The Effect of Fluorescein Angiography on Full-Field Electroretinography Parameters

Mohsen Azarmina, MD; Siamak Moradian, MD; Hossein Azarmina, MD
Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Purpose: To investigate the effect of simultaneously performed fluorescein angiography (FA) on full-field electroretinography (ffERG) parameters.

Method: Scotopic and photopic ffERG were performed immediately and 60 minutes after conventional FA in patients with retinal photoreceptor disorders; a-and b-wave amplitudes were compared between recordings obtained at the two time intervals in each patient.

Results: Ten eyes of five (3 male and 2 female) patients with mean age of 19.6±3.8 (range, 15-25) years were studied. Intravenous fluorescein administration caused an immediate reduction in ERG waves which was most prominent in rod and maximal combined responses. Mean a-wave amplitude in maximal combined response, rod response and cone response ERGs was 46.0±18.8, 8.0±7.0 and 5.1±2.0 µv immediately after FA which was increased to 79.0±30.0, 21.5± 22.5 and 6.5±2.4 µv 60 minutes afterwards, respectively (P<0.005 for all comparisons). Mean b-wave amplitude in the same order was 91.0±17.5, 47.7±17.2 and 17.3±14.7µv which was increased to 145.0±54.3, 91.8±48.1 and 20.0±17.7 µv respectively, 60 minutes after FA (P<0.005 for all comparisons).

Conclusion: The amplitude of ERG a- and b-waves under scotopic and photopic conditions increased significantly one hour after FA. These changes may be explained by disappearance of phototoxic and bleaching effects of strong light exposure from the light source of the angiography machine and fluorescein molecule on retinal photoreceptors.

Keywords: Fluorescein Angiography; Electroretinography

INTRODUCTION

Fluorescein angiography (FA) and electroretinography (ERG) are two of the most important and common paraclinical tests employed for evaluation and diagnosis of retinal and choroidal disorders.1-4 Simultaneous use of FA and ERG may sometimes be considered as the last resort for the diagnosis of these diseases. Many factors such as stimulus duration, size of the illuminated retinal area, interval between stimuli, pupil size, circulation state, drugs, hyperventilation, retinal development, clarity of the media, age, sex, refractive error and anesthesia can affect ERG parameters.5,6

This study was aimed to evaluate the effect of simultaneously performed FA on Ganzfeld full-field electroretinography (ffERG) parameters.
Effect of FA on ERG; Azarmina

METHODS

Five patients including 3 male and 2 female subjects with retinal photoreceptor disorders were enrolled in this study. Conventional FA with a stroboscopic lamp providing flashlight stimulation through a monochromatic blue filter was performed using the Heidelberg Retina Angiography system (Heidelberg Engineering, Germany). Photopic (cone response) and scotopic (rod and maximal combined response) ERGs were obtained according to the methods described by the International Society for Clinical Electrophysiology of Vision (ISCEV) using the Mono Elec2 system (Metrovision Inc., France) in all cases immediately and 60 minutes after FA. The pupils were fully dilated to a diameter of 8 mm with 1% tropicamide and 2.5% phenylephrine eye drops under topical anesthesia with 0.5% tetracaine. The ERGject contact lens electrode was used as the recording electrode and 0.5% methylcellulose was deposited into its concavity; the reference electrode was placed in the center of the forehead and the ground electrode was attached to the ear lobe. The photopic response was recorded after 10 minutes of light adaptation and the scotopic and maximal responses were obtained following dark adaptation for at least 20 minutes. Amplitudes of a and b waves in these two conditions were measured and compared in each patient using Wilcoxon test with significance level set at 0.05.

RESULTS

Ten eyes of five (3 male and 2 female) consecutive patients with mean age of 19.6±3.8 (range, 15-25) years underwent FA in conjunction with ERG. Table 1 summarizes ERG data and clinical findings of the patients. The amplitude of a- and b-waves showed a remarkable decrease shortly after FA but increased significantly after one hour.

Tables 2 and 3 compare a- and b-wave amplitudes shortly and 60 minutes after FA.

Table 1. Clinical data and electrophysiological findings of patients following fluorescein angiography

| Eyes | Age (yr) | Sex | Laterality | Maximal Combined Response | Rod Response | Cone Response | Maximal Combined Response | Rod Response | Cone Response |
|------|----------|-----|------------|---------------------------|--------------|--------------|---------------------------|--------------|--------------|
|      |          |     |            | Early | Late | Early | Late | Early | Late | Early | Late | Early | Late | Early | Late |
| 1    | 15       | M   | OD         | 60.9±18.8; 51.5 (18.8-65.5) | 79.4±30; 72.8 (40.6-146) | 3.1±0.4; 3.2 (2.8-3.6) | 85±3; 83.2 (78-88) | 3.1±0.4; 3.2 (2.8-3.6) | 85±3; 83.2 (78-88) |
| 2    | 17       | F   | OD         | 27.1±0.6; 25.7 (2.2-28) | 40.6±3.2; 39.1 (37.2-42.5) | 7.8±1.2; 7.5 (6.6-8.6) | 9.1±0.2; 8.9 (8.7-9.1) | 7.8±1.2; 7.5 (6.6-8.6) | 9.1±0.2; 8.9 (8.7-9.1) |
| 3    | 20       | M   | OS         | 22.8±1.2; 23.3 (19.8-26.8) | 48.4±3.2; 46.2 (44.1-50.5) | 2.8±0.2; 2.5 (2.3-2.7) | 6.4±0.2; 6.2 (6.0-6.5) | 2.8±0.2; 2.5 (2.3-2.7) | 6.4±0.2; 6.2 (6.0-6.5) |
| 4    | 21       | M   | OS         | 63.5±1.8; 62.3 (59.7-66.1) | 146±3.2; 143 (140-149) | 10.4±0.2; 10.2 (10.0-10.4) | 10.7±0.2; 10.5 (10.3-10.7) | 10.4±0.2; 10.2 (10.0-10.4) | 10.7±0.2; 10.5 (10.3-10.7) |
| 5    | 25       | F   | OS         | 46±2; 45 (43-48) | 68.3±3.2; 66.1 (64.3-69.1) | 4.3±0.2; 4.1 (3.9-4.3) | 7.2±0.2; 7.0 (6.8-7.2) | 4.3±0.2; 4.1 (3.9-4.3) | 7.2±0.2; 7.0 (6.8-7.2) |
| 6    | 20       | M   | OS         | 57±1.2; 56 (54-59) | 72.7±3.2; 70.5 (68.3-74.9) | 4.7±0.2; 4.5 (4.3-4.8) | 7.9±0.2; 7.7 (7.5-8.0) | 4.7±0.2; 4.5 (4.3-4.8) | 7.9±0.2; 7.7 (7.5-8.0) |
| 7    | 21       | M   | OS         | 18.8±2; 18.6 (18.0-19.2) | 68±3.2; 66.1 (64.3-69.1) | 6.3±0.2; 6.1 (5.9-6.3) | 10.2±0.2; 10.0 (9.8-10.2) | 6.3±0.2; 6.1 (5.9-6.3) | 10.2±0.2; 10.0 (9.8-10.2) |
| 8    | 24       | F   | OS         | 54±2; 53 (50-56) | 68±3.2; 66.1 (64.3-69.1) | 6.3±0.2; 6.1 (5.9-6.3) | 10.2±0.2; 10.0 (9.8-10.2) | 6.3±0.2; 6.1 (5.9-6.3) | 10.2±0.2; 10.0 (9.8-10.2) |
| 9    | 25       | F   | OS         | 34±2; 33 (31-36) | 68±3.2; 66.1 (64.3-69.1) | 6.3±0.2; 6.1 (5.9-6.3) | 10.2±0.2; 10.0 (9.8-10.2) | 6.3±0.2; 6.1 (5.9-6.3) | 10.2±0.2; 10.0 (9.8-10.2) |

Table 2. a-wave amplitude (microvolts) immediately (early) and one hour after (late) fluorescein angiography

| Response | M±SD; Median (range) | M±SD (95%CI) Median (95%) | M±SD Median (95%) | *P-value |
|----------|-----------------------|---------------------------|-------------------|---------|
|          | Early | Late | Change | % of change |
| Maximal combined | 46.1±18.8; 51.5 (18.8-65.5) | 79.4±30; 72.8 (40.6-146) | 33.3±23.5 (16.5-50.1) | 24 (12-82.5) | 90±78 | 0.005 |
| Rod | 8±7; 6.3 (1-26) | 21.5±22.5; 12.2 (7.2-80.1) | 13.5±16 (2.1-2.5) | 7.7 (2.9-54.1) | 248±376 | 56 (20-262) | 0.005 |
| Cone | 5.1±2; 4.7 (2.7-9.8) | 6.5±2.4; 6.4 (3-10.7) | 1.4±1.6 (0.2-2.5) | 1 (-0.9 to 4.4) | 29±9 | 22 (-9 to 70) | 0.004 |

F, Female; M, Male; OD, right eye; OS, left eye; Early, electoretinography (ERG) immediately after fluorescein angiography (FA); Late, ERG 60 minutes after FA

* Wilcoxon signed rank test
in terms of maximal combined, rod and cone responses. All changes were statistically significant (P<0.005) under all conditions.

A representative case (#3) demonstrates low α- and β-wave amplitudes shortly after FA in maximal combined, rod, and cone response ERGs (Fig. 1A). ERG in the same patient one hour after FA demonstrated a significant increase in α- and β-wave amplitudes in all three settings (Fig. 1B).

Figure 1. (A) A representative case (#3) demonstrates low α- and β-waves amplitudes shortly after fluorescein angiography in maximal combined response, rod response, and cone response ERGs (upper, middle and lower printouts, respectively). (B) Electroretinography in the same patient 60 minutes after fluorescein angiography shows a significant increase in both α- and β- wave amplitudes.
DISCUSSION

Electrophysiological testing at two time points following FA seem to have different results due to the effect of fluorescein. The idea that repeated recording of ERG together with FA may provide information on dynamic aspects of retinal damage has already been proposed. However, ophthalmologists have generally been discouraged because of the phototoxic and bleaching effect of the strong light emitted from fluorescein molecules.

In 1981, Tamai and Mizuno attempted to detect impairment of retinal vessels with “fluorescein ERG”. They expected to obtain information on the microvascular lesion in the immediate vicinity of the vessels. The basis of their experiment was the assumption that during ERG examination after FA, photoreceptors might be stimulated not only by the blue light (480 nm) flashed onto the retina, but also by the green light (520 nm) emitted by fluorescein which may reflect impairment of blood retinal barrier, damage to photoreceptors and alterations in ERG response.

In an animal study by Bloom and Burian using large doses of orally administered fluorescein in rabbits, there were no significant changes in fundus, ERG or histopathological retinal sections. A similar effect has been reported by fluorescein and indocyanine green angiography on subsequent dark adaptation and ERG.

In the current study, ERG recording revealed considerable amplitude changes at different time points following fluorescein administration. An initial and transient decrease of a- and b-wave amplitude was noted immediately after administration of the dye in all cases which increased one hour thereafter. We can therefore conclude that the initial amplitude reduction may be due to the bleaching and phototoxic effects of the light source of the FA machine or due to the transient phototoxic effect of the fluorescein molecules. In cases requiring both FA and ERG, ERG could be performed prior to FA. However when FA is performed prior to ERG, it is prudent to postpone ERG for at least one hour to avoid the effects of FA on the electrophysiological response.

Conflicts of Interest

None.

REFERENCES

1. Berkow JW, Flower RW, Orth DH, Kelley JS. Fluorescein and Indocyanine Green Angiography. 2nd ed. San Francisco: American Academy of Ophthalmology; 1997.
2. Marmor MF, Holder GE, Seeliger MW, Yamamoto S; International Society for Clinical Electroretinography. Standard for clinical electroretinography (2004 update). Doc Ophthalmol. 2004;108:107-114.
3. Fishman GA, Birch DG, Holder GE, Brigell MG. Ophthalmology Monograph 2-Electrophysiologic testing in disorder of the retina, optic nerve, and visual pathway. 2nd ed. San Francisco: American Academy of Ophthalmology; 2001.
4. Heckenlively JR, Arden GB. Principles and practice of clinical electrophysiology of vision. St Louis: Mosby; 1991.
5. Carr RE, Siegel LM. Electrodiagnostic testing of the visual system: a clinical guide. Philadelphia: FA Davis; 1990.

Table 3. b-wave amplitude (microvolts) immediately (early) and one hour after (late) fluorescein angiography

| Response   | Mean ± Standard Deviation | Median (95% CI) | P-value |
|------------|---------------------------|----------------|---------|
| Maximal combined | 91.8 ± 17.5; 89.1 (60.4-114) | 145.3 ± 54.3; 126 (99.9-292) | 0.005 |
| Rod        | 47.7 ± 17.2; 50 (17.1-72) | 91.8 ± 48.1; 70.4 (57.8-213) | 0.007 |
| Cone       | 17.3 ± 14.7; 13.3 (2.7-40.2) | 20 ± 17.7; 15.6 (3.1-60.4) | 0.075 |

M, mean; SD, standard deviation; CI, confidence interval

* Wilcoxon signed rank test

Table 3. b-wave amplitude (microvolts) immediately (early) and one hour after (late) fluorescein angiography

| Response   | Mean ± Standard Deviation | Median (95% CI) | P-value |
|------------|---------------------------|----------------|---------|
| Maximal combined | 91.8 ± 17.5; 89.1 (60.4-114) | 145.3 ± 54.3; 126 (99.9-292) | 0.005 |
| Rod        | 47.7 ± 17.2; 50 (17.1-72) | 91.8 ± 48.1; 70.4 (57.8-213) | 0.007 |
| Cone       | 17.3 ± 14.7; 13.3 (2.7-40.2) | 20 ± 17.7; 15.6 (3.1-60.4) | 0.075 |

M, mean; SD, standard deviation; CI, confidence interval

* Wilcoxon signed rank test
Effect of FA on ERG; Azarmina

6. Marmor MF, Arden GB, Nilsson SE, Zrenner F. Standard for clinical electroretinography. *Arch Ophthalmol* 1989;107:816-819.

7. Kuwabara T, Gorn RA. Retinal damage by visible light. An electron microscopic study. *Arch Ophthalmol* 1968;72:69-78.

8. Valenzeno DP, Pooler JP. Phototoxicity. The neglected factor. *JAMA* 1979;242:453-454.

9. Putting BJ, Zweypfenning RC, Vrensen GF, Oosterhuis JA, van Best JA. Blood-retinal barrier dysfunctions at the pigment epithelium induced by blue light. *Invest Ophthalmol Vis Sci* 1992;33:3385-3393.

10. Tamai M, Mizuno K. Electoretinogram changes after fluorescein injection: a new method to evaluate blood retinal barrier dysfunction. *Invest Ophthalmol Vis Sci* 1981;20:272-276.

11. Bloome MA, Burian HM. Chronic fluoride ingestion in rabbits. Absence of ocular effects. *Arch Ophthalmol* 1970;83:354-356.

12. Bartz-Schmidt KU, Walter P, Krott R, Brunner R, Esser P, Heimann K. Effect of fluorescein and indocyanine green angiography on subsequent dark adaptation and the electroretinogram. *Klin Monbl Augenheilkd* 1996;208:224-228.

13. Wen F, Yu M, Wu D, Ma J, Wu L. Effect of indocyanine green angiography using infrared fundus camera on subsequent dark adaptation and electroretinogram. *Doc Ophthalmol* 2002;105:51-56.