so confounder bias may be present like tobacco taking or smoking. Genetic susceptibility of effect on eye may not be ruled out. The study has got external validity because the effect of drug in all parts of country will be same, though confounder bias may be there, so it is applicable in prevention of further effect on retina and modifying the line of treatment. Using a slowed down m-sequence, one can readily see and study the variations with the mfERG. These has immense research potential.^{12,13}

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