Abstract  The photopic negative response (PhNR) has recently been shown to be severely affected in central retinal artery occlusion (CRAO), despite relative preservation of the cone b-wave compared to that in the healthy unaffected fellow eye. The aim of this study was to test how the PhNR of the flash electroretinogram (ERG) is affected in human retinal vein occlusion. PhNR was elicited with red stimuli (1 cd s/m², 5 cd s/m², and 7 cd s/m² with 4 ms duration) and blue background (10 cd/m²). Standard Ganzfeld flash ERG was produced according to the ISCEV standard for the clinical electroretinogram (2004). Sixteen patients with central retinal vein occlusion (CRVO), 14 patients with branch retinal vein occlusion (BRVO), and 16 controls were analyzed. The amplitude of the PhNRs was significantly smaller in the CRVO and BRVO eyes than those in the unaffected fellow or control eyes (p = 0.000). There was a significantly greater reduction of PhNR amplitudes than that of other waves including the OPs, rod b-wave, combined a-wave and b-wave, cone a-wave and b-wave, and 30 Hz flicker ERG. Thus, PhNR amplitude in retinal vein occlusion is severely affected. There is a potential role for PhNR in assessing inner retinal damage and evaluating the effect of treatment.

Keywords  Electroretinogram · CRVO · BRVO · Photopic negative response

Introduction

Central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) are among the ocular diseases that markedly reduce vision and are associated with severe complications such as neovascular glaucoma and intraocular hemorrhages. The electroretinogram (ERG) provides an objective measure of the loss of retinal function in affected eyes, but controversy exists regarding which parameter of the ERG is most useful for monitoring patients with retinal vein occlusion [1, 2].

Recent studies in monkeys and cats have shown that the slow negative potential, the photopic negative response (PhNR), which follows the b-wave, originates from the inner retina [3, 4]. The results in monkeys—whose retinæ are very similar to those of humans—raised the possibility that the PhNR may be a sensitive index of retinal dysfunction in patients with diseases that affect the inner retina. Thereafter, some researchers used PhNR to detect and monitor glaucomatous...
damage for the possibility that PhNR may be a consequence of spiking activity of retinal ganglion cells [5–7]. A more recent study by Machida et al. [8] found that the PhNR was severely affected in central retinal artery occlusion (CRAO) despite relative preservation of the cone b-wave.

In the present study, the PhNR of the photopic ERG and the standard ERG responses were evaluated in eyes with CRVO, BRVO, as well as unaffected fellow eyes and control eyes. The purpose of our study was to determine the features of PhNR in CRVO and BRVO eyes. In addition, we compared standard ERG responses between affected eyes and unaffected fellow eyes. The results of present study showed selective reduction of PhNR in affected eyes compared to unaffected fellow eyes and control eyes.

Materials and methods

Subjects

Sixteen cases of unilateral CRVO (6 females and 10 males, aged 42–71, mean 53.5 ± 8.1 years old) and 14 cases of unilateral BRVO (2 females and 12 males, aged 44–74, mean 59.3 ± 10.8 years old) from the Zhongshan Ophthalmic Center of Sun Yat-sen University participated in the study. All patients were examined with fundus fluorescein angiography (FFA) in both eyes 1–7 days before the ERG was recorded. The time from the onset of the disease to the ERG test ranged from 3 months to 1 year. In CRVO cases, only one patient showed apparent retinal capillary non-perfusion in FFA. In BRVO cases, the smallest affected vein was the second-order branch. Patients who suffered from diabetes, other systemic disease or retinal degeneration that might influence the ERG results were excluded from this study. None of the patients had laser photocoagulation history or showed apparent vitreous hemorrhage. ERGs were also recorded in 16 visually normal age-matched controls (2 females and 14 males, aged 37–71, mean 55.3 ± 11.6 years old). The 30 unaffected eyes from the CRVO and BRVO patients were classified as unaffected fellow eyes. Sixteen right eyes from normal controls were classified as control eyes.

Informed consent was obtained from every subject or patient after the procedures used in the study were fully explained.

Stimulus

PhNR and standard Ganzfeld ERG were performed using the Espion visual testing system (Diagnosys). PhNR was produced with red stimuli (peak wavelength 635 nm) and blue background (peak wavelength 465 nm). Flashes were produced by light-emitting diodes with duration of 4 ms and intensity of 1 cd s/m², 5 cd s/m², and 7 cd s/m², respectively. The background intensity was 10 cd/m². Standard Ganzfeld ERG was produced according to the ISCEV standard for the clinical electroretinogram (2004).

Recording

After the pupils were maximally dilated with topical 0.5% tropicamide and 0.5% phenylephrine hydrochloride, topical corneal anesthesia was induced with 1% dicaine hydrochloride. ERGs were recorded binocularly with contact-lens electrodes referenced to both ear lobes, and the forehead was grounded. Scotopic ERGs were first recorded after 20 min dark adaptation, and then the patient was light adapted under the background light of 30 cd/m² for 10 min before recording photopic ERGs. After another 1-min blue background light adaptation, PhNRs were recorded at three different red light stimulus intensities (1 cd s/m², 5 cd s/m², and 7 cd s/m²).

The amplitude of PhNR was measured from baseline to the trough immediately after the b-wave according to the study of Viswanathan et al. [3, 4, 7]. The sum amplitude of OP₁, OP₂, OP₃, and OP₄ was calculated.

Statistical evaluation

The data for each ERG response were analyzed with SPSS 11.0. The statistical significance of the data was calculated using the independent-samples t test. Receiver operating characteristic (ROC) analysis was performed by computer on each ERG response to determine the area under the ROC curve.