Topical Fundus Pulsation Measurement in Patients With Active Central Serous Chorioretinopathy

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Objective: To determine regional pulsatile choroidal blood flow using laser interferometry in patients with active central serous chorioretinopathy (CSC).

Method: The study compared an equally sized age-, sex-, and refractive error–matched control group of healthy volunteers obtained from the Department of Clinical Pharmacology with 18 consecutive patients who had newly diagnosed active, unilateral CSC obtained from the University of Vienna Eye Clinic, Vienna, Austria.

Main Outcome Measures: Regional fundus pulsation amplitude as assessed using laser interferometry.

Results: The median age of the patients was 40 years; the male-female ratio was 16:2. Foveal fundus pulsation amplitude was significantly higher in eyes with CSC (mean [SD], 5.5 [1.7] µm) than in the eyes of the control subjects (4.1 [1.1] µm; \( P = .005 \)). In addition, eyes with CSC had a significantly higher variability in fundus pulsation amplitude (mean [SD], 48% [20%]) assessed at different fundus locations around the leak than the controls did (20% [9%]; \( P < .001 \)).

Conclusions: To our knowledge, this is the first study that measures topical fundus pulsations in patients who have active, unilateral CSC. These data indicate a generally increased foveal pulsatile choroidal blood flow and an abnormal distribution of fundus pulsation amplitude in the area close to the leak. Whether these findings reinforce the concept that choroidal perfusion abnormalities play a role in the pathogenesis of CSC remains to be established.

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CENTRAL SEROUS chorioretinopathy (CSCR) is an exudative macular disease that predominantly affects young to middle-aged men. The characteristic neurosensory detachment on the posterior pole is caused by leakage of fluid seen at the level of the retinal pigment epithelium. Mental stress1-3 and hypercortisolism4-7 are factors frequently associated with the precipitation or aggravation of CSCR. Cardiovascular factors that have been linked to CSCR are a type A personality,8 systemic hypertension,9 and an increased variable heart beat.10 It is believed that psychological stress, especially in men, leads to a hyperactivation of the sympathetic nervous system with an abnormal neuroendocrine response of endogenous catecholamine and cortisol concentrations.11,12 In fact, experimental studies on animals were able to create an ocular condition similar to CSCR owing to repeated injections of these hormones.13 Angiographic images of the fundus seen in patients who have CSCR frequently reveal vascular patterns like choroidal hyperpermeability,14,15 localized choroidal filling delays, or venous congestion that may be characteristic of CSCR.16,17 Despite the current technical limitations in choroidal angiography, these observations raised the discussion about whether the choroid is involved in the pathophysiology of CSCR. Given the fact that there is only little quantitative data about choroidal hemodynamics in this ocular disease, our aim was to investigate regional pulsatile choroidal blood flow using laser interferometry in patients who had active, unilateral CSCR.

METHODS

PATIENTS AND HEALTHY CONTROL SUBJECTS

The study protocol was approved by the ethics committee of University of Vienna School of Medicine, Vienna, Austria, and followed the guidelines of the Declaration of Helsinki. All participants signed a written informed consent. All patients were seen and their conditions were diagnosed in the medical retina referral center of the university eye clinic.
Fundus pulsation synchronous with the cardiac cycle was recorded using laser interferometry. In previous studies, this has been shown to be discernible in all patients. All patients were newly diagnosed for active, unilateral CSC, meeting the inclusion criteria. The clinically unaffected partner eyes of the patients with CSC served as a second control group.

DEFINITIONS

To meet the inclusion criteria of this study, all participants had to have an unremarkable general medical and ocular history with no present use of medications or tobacco. A complete ophthalmic examination was performed, including slitlamp biomicroscopy and indirect ophthalmoscopy. An acute, unilateral neurosensory detachment localized in the macula had to be discernible in all patients. All patients were newly diagnosed as having CSC with no documented history of the disease. Any participant with ametropia higher than 3.0 diopters (D) in either eye was excluded from the study. To establish the diagnosis, standard fluorescein angiography was performed to document that the localized macular detachment is attributed to a distinct leak or leaks within the temporal vascular arcades typically evident in active CSC. Other possible causes for the exudation such as inflammation, infiltration, or choroidal neovascularization ruled out a candidate.

FUNDUS PULSATION AMPLITUDE, MEAN ARTERIAL BLOOD PRESSURE, AND PULSE RATE

Fundus pulsation synchronous with the cardiac cycle was recorded using laser interferometry. In previous studies, this noninvasive method has proven to detect small hemodynamic changes with excellent reproducibility. Laser interferometry uses a coherent laser beam with a wavelength of 780 nm and 80 µW of power. The coherent laser beam illuminates the eye along the optical axis producing a 20- to 50-µm measurement spot on the retina. The laser light gets reflected from the anterior surface of the cornea and the fundus. This allows for the recording of interference fringes generated from the pulse synchronous relative distance changes between cornea and retina. The maximum distance change between the cornea and the fundus during a cardiac cycle is termed “fundus pulsation amplitude” (FPA). Fundus pulsation amplitude served as the main outcome factor in the present study and estimates local pulsatile blood flow. The interferometer is coupled to a fundus camera (model FK 30; Karl Zeiss, Oberkochen, Germany), which allows continuous visual control of the topographic alignment and focus of the laser spot on the retina. According to the protocol, FPA was measured in the fovea by asking the subject to fixate directly at the beam, which appeared as a red dot to the participant. In addition, the FPA was assessed at preselected points that were chosen based on fundus photographs and fluorescein angiograms. One measurement locus was the leak itself and up to 4 additional retinal measurement points were selected that were located within 1 disc diameter around the leak. In the controls just the right eyes were studied, where fundus pulsations were detected at corresponding fundus locations.

The mean arterial blood pressure was measured with an automated oscillometric device on the participant's right arm (CMS-patient monitor; Hewlett-Packard, Palo Alto, Calif). Pulse rate was automatically recorded from a finger-oxyometric device (CMS-patient monitor; Hewlett-Packard).

STATISTICAL ANALYSIS

Data were analyzed with descriptive statistics. A sample size calculation was considered to find a 10% difference of the main outcome measure to be statistically significant at \( \alpha = .05 \). \( \chi^2 \) Analysis with continuity correction was used for categorical analysis. The paired and unpaired \( t \) tests were used to compare group means of continuous variables. All statistical analyses were performed using the Statistica software package (Release 4.5; StatSoft Inc, Tulsa, Okla). All tests used were 2-sided with statistical significance set at \( P < .05 \). Data are given as mean (SD).

RESULTS

Based on the exclusion-inclusion criteria a total of 18 patients with active, unilateral CSC and 18 controls were included in the study. The descriptive characteristics of the patients who had active, unilateral CSC are given in Table 1. Both study groups had a male-female ratio of 16:2. The mean age of the patients who had CSC was 42 (10) years (age range, 31-68 years). The mean age of the controls was 40 (16) years (age range, 24-71 years; \( P = .65 \)). The mean arterial blood pressure tended to be higher in patients with CSC (99 [13] mm Hg) than in the controls (94 [13] mm Hg), but this value was not significantly different (\( P = .18 \)). Pulse pressure amplitude (64 [8] mm Hg in patients with CSC; 62 [7] mm Hg in the controls, \( P = .77 \)) and pulse rate (patients with CSC, 77 [13]/min; controls, 76 [11]/min; \( P = .87 \)) were comparable between the 2 study groups.

Typical measurement locations as selected in 1 patient are shown in the Figure. Table 2 lists individual foveal FPA measurements for both groups. Foveal FPA was significantly higher in the eyes of patients who had CSC (5.5 [1.7] µm) than in the eyes of the controls (4.1 [1.1] µm; \( P = .005 \)). Foveal FPAs in the eyes of the patients who had CSC were also elevated compared with the patients’ unaffected partner eyes (4.6 [1.2] µm; \( P = .047 \)). However, there was some, but a statistically insignificant, difference between the foveal FPA in the eyes of the controls and the one in the unaffected partner eyes of patients who had CSC (\( P = .07 \)).
The FPA, as measured directly on the leak, was 5.3 (1.8) µm. In healthy subjects the FPA values measured on the corresponding fundus locations were significantly lower (3.9 [0.8] µm; \(P = .007\)). The coefficient of variation of FPAs around the leak was also calculated. This point-to-point variability was significantly higher in patients with active CSC (48% [20%]) than in the controls (20% [9%]; \(P < .001\)).

**COMMENT**

In the present study laser interferometric measurement of fundus pulsation was chosen to gain insight into choroidal circulation in patients with CSC. In this study 18 consecutive patients with active, unilateral CSC were compared with an equally sized control group of healthy volunteers to assess the magnitude of the pulsatile choroidal blood flow in active CSC. The results clearly indicate that patients with active CSC have higher than normal amplitudes of ocular fundus pulsation in the macular area compared with healthy control eyes and with the unaffected partner eye. In addition, the local variability of FPA in the area of the leak is larger in the patients with CSC than in the controls. These results suggest that at least the pulsatile component of choroidal blood flow is altered in active CSC.

In general, blood flow is determined by the perfusion pressure, the tone of the peripheral resistance vessels, and rheological properties. As the pulsatile blood flow is a part of the entire blood flow, one may speculate that the alteration of the pulsatile choroidal blood flow in CSC must be caused by at least one of the above-mentioned factors. Under stress, human circulation and homeostasis undergo numerous changes, which may, in turn, alter systemic hemodynamics. However, none of the systemic factors measured in this study showed any significant difference between the patients with active CSC and the controls. This is particularly true for pulse pressure amplitude, which is the driving force of pulsatile blood flow. Hence, we assume that the detected phenomenon of increased FPA is unlikely to be only a propagated cardial phenomenon. The high regional variability in FPA also suggests that our observation represents more of a localized problem.

Since this disease occurs rather early in a person's life, we assume that tonal flexibility of the choroidal vessels may be of certain relevance, especially compared with arteriosclerotic and hypertensive changes in the choroid that appear later in life. Although it is said that the choroidal circulation is under neural control, we do not know until now to what extent. However, recent studies clearly indicate neural control mechanisms occur in the human choroid. Our observation may be compatible with the concept that the choroidal regulatory abilities are limited or are altered in CSC. Recently, a study provided evidence for altered endothelial function in patients with CSC and increased plasma endothelin 1 levels were reported. Because the level of endothelin 1 is typically elevated when shear stress on the endothelium is evident, this, indeed, may be compatible with our results and angiographic observations that there is a strong local variability of choroidal blood flow around the leak with choroidal hyperperfusion. Furthermore, plasma levels of plasminogen activator inhibitor-1 are found to be significantly increased in patients who have CSC, thus, supporting the concept that the choroidal vasculature is involved in the pathogenetic process. However, to our knowledge, in vivo studies on endothelial dysfunction in patients with CSC have not yet been performed.

The angiographic appearance of active as well as chronic CSC is clearly described. Our findings may reflect what is seen in angiographic studies. The strong regional differences of the FPA indicate higher than normal variability in choroidal hemodynamics. In the con-

<table>
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<tr>
<th>Patient and Control Subject No.</th>
<th>Foveal FPA, µm</th>
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<th>Control Subjects</th>
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Controls the FPA is higher in the fovea than in peripheral parts of the retina. In an area of 15° around the fovea, there is, however, little variation of FPA in healthy subjects as also evidenced from the results of the present study. The regional variability of the FPA in patients with CSC may indicate local perfusion abnormalities in the choroid of eyes with CSC. Local perfusion changes were also proposed based on angiographic findings with the numerous patches of discrete choroidal hyperfluorescence attributed as multifocal choroidal hyperpermeability. Hayashi et al demonstrated localized perfusion abnormalities presumed as focal choroidal ischemia. Focal leakage of indocyanine green dye at the level of the choriocapillaris and patches of hyperfluorescence in otherwise unaffected areas in late-transit phases were described. Most authors share the impression that this multifocal choroidal vascular hyperpermeability seen on indocyanine green angiography is common and, therefore, a characteristic feature in patients with CSC. Prunte and Flammer formulated a causal chain of pathophysiologic changes where a lobular arterial filling delay causes focal ischemia followed by capillary and venous congestion leading to choroidal hyperpermeability. Moreover, Prunte and Flammer postulated that choroidal hyperpermeability was only detected in areas of previous vascular congestion. Direct comparison of FPA measurements with angiographic findings is, however, difficult. On the one hand, the sites of FPA measurements were chosen directly adjacent to the leakage point which hampers local correlation with indocyanine green angiograms. On the other hand, it is difficult to extract quantitative data of choroidal blood flow based on angiography. Hence, focal ischemia as proposed by several authors is not a contradiction to increased choroidal blood flow as indicated based on our results.

CONCLUSIONS

We have shown that patients with active, unilateral CSC have increased FPA in the fovea compared with controls. In addition, our data indicate an abnormal local variability of FPA in the region of the leak. This may reinforce the concept that CSC is a widespread choroidal disease.

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