Ocular pulse amplitude in diabetes mellitus

Karl-Georg Schmidt, Andrea von Rückmann, Bettina Kemkes-Matthes, Hans-Peter Hammes

Abstract

Background—The influence of diabetes mellitus on ocular pulse amplitude (OPA), an indirect measure of choroidal perfusion, is unclear.

Methods—OPA, using the Langham ocular blood flow (OBF) system, application intraocular pressure (IOP), systemic blood pressure (BP), heart rate, and haemoglobin (Hb) A1c were measured in patients with insulin dependent diabetes mellitus (IDDM) with no (DR-0, n = 22) non-proliferative (DR-1, n = 24), and proliferative (DR-2, n = 18) diabetic retinopathy.

Results—Neither local (OPA, IOP) nor systemic perfusion parameters (BPs, HR) nor HbA1c were significantly altered in DR-0, DR-1, or DR-2 IDDM patients.

Conclusion—Choroidal circulation remains unaffected as diabetic retinopathy advances.

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Diabetic retinopathy (DR) is the major cause of blindness in adults aged 25–74 years.1 With increasing duration of this disease, the inner retina is progressively affected by microvascular occlusions leading to reduced oxygen supply and eventual retinal neovascularisation.2 Although the underlying cause of DR is related to chronic hyperglycaemia, the exact sequence of events and the relative contributions of abnormalities within the vessel3–5 and the vessel wall are undetermined.6 7

Changes in retinal perfusion, its regulation, and the factors that mediate them have been studied in diabetes mellitus (DM) by many investigators.8–12

A review of the literature also suggests a pathogenetic role for the choroid in the initiation and propagation of DR. Using scanning electron microscopy in necropsy eyes from patients with long standing insulin dependent DM (IDDM), Fryczkowsky et al13 noted increased tortuosity, focal vascular dilations and narrowings, vascular loops and microaneurysm formation, dropout of choriocapillaries, and sinus-like structure formation between choroidal lobules in the equatorial area. They concluded that changes in the choroid, especially in the choriocapillaris, may be a contributing factor in DR, resulting in decreased oxygenation of the outer layers of the retina.

High resolution histological analysis of the human choroidal vasculature revealed capillary dropout, beaded capillaries, and neovascularisation,14 fluorescein angiography showed delayed choroidal perfusion, and electroretinograms with abnormal oscillatory potentials in the same DM patients.15

The choroid supplies 80% of total retinal oxygen16 and glucose,17 and all of the nutrients to the macula and optic disc region,18 and maintains a constant thermal environment for the retina.19 20

Reduced blood flow can result in tissue hypoxia, leading in extreme situations to cell/tissue death—for example, in myocardial or cerebral tissue infarctions. Results from clinical studies showed reduced choroidal perfusion in DR,19 retinitis pigmentosa,20 and normal tension glaucoma.21–23 Associated with functional (visual field defects) and morphological (nerve fibre layer loss) damage.20 22

Increased choroidal perfusion as noted in ocular hypertensive patients24 25 and following application of nifedipine26 27 and dorzolamide28 may be interpreted as a protective mechanism.

This study was designed to evaluate ocular pulse amplitude (OPA), in IDDM patients with different stages of DR.

OPA is an indirect measure of choroidal perfusion. A bolus of blood entering the eye corresponding to the cardiac pulse represents a change of intraocular pressure (IOP) as a function of time reflecting the pulsatile component (approximately 70%)29 of intraocular blood flow,30 31 85% of which is choroidal.32

Materials and methods

Sixty four patients with type 1 insulin dependent diabetes mellitus (IDDM) taking intensified insulin therapy were investigated. Patients with systemic hypertension, hypercholesterolaemia, neurological deficits, typical migraine headache, and ocular or systemic disease, other than the category selected for, were excluded from the study. The IDDM patients selected had a history of IOP < 21 mm Hg, typical fundus appearance (DR-0: normal fundus, DR-1: background diabetic retinopathy characterised by microaneurysms, haemorrhages, exudates, oedema, nerve fibre layer infarcts, venous beading, and/or intraretinal microvascular abnormalities; DR-2: proliferative diabetic retinopathy characterised by an area of epipapillary neovascularisation larger than a quarter of disc diameter and/or areas of epiretinal neovascularisation larger than a diameter of half a disc). None of the patients or controls had received ocular surgery or laser treatment of any kind and were taking no ocular therapy.

Patients with DR-0 (n = 22, male: 12, age: 23.3 (SD 2.2) years, duration of diabetes: 5.5 (1.8) years, HBA1c: 6.1 (0.5)); DR-1 (n = 24, male: 11, age: 28.4 (2.6) years, duration of...
Results

When compared with respective subgroups from a pool of healthy controls (n = 72), IOP, OPA (Fig 1), systolic and diastolic blood pressures, and heart rate (Table 1) were not significantly (p>0.01) altered in any of the three IDDM groups investigated. Also, when IDDM patient groups were compared with each other, OPA (Fig 1), systolic and diastolic blood pressures, heart rate, and HBA1c, were not significantly (p>0.01) altered in any of the three IDDM groups (Table 1).

Discussion

OPA, a haemodynamic parameter reflecting overall choroidal perfusion is unchanged in IDDM patients independent of the degree of retinopathy which is in contrast with another study reporting a reduction of OPA with the severity of the retinopathy.32

The functional integrity of the choroid in DR even in advanced stages, as demonstrated by our data, is confirmed by clinical evidence that the function of the photoreceptors as measured by visual field examination is unaltered in DR.31

In parallel with the anatomy and the physiological function of both vascular systems, DR is confined to the inner parts of the retina,13 the outer plexiform layer, the watershed zone between retinal and choroidal vascular system, being the most outer zone affected,13 whereas the outer retina beginning at the outer plexiform layer, supplied by the choroid,13 remains mostly unaltered.13

Despite similar metabolic changes affecting both retinal and choroidal vascular beds,12 one interesting finding is that pericyte dropout, a hallmark of early diabetic retinopathy does not occur in choroidal capillaries.12 The primary surplus of choroidal vessels and blood flow, responsible for the nutrition and waste removal of the crucial outer retinal parts, may in part explain the relative resistance to degenerative influences from disease such as diabetic retinopathy.

Statistics

All data represent arithmetic mean (SD); Student’s unpaired two tailed t test was used for statistical analysis. Measurements were performed on both eyes of each subject. The level of significance was 5%. IDDM patient groups (DR-0, DR-1, DR-2) were compared with matched subgroups (MCTL) of healthy volunteers (CTL), and with each other.

Table 1 Comparison of perfusion parameters (mean (SD)) of patients with insulin dependent diabetes mellitus (IDDM) with different stages of diabetic retinopathy, no (DR-0, n = 22), non-proliferative (DR-1, n = 24), and proliferative (DR-2, n = 18) diabetic retinopathy compared with matched subgroups (MCTL) from a pool of healthy controls (CTL, n = 72).

<table>
<thead>
<tr>
<th></th>
<th>OPA (nm Hg)</th>
<th>IOP (nm Hg)</th>
<th>Blood pressure (systolic, mm Hg)</th>
<th>Blood pressure (diastolic, mm Hg)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (CTL)</td>
<td>2.2 (0.5)</td>
<td>15.1 (1.5)</td>
<td>125.1 (14.2)</td>
<td>78.2 (10.7)</td>
<td>77.0 (15.0)</td>
</tr>
<tr>
<td>DR-0</td>
<td>2.4 (0.7)</td>
<td>15.8 (4.3)</td>
<td>129.4 (17.6)</td>
<td>78.6 (10.9)</td>
<td>76.2 (20.5)</td>
</tr>
<tr>
<td>Matched CV</td>
<td>2.2 (0.7)</td>
<td>14.9 (2.4)</td>
<td>123.4 (24.9)</td>
<td>77.4 (8.8)</td>
<td>77.7 (16.8)</td>
</tr>
<tr>
<td>Matched CTL</td>
<td>2.2 (0.8)</td>
<td>16.4 (5.2)</td>
<td>125.0 (23.1)</td>
<td>80.1 (10.3)</td>
<td>79.9 (9.5)</td>
</tr>
<tr>
<td>DR-1</td>
<td>2.2 (0.8)</td>
<td>15.0 (2.6)</td>
<td>127.1 (20.4)</td>
<td>76.7 (10.2)</td>
<td>76.3 (12.5)</td>
</tr>
<tr>
<td>Matched CTL</td>
<td>2.2 (0.8)</td>
<td>16.2 (5.4)</td>
<td>119.7 (22.3)</td>
<td>75.7 (13.9)</td>
<td>77.1 (19.2)</td>
</tr>
<tr>
<td>DR-2</td>
<td>2.1 (0.7)</td>
<td>16.4 (5.2)</td>
<td>125.0 (23.8)</td>
<td>80.1 (10.3)</td>
<td>79.9 (9.5)</td>
</tr>
<tr>
<td>Matched CTL</td>
<td>2.3 (0.5)</td>
<td>15.2 (2.4)</td>
<td>124.5 (24.2)</td>
<td>78.9 (17.9)</td>
<td>76.6 (15.1)</td>
</tr>
</tbody>
</table>

There were no significant changes in any of the parameters using Student’s unpaired two tailed t test.

Diabetes: 11.3 (2.6) years, HBA1c: 5.8 (0.4); and DR-2 (n = 18, male: 9, age: 33.1 (2.5) years, duration of diabetes: 16.1 (3.2) years, HBA1c: 6.3 (0.7)) were compared with respective matched control subgroups (MCTL) selected from a pool of 72 healthy volunteers with no known ocular or systemic disease, who showed no visual field defects and/or disc alterations and had IOPs < 21 mm Hg matched for age (SD 3 years), sex, IOP (2) mm Hg), and refraction (1.5 dioptres spherical equivalent).

The study has been approved by the institutional review board and informed consent was obtained from each patient/volunteer following complete explanation of the procedure.

The ocular blood flow (OBF) system (OBF Labs Ltd, Wiltshire) has been described in detail elsewhere.31

In addition to pneumotonometric values, IOP was measured by Goldmann application tonometry. Brachial artery pressures were measured non-invasively (Riva-Rocci) using a blood pressure cuff and a stethoscope after 5 minutes resting. Heart rate (HR) was measured manually using a stopwatch. Application IOP, blood pressure (BP), and HR were taken before OPA measurements. All measurements were performed in a seated position, respective measurements were taken by the same examiner.

Statistics

All data represent arithmetic mean (SD); Student’s unpaired two tailed t test was used for statistical analysis. Measurements were performed on both eyes of each subject. The level of significance was 5%. IDDM patient groups (DR-0, DR-1, DR-2) were compared with matched subgroups (MCTL) of healthy volunteers (CTL), and with each other.

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Proprietary interest: none.


Figure 1 Ocular pulse amplitudes (OPA; mean (SD)) of patients with insulin dependent diabetes mellitus (IDDM) with different stages of diabetic retinopathy, no (DR-0, n = 22), non-proliferative (DR-1, n = 24), and proliferative (DR-2, n = 18) diabetic retinopathy compared with matched subgroups from a pool of healthy controls (n = 72). There were no significant changes in any of the parameters shown in this diagram using Student’s unpaired two tailed t test.

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