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Short communication

Retinal nerve fibre layer thickness in conditions of severe ischemia in patients without glaucoma

JOSIP PAVAN
ADRIAN LUKENDA
MIRKO ŠARLIJA
SNJEŽANA KAŠTELAN
IGOR KNEZOVIĆ
JASMINKA SALOPEK-RABATIĆ
MARKO ĆURKOVIĆ

Department of Ophthalmology
University Hospital Dubrava
Av. G. Šuška 6,10000 Zagreb

Correspondence:
Josip Pavan
Department of Ophthalmology
University Hospital Dubrava
Av. G. Šuška 6, 10000 Zagreb
E-mail: josip.pavan@zg.htnet.hr

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Abstract

Introduction: *Ischemia, most often caused by carotid disease, contributes to or causes a numerous ocular changes including optic nerve and ganglion cell damage, glaucoma, anterior and posterior segment changes. The perimetric changes in ischemia partially overlap with those caused by glaucoma. New diagnostic tools such as scanning laser polarimetry can detect retinal nerve fiber layer loss in glaucoma up to 6 years earlier than the first perimetric changes. Still, it is not yet clear if and up to what level laser polarimetry can show changes in RNFL caused by ischemia only, and whether these changes differ from the pure glaucomatous ones. In our pilot study we tried to investigate influence of significant carotid stenosis on retinal nerve fiber layer.*

Materials and Methods: *Eight consecutive patients with carotid stenosis of more than 70% and no other eye disease influencing optic nerve.*

Results: *RNFL loss can be found in the most of analyzed patients. The level of the RNFL impairment is not equal in the both eyes of patients having a different degree of stenosis on two sides probably due to the factors such as microvascular status.*

Conclusion: *RNFL suffers changes in carotid stenosis. The results demand further investigation because the possibility of the precise estimation of ischemical damage to the RNFL can be of crucial importance in diagnosing and treatment of patients having glaucoma and ocular ischemia at the same time.*

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INTRODUCTION

A severe prolonged ischemic, most often caused by carotid disease but also with other vasculopathies, causes a large spectrum of ocular changes known as ocular ischemic syndrome, OIS *(1)*. The syndrome most commonly consists of ocular and orbital pain, visual loss, conjunctival angiopathy and iris dystrophy, pseudoexfoliation, pale optical disc and tortuous retinal veins *(1–3)*. The presence of ocular ischemic syndrome implies in many cases also a significant risk of cerebrovascular morbidity *(1, 4)*. Due to large variety of symptoms and severity of presentation, ocular ischemic syndrome is relatively difficult to be diagnosed *(1)*. MSCT and ultrasound are two major techniques in evaluation of carotid stenosis, but reduced blood flow to the orbit and the eye can be detected also by fluorescein angiography and ophtalmodynamometry *(4)*. Recent investigation showed that the diastolic central retinal artery pressure was significantly ($p<0.001$) lower in the affected eye *(5)*.

The mechanism of eye damage is oxidative stress which encompasses elevation of oxidative metabolites and a relative deficiency of anti-oxidants *(6)*. The eye is known to be at high risk to be damaged by oxidative mechanisms due to the biochemical composition of ocular structures, especially that of retina and content of unsaturated fatty acids. Most prominent entities initiated or propagated by oxidative processes, ocular ischemia or hypoxia besides OIS are diabetic retinopathy and glaucoma *(7)*.

In many cases where carotid stenting was performed and arterial perfusion restored before significant anterior segment involvement, visual function and other ocular signs of the disease recovered within a few weeks *(8, 9)*.

Ischemia plays also a significant role in onset and development of glaucoma *(7)*. Having an elevated intraocular pressure as a main sign threw out the history; glaucoma is nowadays defined as multifactorial optic neuropathy with an elevated intraocular pressure as a primary risk factor. Ischemia on the other hand, is recognized as an important factor in optic nerve changes and consequently visual field deterioration *(10)*. Recent data clearly showed changes in ocular blood flow and resistivity index in ciliary artery, central retinal artery and ophthalmic artery in glaucoma patients. Vascular insufficiency and elevated IOP together or each of them alone can lead to structural changes of the optic nerve head and retinal fibre layer. These changes, in the beginning reversible but later irreversible are manifested as retinal fibre layer loss and progressive disc couping *(7)*. Which of two mentioned factors, IOP or ischemia prevails in glaucoma onset in each particular case remains unclear.

Clinical picture of primary open-angle glaucoma (POAG) in patients with significant stenosis of the extracranial segment of the internal carotid artery (ICA) on the side of the glaucomatous eye is similar to the one of the POAG patients with normal carotid function but IOP tends to be less reactive to the drug therapy or antiglaucomatous surgical procedures. After restoring a perfusion, IOP decreases although worsening of the symptoms can sometimes be seen for a shorter period of time *(11)*.

Based on the fact that changes of the RNFL are one of the earliest signs of glaucoma *(12, 13)* and precede visual field loss or changes in optic disc appearance, scanning laser polarimetry has been developed as an efficient tool in glaucoma assessment. Furthermore, 88% of eyes that convert into glaucoma have had RNFL defect at the time it was detected by standard automated perimetry, and 60% of them had RNFL defect 6 years prior to the visual field defect *(14)*. Although polarimetry has a high sensitivity, reproducibility and specificity, a border between RNFL loss in suspicious glaucoma patient and patient with other / ischemical cause of nerve damage remains unclear.

For all above mentioned reasons we assumed that RNFL change measured by scanning laser polarimetry can be an objective and early parameter in detection of the possible ischemical damage to the optic nerve. As ischemia plays an important role in onset and development of glaucoma, objectification of the degree of ischemical damage by standard glaucoma diagnostic tools can be in the future helpful in distinguishing ischemical component from the others.

MATERIALS AND METHODS

Eight consecutive patients suffering internal carotid stenosis of more than 70%, monolateral or bilateral were observed. Due to the significant impairment of the circulation all of them were hospitalized for surgical treatment of carotid stenosis. After a full preoperative systemic evaluation, a detailed ophtalmic examination was performed. It consisted of visual acuity (without correction and best corrected visual acuity), anterior and posterior segment evaluation and intraocular pressure. Excluding criteria were following: PNO abnormalities, history of opticoneuropathy, disturbances in visual axis resulting in best corrected visual acuity of less than 0,30, myopia of –4 D or more, diagnosed glaucoma, IOP more or equal to 20 mm in two consecutive measurements. In all observed patients GDX VCC was performed.

Control group consisted of 20 age and sex- matched subjects with no glaucoma or ischemia signs and a normal carotid status.

Carotid stenosis was measured by MSCT and/or ultrasound.

Retinal nerve fibre layer was measured with GDx with variable corneal compensation (GDxVCC, Zeiss, Germany).

The differences in RNFL status are going to be explained threw IES, inter-eye symmetry measures and P values.

IES, inter-eye symmetry measures the degree of symmetry between the right and left eyes by correlating the TSNIT functions from two eyes. Values range from –1 to 1, where values near one represent good symmetry. Normal eyes have good symmetry with values around 0,9. This measure is the Pearson Product correlation coefficient (r-value) from the correlation of the TSNIT curves of the two eyes. TSNIT stands for temporal-superior-nasal-inferior-temporal and displays the RNFL thickness values along the calculation circle starting temporally.

P value, in the GDxVCC printout displayed as deviation map reveals the location and magnitude of RNFL defects over the entire thickness map. Map analyzes a 128x128 pixel region (20°x20°) centered on the optic disc. P value in a certain location of less than 5 means that there is less than 5 % probability that such RNFL deviation can be found in a normal subject.

RESULTS

In Table 1. Results for all patients have been listed.

Parameter age shows that all the patients are in the age of 55–82. This has been expected due to the nature of

TABLE 1

Summary data for the observed patients.

Patient	Sex	Age	Stenosis R	Stenosis L	Hypertension	Triglycerides	Smoking	Pdex.	P sin.	IES
U.J.	M	68	80–90%	40%	+	N	+	p < 1%	p < 1%	0.54
T.J.	M	82	50%	80%	+	elevated	+	p < 5%	p < 1%	0.58
B.V.	Ma	77	85%	40–50%	+	elevated	+	p < 2%	p < 2%	0.85
Lj.C.	F	55	subtotal	60–70%	–	elevated	?	p < 5%	p <0.5%	0.68
A.G.	M	69	70%	85%	+	elevated	+	p < 5%	p <0.5%	0.90
S.K.	M	68	85%	none	+	elevated	+	p > 5%	p < 5%	0.85
M.V.	M	60	60	none	+	elevated	+	p < 5%	p < 5%	0.97
P.S.	F	71	80	60–70	+	elevated	–	p < 1%	p < 2%	0.72

vascular stenosis which affects predominantly people of the older age. All but one patient had arterial hypertension and elevated triglycerides. All but one patient are or have been cigarette smokers except in the case of the patient who didn't want to express himself. It is obvious in the most of the cases that depth of the RNFL defect in both sides varies depending on degree of stenosis.

DISCUSSION

The ischemic damage to the optic nerve and other eye structures that occurs in the most of the cases due to the carotid stenosis causing retinal ganglion cell loss is a well known fact *(15–18)*. Still, the correlation between ischemia and changes in the eye cannot always be exactly quantified. The most important tools in diagnosing of ischemia are doppler of the carotid artery, ciliary artery, central retinal artery and ophthalmic artery where alterations in ocular blood flow and resistivity index can be prominent, MSCT of the carotid and visual field testing where typical changes can be found in a relatively early stage *(1, 3, 4, 10)*. Still, some newer diagnostic tools predominantly designed for glaucoma detection can also be of potential benefit. Retinal nerve fiber layer is the one that suffers changes in glaucoma in the very early stage due to the direct mechanical damage by elevated intraocular pressure or/and microvascular dysfunction *(12, 13, 14)*. Based on the fact that changes in RNFL are presently first detectible changes that can be objectively measured, a scanning laser polarimetry, GDxVCC (Zeiss) was designed and implemented *(19, 20)*. Up to the available data it has a high sensitivity (89%) and specificity (98%) *(21)* and therefore detects glaucomatous (multifactorial) RNFL loss up to 6 years before visual field testing *(14),* but there are very few data describing the role of GDX in detecting only ischemical RNFL loss *(22)*. Moreover, glaucoma onset and progression are very much dependent on the ocular blood flow *(23, 24)*. Role of ischemia in glaucoma as a multifactorial neuropathy among ophthalmologists is widely accepted as significant but it still isn't clear up to what point it contributes in glaucoma in each particular case compared to the other factors (e.g. intraocular pressure, heritage).

In this trial, a degree of damage of the optic nerve in patients with carotid stenosis but no glaucoma tried to be quantified. Even in a small group of patients it is obvious that RNFL defects, sometimes of an important level are often present. Another confirmation of the ischemical origin of the defect is a difference in RNFL thickness in the eyes of the same patient with a different degree of carotid stenosis in two sides. Presumably, unilateral stenosis is going to be cause of changes on the same side, but changes seen on the contra lateral side can have it's origin in more peripheral vessels, status of circulus Wilisii or other causes. This is more probable having in mind the fact that almost all patients were smokers and had elevated cholesterol values. Certainly, these results are motivating and demand further investigation on bigger group of patients as well as repetition of laser polarimetry after operative resuscitation of the circulation because several reports have shown positive effects of endaeterectomy on perimetric findings *(25, 26)*. Possibility of the precise estimation of ischemical damage to the RNFL can be of crucial importance in diagnosing and treatment of patients having glaucoma and ocular ischemia at the same time.

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