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Study of normative data of ephios handheld electroretinogram

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Abstract

Objective:

1) To analyse normative data from Ephios Handheld Electroretinogram.
2) To compare the obtained normative data with that of existing data of both handheld and table top Electroretinogram.

Method: Electroretinograms was measured in 45 normal subjects in accordance with the International standardisation Protocol by ISCEV. The mean, median and standard deviation of each wave was calculated and these were compared with the results from other studies. The repeatability of handheld ERG was also tested by repeating the test in 10 subjects after 3days of first examination.

Results: The mean b-wave amplitude of dark adapted 0.01 waves was 124.19 ±47.32uV and implicit time of b-wave obtained was 70.74 ±8.72ms.The average a-wave and b-wave amplitudes and implicit time obtained for dark adapted 0.01 b-wave was 167.16 ±39.3uV, 290.81 ±73.96uV and 18.37 ±2.37ms, 43.72 ±4.33ms. The same obtained for light adapted 3.0wave was 40.15 ±20.89uV, 130.95 ±37.89uV and 15.75 ±1.05ms, 33.41 ±1.99ms. The mean b-wave amplitude and implicit time for light adapted flicker was 114.61 ±32.96uV and 30.13 ±3.6ms. The values represent mean ±standard deviation.

Conclusion: Handheld ERG is portable and fully integrated device. It is an easy to use, handy instrument, relatively inexpensive and can be used for testing both adults and children and in bedside patients. However, the use of handheld ERG has not become very widespread and hence normative data is not available. ISCEV recommends that each laboratory establish normal values based on its own equipment and patients. This study aims to bridge these lacunae in our knowledge.

Keyword: Handheld, Normative, Electroretinogram.

Introduction

Electrophysiological test is an objective method to analyze the functional integrity of neurosensory retina in various retinal disorders.[(1)] Full-field electroretinography gives a mass response generated by the cells across the entire retina in response to light flash.[(2)] International Society for Clinical Electrophysiology of Vision (ISCEV) is an organization for the standardization of clinical protocols for electrophysiological examinations.[(3)] Based on ISCEV standards, several devices are now available for clinical purposes, in the form of both table-top, which is commonly available and hand-held, which can be used in bedside patients and paediatric patients.[(1,3)] The hand-held device is used for confirmation of ophthalmic and neurologic diseases, paediatric neurology, animal studies, inherited visual disorders etc.[(3)] ISCEV recommends, each laboratory establish normal values are required for its own equipment.[(4)] The aim of this study is to obtain a normative data for Ephios hand-held ERG, to compare the results with existing data of both hand-held and table-top devices.

Materials and Methods

A prospective, observational study was conducted in 90 eyes of 45 subjects. The subjects underwent a complete ophthalmology examination including vision, slit lamp examination and dilated fundus examination with an indirect ophthalmoscope to rule out any ocular pathology. Patients with best corrected visual acuity of 6/6, with a refractive error ±1D and having normal anterior and posterior segments were selected for the study. Patients with any systemic diseases were excluded. Written, informed consent was obtained.

1% tropicamide plus was used for dilating the eyes. The handheld electroretinogram (Ephios) was used for recording the ERG. The Burien-Allen bipolar contact lens electrode, which has both active and reference electrode was used for recording ERG. Gold-cup skin electrode, was placed on the ear as ground electrode.[(1,3)]

After dilatation, patient was dark adapted for a period of 20 minutes and scotopic responses were obtained in a dark room. After attaining scotopic responses from both the eyes, patient was light adapted for 20 minutes for measuring photopic responses. According to ISCEV, there are 5 standard wave forms which are dark adapted 0.01 ERG (rod response), dark adapted 3.0 ERG (combined rod-cone response), dark adapted 3.0 oscillatory potential, light adapted 3.0 ERG (cone response) and light adapted 3.0 flicker (30Hz flicker).[(1,3-5)] Oscillatory potentials are then eliminated by the software provided by Ephios handheld ERG. The device composed of a flash stimulator along with a fixation target, which is connected to the electrodes via a cable. Another cable sends the obtained curves to a computer, for further analysis. The flash strength varies from 0.002 to 32cd.s.m^{-2}. The white light emitting diode acts as the stimulus source. A flash intensity of -

2.4log unit (0.0078cd.s.m^{-2}) was used to obtain dark adapted 0.01 ERG and that of 0 log unit (2.0cd.s.m^{-2}) was used for other responses. White background illumination of the stimulator varies from 28.0 to 30.0cd/m^2. Artefacts are eliminated by the examiner herself.[3] Same examiner performed ERG for all the 45 patients. Repeatability of this device was also tested. For this, 10 patients were selected randomly and repeat ERG was done for both eyes after three days of first examination. The amplitude and implicit time thus obtained were compared with the previous test.

Statistical analysis was performed by IBM SPSS version 20.0 software. Categorical variables are presented using frequency and percentage. Numerical variables are expressed using mean, median and standard deviation. To test the statistical significant mean change of amplitude and implicit time of each wave between males and females, two sample test was used. The statistical significance of inter-ocular difference of all responses, was tested using two sample test and Mann Whitney U test. To check the repeatability of Ephios hand-held device, wilcoxon signed rank test was used.

Result

The study was conducted in 90 eyes of 45 normal subjects with mean age of 21.62±2.39 years .Since ISCEV recommends a median value to describe the limits of normal, the median value was also calculated.[4] The given value represents mean ± standard deviation. The mean b-wave amplitude and implicit time of dark adapted 0.01 wave were 124.19±47.32uV and 70.74±8.72ms and the median value were 117.5uV and 70ms respectively. The mean a-wave and b-wave amplitude for dark adapted 3.0 responses were 167.16±39.3uV and 290.81±73.96uV. The median value for the same is 167.5Uv and 278uV. The mean implicit time for the same wave is 18.37±2.37ms and 43.72±4.33ms and the median is 17ms and 45ms respectively. 40.15±20.89uV and 130.95±37.89uV was the mean obtained for the amplitude of light adapted 3.0 responses. At the same time, the median values were 35.75uV and 131.75uV respectively. The implicit time for the same was 15.75±1.05ms and 33.41±1.99ms. The median values for light adapted 3.0 waves were 16ms and 33ms. The mean and median value for light adapted flicker b-wave amplitude was 114.61±32.96uV and 111.25uV and that of implicit time was 30.13±3.6ms and 29ms.

Fig. 1 shows the normal pattern of ERG obtained from Ephios hand-held device.

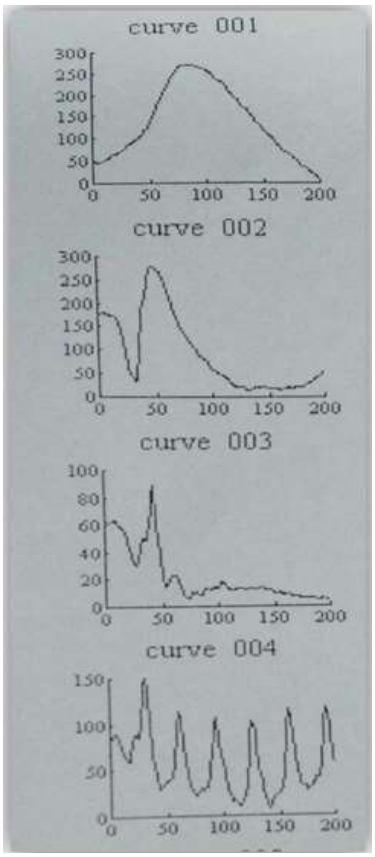

Fig. 1

Out of 45 subjects, 30 (67%) were females and the rest 15 (33%) were males. A comparative study had been conducted between males and females and was observed that, there was no significant difference between them. The mean value obtained for dark adapted 0.01 b-wave amplitude for males and females were 136.40±47.76uV and 118.08±46.29uV. The implicit time value for the same response, in males and females were 71.77±7.96ms and 70.23±9.1ms. In case of dark adapted a and b wave amplitude, the mean obtained for males and females were 165.35±41.45uV, 168.06±38.57uV and 292.87±75.25uV, 289.78±73.93uV respectively. The mean implicit time for the same wave in males and females were 19.10±2.50ms, 18.00±2.24ms and 43.10±5.31ms, 44.03±3.76ms. The mean value for light adapted 3.0 a-wave amplitude and implicit time in males were 35.90±10.54uV, 15.73±1.11ms and in females, it was 42.28±24.28uV and 15.77±1.03ms. In case of light adapted 3.0 b-waves the amplitude and implicit time for males and females were 123.78±34.80uV, 134.54±39.06uV and 33.53±1.46ms, 33.35±2.21ms respectively. The mean amplitude and implicit time of light adapted flicker in males and females were 113.17±33.64uV, 115.33±32.88uV and 30.73±3.38ms, 29.78±3.70ms. The gender comparison showed that all values were similar in males and females except dark

adapted 3.0 a-wave implicit time with a border line significant(p value = 0.05).

Table I: Gender comparison of ISCEV protocols

ISCEV protocol	P value	
	Amplitude (Uv)	Implicit time(ms)
Dark adapted 0.01 b-wave	0.08	0.44
Dark adapted 3.0 a-wave	0.76	0.05
Dark adapted 3.0 b-wave	0.85	0.39
Light adapted 3.0 a-wave	0.17	0.89
Light adapted 3.0 b-wave	0.21	0.68
Light adapted flicker b-wave	0.77	0.24

Repeatability of Ephios hand-held device was analysed by repeating the test for selected 10 patients after three days of first examination. The result showed no significant difference between test 1 and test 2.

Table 2: Repeatability of Ephios hand-held ERG

ISCEV protocol	p value	
	Amplitude (Uv)	Implicit time(ms)
Dark adapted 0.01 b-wave	0.86	0.12
Dark adapted 3.0 a-wave	0.89	0.27
Dark adapted 3.0 b-wave	0.52	0.49
Light adapted 3.0 a-wave	0.59	0.12
Light adapted 3.0 b-wave	0.18	0.82
Light adapted flicker b-wave	0.24	0.26

The inter-ocular differences of all responses were analysed. It is an important parameter for the clinical evaluation of patients with asymmetric retinal eye diseases, for determining the sample size in treatment trials and for monitoring possible therapeutic effects in future clinical treatment trials for hereditary retinal diseases.[6] The comparison between the right and left eye parameters shows no significant difference between the two, except in case of light adapted flicker amplitude (p value = 0.04).

Table 3: Inter-ocular differences of ISCEV protocols

ISCEV protocol	p value	
	Amplitude (Uv)	Implicit time(ms)
Dark adapted 0.01 b-wave	0.08	0.17
Dark adapted 3.0 a-wave	0.42	0.89
Dark adapted 3.0 b-wave	0.31	0.68
Light adapted 3.0 a-wave	0.53	0.84
Light adapted 3.0 b-wave	0.13	0.79
Light adapted flicker b-wave	0.04	0.15

Discussion

A study was conducted by Ramya Sachidanandam et al in 2015 with a sample size of 47 subjects with the title, Comparison between Fullfield Electroretinography obtained from hand-held and table-top devices in normal subjects. Our normative data was compared with their normative data obtained from Veris table-top devices. This comparison shows similarity with their comparison between Veris and Ephios. The amplitude of all scotopic responses that we obtained shows a considerable reduction when compared to the Veris values. The mean amplitude for dark adapted 0.01 b-waves was 286.8 ± 62.0uV for them. The mean value for a and b wave amplitude in dark adapted 3.0 wave was 22.03±52.6uV and 471.5±84.3uV. The study of Ramya Sachidandam itself shows the reason for this reduction. The area of retina stimulated is less in Ephios when compared to Veris, also the flash strength is weak in Ephios than Veris.

The mean implicit time in both scotopic and photopic responses shows delay when compared to their value, except for dark adapted 3.0 b-wave and light adapted 3.0 a-wave, where their mean was 44.7±2.5ms and 16.6±0.8ms. The mean implicit time for dark adapted 0.01 b-wave was 65.1±3.9ms and that of dark adapted 3.0 a-wave was 17.4±0.8ms. Light adapted 3.0 b-wave shows a mean value of 27.4±1.3ms and 25.2±1.0ms was shown by light adapted flicker.

The amplitude of our photopic responses when compared with them shows an increase in value. The mean amplitude for light adapted 3.0 a-wave for them was 30.4±7.7uV and that of b-wave was 109.1±31.7uV. Light adapted flicker response shows mean amplitude of 69.1±18.8uV.

The Ephios hand-held ERG used in the same study of Ramya Sachidanandam was also compared with our study and the result shows our normative data falls within the range of their normative data.[1] The mean amplitude and implicit time for dark adapted 0.01 wave in their study was 128±37.7uV and 79.2±6.2ms. At the same time their mean value for amplitudes of dark adapted 3.0 a-wave and b-wave was 152.6±34.2uV and 379.7±75.9uV. The same for implicit time was 17.9±1.1ms and 46.7±2.8ms. When we take the photopic values for comparison, the amplitude of light adapted a-wave and b-wave also falls within our data. The mean obtained for this was 34.4±8.6uV and 116.3±32.0uV. The mean implicit time for the same response was 15.7±0.9ms and 30.8±1.4ms. Light adapted flicker amplitude and implicit time shows a mean of 92.7±27.9uV and 28.1±2.0ms in their study which lies within our normative data.

Another study was conducted by Parvaresh et al in 2009 with the title Normal Values of Standard Fullfield Electroretinography in an Iranian Population with a sample size of 170 normal subjects.[5] Their study included subjects of age from 1 to 8 0, in which they divided it into 8 age strata with an interval of 10. They

found out the median of each parameter in different age groups separately among males and females. So our median values were used to compare with age differentiated data. Because of our limited data and age groups, we divided our subjects into 2 age strata that is 18-20 and 21-25, that falls within their age group of 11-20 and 21-30.

The males of our age group 18-20, were compared with their age group 11-20.The comparison showed no significant change between two studies. When the female subjects were compared some values showed significant differences. Table IV gives statistical significance of all waves.

Table 4: Comparison of ISCEV protocols of the age group 18-20

ISCEV protocol	Male subjects		Female subjects	
	p value		p value	
	Right eye	Left eye	Right eye	Left eye
Dark adapted 0.01 b-wave amplitude Uv	0.07	0.14	0.03	0.003
Dark adapted 0.01 b-wave Implicit time ms	0.07	0.66	0.19	0.002
Dark adapted 3.0 a-wave amplitude Uv	0.14	0.68	0.002	0.006
Dark adapted 3.0 a-wave implicit time ms	0.1	0.7	0.32	0.5
Dark adapted 3.0 b-wave amplitude Uv	0.67	0.07	0.39	0.004
Dark adapted 3.0 b-wave implicit time ms	0.27	0.71	0.003	0.13
Light adapted 3.0 a-wave amplitude uV	0.71	0.71	0.17	0.16
Light adapted 3.0 a-wave implicit time ms	0.14	0.16	0.002	0.59
Light adapted 3.0 b-wave amplitude uV	0.59	0.07	0.38	0.01
Light adapted 3.0 b-wave implicit time ms	0.1	0.07	0.001	0.003
Light adapted flicker b-wave amplitude uV	0.71	0.71	0.08	0.38
Light adapted flicker b-wave implicit time ms	0.18	0.1	0.005	0.007

When the normative data of males, in our age group 21-25 was compared with their age group 21-30, some waves showed significant difference while some showed comparable values. The differences may be due to the large sample size in their study and the difference in instrument used for recording ERG.

Table 5: Comparison of ISCEV protocols of the age group 21-25

ISCEV protocol	Male subjects		Female subjects	
	p value		p value	
	Right eye	Left eye	Right eye	Left eye
Dark adapted 0.01 b-wave amplitude Uv	0.17	0.07	0.01	0.004
Dark adapted 0.01 b-wave Implicit time ms	0.005	0.007	0.001	<0.001
Dark adapted 3.0 a-wave amplitude Uv	0.005	0.005	<0.001	0.001
Dark adapted 3.0 a-wave implicit time ms	0.005	0.36	0.002	0.001
Dark adapted 3.0 b-wave amplitude uV	0.02	0.01	<0.001	<0.001
Dark adapted 3.0 b-wave implicit time ms	0.01	0.41	0.006	0.01
Light adapted 3.0 a-wave amplitude uV	0.71	0.54	0.91	0.43
Light adapted 3.0 a-wave implicit time ms	0.007	0.02	0.02	<0.001
Light adapted 3.0 b-wave amplitude uV	0.013	0.01	0.17	0.002
Light adapted 3.0 b-wave implicit time ms	0.005	0.005	0.001	0.002
Light adapted flicker b-wave amplitude uV	0.11	0.44	0.46	0.88
Light adapted flicker b-wave implicit time ms	0.01	0.005	0.04	<0.001

Conclusion

Hand-held ERG is an easily portable and fully integrated device. It is an easy to use, handy instrument, relatively inexpensive and can be used for testing both adults and children and in bedside patients. However, the use of hand-held ERG has not become very popular and hence normative data is not available. International Society for Clinical Electrophysiology of Vision recommends that each laboratory establish normal values based on its own equipment. This study aims to bridge this lacunae in our knowledge. More studies

with greater number of patients will be required in future to establish a normative data conclusively.

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