Principles and Practice of Clinical Electrophysiology of Vision

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21

Nonphotic Standing Potential Responses: Hyperosmolarity, Bicarbonate, and Diamox Responses

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The light peak/dark trough ratio (L/D) (Arden ratio[1]) is widely accepted as useful for evaluating retinal pigment epithelium (RPE) activity since the light peak and dark trough represent mainly the changes of the RPE membrane potentials. It also depends on the photoreceptor activity and RPE-receptor attachment, because the photoreceptors and their attachment with the RPE are essential for evoking the light peak. The L/D is also changed by occlusion of the central retinal artery, which nourishes the middle and inner layers of the retina. Therefore, abnormal L/D alone does not necessarily indicate RPE disorders. So far as a photic stimulus to the photoreceptors is used, the response obtained is not solely specific to the RPE.

The ocular standing potential, which mainly comes from the transepithelial potential (TEP) of the RPE, can be changed by nonphotic stimuli. For example, hyperosmolarity,[5, 8, 10] bicarbonate,[11, 12] and acetazolamide[3] (Diamox) decrease the TEP in vitro and the ocular standing potential in vivo. We call these responses the hyperosmolarity response, bicarbonate response, and Diamox response, respectively. The standing potential is changed by breathing a hypoxic mixture of oxygen and nitrogen.[9] These responses are recordable by conventional electro-oculographic (EOG) technique in the dark.

Figure 21–1 shows these three responses in normal human subjects. The EOG amplitude is virtually stabilized (V_0) usually about in 30 minutes in the dark. Then, a hypertonic solution (e.g., 20% mannitol or Fructmanit, see legend for Fig 21–1), 7% sodium bicarbonate solution (Meylon), or Diamox is given intravenously. These procedures decrease the EOG amplitude in the dark down to the minimum (V_{min}) approximately 8 to 20 minutes after the onset of administration. The amplitude of the response is defined as the percent amplitude change of the EOG: $100 \times (V_0 - V_{min})/V_0$. The distribution of the amplitudes of these responses in the normal subjects is approximated by the normal distribution. Thus, their normal range is the mean ± 2 SD of the amplitude in the normal subjects; 22.8% to 45.2% for the hyperosmolarity response, 15.2% to 28.6% for the bicarbonate response, and 32.1% to 52.9% for the Diamox response (the dose of each stimulant is described in the legend for Fig 22–1).

The amplitudes of the hyperosmolarity response and bicarbonate response are frequently decreased in retinitis pigmentosa,[15] rhegmatogenous retinal detachment even in a localized area,[2] diabetic retinopathy[4] (occasionally abnormal even in diabetics without visible retinopathy), angioid streaks, Stargardt's disease-fundus flavimaculatus,[14, 16] vitelli-

TABLE 21–1.

Characteristics of Responses Related to the Retinal Pigment Epithelium

	Hyperosmolarity Response	Bicarbonate Response	Diamox Response	Light Rise	C-Wave
	Nonphotic Stimulus			Photic Stimulus	
Characteristic	Hyperosmolarity	HCO_3^-	Diamox		
Origin	Mainly hyperpolarization of RPE basal membrane	Mainly depolarization of RPE apical membrane		Mainly depolarization of RPE basal membrane	Hyperpolarization of RPE apical membrane modified by slow PIII from Müller cell
By hyperosmolarity				Suppressed to abolished	Enhanced
By Diamox				Not suppressed	
By ketamine hydrochloride			Suppressed to abolished	Suppressed	
Retinitis pigmentosa	Suppressed to abolished		Not suppressed		
Pigmented paravenous retinochoroidal atrophy	Suppressed				
Fundus albipunctatus	Suppressed		Not suppressed	Suppressed in some cases	
Familial drusen	Suppressed				
Stargardt's disease and fundus flavimaculatus	Suppressed in some cases				
Angioid streaks					
Vitelliform macular dystrophy	Suppressed		Suppressed in some cases	Suppressed	
Carrier of vitelliform macular dystrophy	Suppressed in some cases		Not suppressed	Suppressed	
Cone dystrophy	Not suppressed		Not suppressed		
Diabetic retinopathy	Frequently suppressed				
Rhegmatogenous retinal detachment	Suppressed		Not suppressed	Suppressed	
Harada's disease	Occasionally suppressed			Occasionally suppressed	
X-linked juvenile retinoschisis	Not suppressed in cases without peripheral schisis		Not suppressed in cases without peripheral schisis		
After cataract extraction	Temporarily suppressed				
Occlusion of the central retinal artery	Suppressed			Suppressed in some cases	
Choroideremia	Suppressed		Not suppressed	Suppressed	

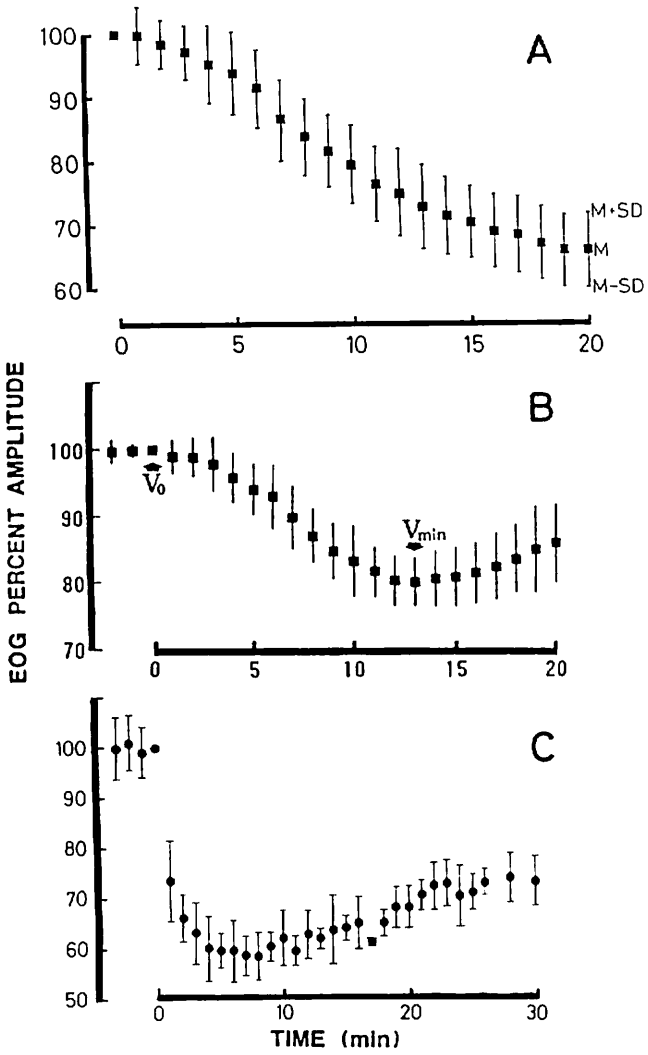

FIG 21–1.
Hyperosmolarity response **(A)**, bicarbonate response **(B)**, and Diamox response **(C)** in normal human subjects. The mean and standard deviation of the EOG amplitude as a percentage of the stabilized amplitude (so-called base value) after dark adaptation of 30 minutes are shown. The hyperosmolarity response was recorded in 50 eyes of 30 subjects, bicarbonate response in 70 eyes of 45 subjects, and Diamox response in 36 eyes of 24 subjects. To evoke the hyperosmolarity response Fructmanit (10% fructose, 15% mannitol) was given intravenously. The solution was administered for 15 to 20 minutes at a rate of 11% of the subject's total blood volume per hour. The total blood volume (liters) was calculated by the following formulas: $0.168H^3 + 0.05W + 0.444$ in males or $0.25H^3 + 0.063W - 0.662$ in females, where H is the height in meters and W is weight in kilograms. To evoke the bicarbonate response 0.83 mL/kg of 7% sodium bicarbonate (Meylon) was intravenously given in 5 minutes. To evoke the Diamox response 500 mg of Diamox was given intravenously in 1 minute. No light was used except for two dim miniature lamps to alternatively fixate the eye for the conventional EOG procedure. The onset of stimulant application was at 0 minutes on the abscissa.

form macular dystrophy (Best's disease[13]), Vogt-Harada-Koyanagi disease,[7] and temporarily after cataract extraction[6] (especially after intracapsular extraction) (Table 21–1). The hyperosmolarity response is more frequently abnormal than the L/D in the aforementioned diseases. The Diamox response remains within the normal range in most of the diseases described above and predominantly depends on the RPE in the posterior region of the ocular fundus since this response is suppressed in patients with severe macular atrophy (e.g., advanced stage in Stargardt's disease).[14]

REFERENCES

1. Arden GB, Barrada A, Kelsey JH: New clinical test of retinal function based upon the standing potential of the eye. *Br J Ophthalmol* 1962; 46:449–467.
2. Kawasaki K, Madachi-Yamamoto S, Yonemura D: Hyperosmolarity response of ocular standing potential as a clinical test for retinal pigment epithelium activity—Rhegmatogenous retinal detachment. *Doc Ophthalmol* 1984; 57:175–180.
3. Kawasaki K, Mukoh S, Yonemura D, Fujii S, Segawa Y: Acetazolamide-induced changes of the membrane potentials of the retinal pigment epithelial cell. *Doc Ophthalmol* 1986; 63:375–381.
4. Kawasaki K, Yonemura D, Madachi-Yamamoto S: Hyperosmolarity response of ocular standing potential as a clinical test for retinal pigment epithelium activity—Diabetic retinopathy. *Doc Ophthalmol* 1984; 58:375–384.
5. Kawasaki K, Yonemura D, Mukoh S, Tanabe J: Hyperosmolarity-induced changes in the transepithelial potential of the human and frog retinae. *Doc Ophthalmol* 1983; 37:29–33.
6. Kawasaki K, Yonemura D, Yanagida T, Segawa Y, Wakabayashi K, Mukoh S, Ishida H, Fujii S, Takahara Y: Suppression of the hyperosmolarity response after cataract surgery. *Doc Ophthalmol* 1986; 63:367–373.
7. Madachi-Yamamoto S, Kawasaki K, Yonemura D:

Retinal pigment epithelium disorder in Vogt-Koyanagi-Harada disease revealed by hyperosmolarity response of ocular standing potential. *Jpn J Ophthalmol* 1984; 28:362–369.
8. Madachi-Yamamoto S, Yonemura D, Kawasaki K: Hyperosmolarity response of ocular standing potential as a clinical test for retinal pigment epithelium activity—Normative data. *Doc Ophthalmol* 1984; 57:153–162.
9. Marmor MF, Donovan WJ, Gaba DM: Effects of hypoxia on the human standing potential. *Doc Ophthalmol* 1985; 60:347–352.
10. Mukoh S, Kawasaki K, Yonemura D: Hyperosmolarity-induced hyperpolarization of the membrane potential of the retinal pigment epithelium. *Doc Ophthalmol* 1985; 60:369–374.
11. Segawa Y, Mukoh S, Tanabe J, Kawasaki K: Bicarbonate-induced response from the retinal pigment epithelium for electrodiagnosis. Presented at the 26th International Symposium on Clinical Electrophysiology of Vision, Estoril, Portugal, May 23, 1988.
12. Steinberg RH, Miller SS: Transport and membrane properties of the retinal pigment epithelium, in Marmor MF, Zinn KH (eds): *The Retinal Pigment Epithelium*. Cambridge, Mass, Harvard University Press, 1979, pp 205–225.
13. Wakabayashi K, Yonemura D, Kawasaki K: Electrophysiological analysis of Best's macular dystrophy and retinal pigment epithelial pattern dystrophy. *Ophthalmic Paediatr Genet* 1983; 3:13–17.
14. Wakabayashi K, Yonemura D, Kawasaki K: Electrophysiological analysis of Stargardt's disease fundus flavimaculatus group. *Doc Ophthalmol* 1985; 60:141–147.
15. Yonemura D, Kawasaki K, Madachi-Yamamoto S: Hyperosmolarity response of ocular standing potential as a clinical test for retinal pigment epithelium activity—Chorioretinal dystrophies. *Doc Ophthalmol* 1984; 57:163–173.
16. Yonemura D, Kawasaki K, Wakabayashi K, Tanabe J: EOG application for Stargardt's disease and X-linked juvenile retinoschisis. *Doc Ophthalmol Proc Ser* 1983; 37:115–120.