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Use of color Doppler ultrasonography in primary vasospastic syndrome and assessment of ocular blood flow in patients with transient monocular blindness

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Summary

Background: Transient monocular blindness (TMB) may appear as a consequence of vasospasm called the primary vasospastic syndrome. Because of pathogenesis of this disorder it is an essential diagnostic procedure in evaluation of hemodynamic disturbances in eyeball circulation system in group of TMB patients. The aim of this study was to investigate the changes in eyeball circulation in patients with TMB, using colour Doppler ultrasound imaging method (CDI).

Material/Methods: 89 patients (59 women and 30 men) aged 34 to 56 (avg. 49.53, sd 3.15) with symptoms of transient blindness were examined using Acuson 128XP apparatus and sector probe frequency of 7.5 MHz. In ophthalmic artery (OA), central retinal artery (CRA) and short posterior temporal ciliary artery (SPTCA), the following parameters of blood flow were determined: peak systolic velocity (PSV, m/s), peak end – diastolic velocity (EDV, m/s), vascular pulsation index (PI) and resistance index (RI). The determined blood flow parameters were compared with the same blood flow indicators in the group of healthy individuals, matched for sex and age with the study group.

T-Student test was applied in the statistical analysis of the differences between studied ocular blood flow parameters. In case of lack of normal variance, non – parametric U-Mann-Whitney test was used.

Results: Statistical diminishing of average values of PSV ($p = 0.0001$) in CRA and SPTCA; RI ($p = 0.0001$ in CRA and $p = 0.0003$ in SPTCA) and PI (in OA $p = 0.0005$, in CRA $p = 0.0001$, in SPTCA $p = 0.0004$) of examined eyes in comparison to healthy subjects was revealed. Peak-diastolic and mean velocities did not indicate statistically relevant difference in the control group.

Conclusions: The statistically significant decrease of peak systolic parameters of blood flow velocity, pulsation and resistance indices in eyeball arteries were observed in patients with transient monocular blindness. Color Doppler ultrasonography was an effective and helpful method in assessing blood flow changes of eyeball microcirculation in transient monocular blindness.

Key words: transient monocular blindness • ocular blood flow • primary vasospastic syndrome • vascular dysregulation • color Doppler ultrasonography

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Background

Transient symptoms of blindness produced by vascular spasms can occur in patients of various ages but they appear most frequently in young and middle-aged people. Clinical symptoms of blindness last from a few seconds to several minutes, usually occur in one eye and are not associated with other clinical symptoms. Endothelin – 1, a peptide produced by endothelial cells, plays an important role in pathogenesis of this disease as it can bring about

a powerful and prolonged vasospasm [1]. The vasospasm has major role in the pathogenesis of different diseases, including the eyeball. This symptom is defined as constriction or dilatation of small retinal and choroidal vessels in insufficient microcirculation of eyeball. The vasospasm is accompanied by a reaction from the surrounding vessels causing dilatation of arteries, venules or capillaries in eyeball vascular bed. The set of phenomena appearing in eyeball microcirculation is known as vascular dysregulation (VD) [1, 2]. VD occurs with different intensification in various organs. The most common symptom occurs in fingers and toes, heart, brain and eye.

In ophthalmologic practice there are patients regarded as healthy, however exhibiting ocular symptoms of transient blindness. Due to the lack of data in literature concerning the above presented phenomenon, the authors delivered early outcomes of their own studies.

One of the methods enabling direct and noninvasive assessment of blood flow in ophthalmic vessels is color Doppler ultrasound.

The aim of this study was to assess and analyze the mean values of blood flow velocity parameters and vascular pulsation as well as resistance indices in retrobulbar arteries in patients with transient monocular blindness using color Doppler ultrasonography (CDI). The received results were then compared with blood flow parameters in the same arteries in the group of healthy individuals.

Materials and methods

The study group consisted of 89 patients, in whom 117 eyes were examined. The age of the patients was between 34 to 56 years old, mean 49.53 (sd. 3.15). In all cases the disease symptoms occurred in 1 eye; however, in 28 patients blindness occurred alternatingly in each of the eyes, but not in both of them at the same time. Therefore, those 28 eyes were included in the examined group. The examined patients were mostly regarded as healthy with recognized short term, repeating blindness. Additionally, during the interview frequent headaches, cold hands, migraine and low arterial blood pressure were observed. CDI ocular blood flow examination was performed after 7–10 days from the disappearing of short term loss of vision symptoms. Ultrasonographic examinations were conducted after receiving earlier consent from patients. In the studied group atheromatosis pathological changes which could disturb the blood flow in carotid arteries did not occur during CDI examination.

As for basic ophthalmic determination, the following examinations were performed: visual acuity on Snellen chart, anterior segment investigation in slit lamp, measurement of intraocular pressure and indirect fundoscopy.

Ocular blood flow velocity was determined by CDI of the ophthalmic artery (OA), central retinal artery (CRA) and short posterior temporal ciliary artery (SPTCA) using the Acuson 128XP apparatus, with a multifrequent 7.5 MHz sector probe. The examination was performed typically for the evaluation of blood flow in eyeball arteries described by different authors, as well as by the authors of this research [3, 4, 5, 6]. Ophthalmic artery (OA) was found in the orbital space behind the posterior pole of eyeball, along the temporal part of optic nerve, or in place where optical nerve crosses this artery. The depth of spot where ophthalmic artery was most often situated varied from 1.5 cm to 1.8 cm. Furthermore, central retinal artery (CRA) ranging from 0.2 mm to 0.3 mm from the entrance of optical nerve head into eyeball was examined. The course of both central retinal artery and central retinal vein was the most common site of this vessel investigation. Temporal branch (SPTCA) of short posterior arteries (SPCAs) was the most repeatable in choroidal blood flow evaluation, thus CDI was applied to this vessel. SPTCA was found in the distance of 0.2 to 0.4 mm from posterior pole of eyeball along the temporal part of optic nerve. In our opinion, CDI examination of ocular vessels is complicated, time consuming and demands a lot of experience from the investigator. In our facility the evaluation of the ocular blood flow has been performed using CDI method since 1992 and so far the Doppler ultrasonography in retrobulbar arteries has been used in examinations of about 2.5 thousand patients. Angle correction was applied to the pulsed Doppler recordings to minimize errors in the examined velocities. CDI measured the following blood flow parameters: peak systolic velocity (PSV, m/s), end-diastolic velocity (EDV, m/s), pulsation index (PI) and resistance index (RI).

The blood flow spectrum in examined arteries was compared in the study and control groups, where control group consisted of 29 healthy volunteers, 15 women (51.7%) and 14 men (48.3%), aged 29–57. The average age of the control group was 47.31 (sd.2.97). In the group of healthy individuals cardiovascular diseases and carotid artery blood flow disturbances were excluded.

The T-student test was used for the statistical analysis of the comparison of mean blood flow parameters. In cases of deviation from the normal variance, U Mann-Whitney test was applied. In the tables the level of significance was indicated as p-value; $p \leq 0.05$ supported the assumed hypothesis.

Results

The results based on the interviews with the patients showed that blindness occurred mostly in one eye and lasted from a few to several seconds. Short term loss of vision was not accompanied by additional clinical symptoms in other organs. Medical interview revealed that blindness mostly appeared after emotional stress or without any relevant cause and repeated several times. Additionally, intervals between the symptoms of blindness appeared in different time periods.

In the study group no systemic diseases of vascular origin and insufficiency of carotid circulation were found. According to the case histories they were healthy individuals. Arterial hypotension was present in majority of patients (89.8 %). The arterial systolic pressure did not exceed values from 80 to 100 mm Hg. The diastolic blood pressure values ranged from 50 to 70 mm Hg. All patients

Table 1. Average value of peak systolic velocity (PSV) in examined arteries of the eye-ball in affected eye group (n_1) and healthy eye group (n_2), sd_1 – standard deviation in group 1, sd_2 – standard deviation in group 2, p – statistical significance was indicated as p value $p \leq 0.01$ and $p \leq 0.05$.

Studied arteries	PSV (m/s) Affected eyes (n_1=117)	sd_1	PSV(m/s) Healthy eyes (n_2=29)	sd_2	P
Ophthalmic artery	0.41	0.14	0.43	0.12	0,3918
Central retinal artery	0.11	0.04	0.17	0.005	0,0001
Short temporal posterior ciliary artery	0.19	0.10	0.27	0.09	0,0001

Table 2. Average value of RI in examined arteries of the eye-ball in affected eye group (n_1) and healthy eye group (n_2), sd_1 – standard deviation in group 1, sd_2 – standard deviation in group 2, p –statistical significance was indicated as p value $p \leq 0.01$ and $p \leq 0.05$.

Studied arteries	Affected eyes (n_1=117)	sd_1	Control group (n_2=29)	sd_2	P
Ophthalmic artery	0,68	0.09	0.73	0.07	0.0143
Central retinal artery	0,61	0.11	0.75	0.09	0.0001
Short temporal posterior ciliary artery	0,62	0.11	0.71	0.10	0.0003

Table 3. Average value of PI in examined arteries of the eye-ball in affected eye group (n_1) and healthy eye group (n_2), sd_1 – standard deviation in group 1, sd_2 – standard deviation in group 2, p – statistical significance was indicated as p value $p \leq 0.01$ and $p \leq 0.05$.

Studied arterie	PI Affected eyes (n_1=117)	sd_1	PI Control group (n_2=29)	sd_2	p
Ophthalmic artery	1.34	0.41	1.63	0.25	0,0005
Central retinal artery	1.06	0.34	1.50	0.29	0,0001
Short temporal posterior ciliary artery	1.09	0.35	1.34	0.35	0,0004

who underwent the ophthalmologic examination had normal visual acuity after using ophthalmic correction glasses, determined by Snellen's chart. The anterior section of the eye was found to be within the standard limit and the intraocular pressure, did not exceed 21 mm Hg. As for fundoscopy, no abnormalities were found in majority of patients, except for the narrowing and straightening of arterial vessels. Although two patients were diagnosed with thrombotic changes in branch of central retinal vein, these changes were deemed to have no influence on visual disturbance in those patients.

All patients examined with CDI showed alterations of blood flow in OA, CRA and SPTCA. These results were statistically significant for PSV in CRA and SPTCA compared with healthy eyes of the control group ($p = 0.0001$), table 1.

The analysis of the RI parameter in the examined arteries showed diminished values of this index in all eyeball arteries, when compared to the same arteries of the control group. The most significant differences of the average value of this index were visible in CRA ($p = 0.0001$) and in SPCTA ($p = 0.0003$), where similar results occurred, table 2.

The analysis of mean value of PI in assessed arteries revealed statistically significant decrease of this index in all ocular arteries in comparison to the same arteries of the control group. Statistically significant differences in this index were observed in OA ($p = 0.0005$), in CRA ($p = 0.0001$) and in SPTCA ($p = 0.0004$), table 3.

The remaining parameters of blood flow velocity such as end-diastolic velocity (EDV) and mean velocity (MV) did not differ significantly in the examined eyes. Blood flow spectrum in US Doppler revealed a diminished amplitude of the blood flow velocity and a disturbance of the flow pattern in the arteries within the examined group (fig. 1B, 2B, 3B), as compared to the control group (fig. 1A, 2A, 3A).

Discussion

Color Doppler US is one of few noninvasive methods applied in medical practice, that can assess the blood flow in the ocular arteries and retrobulbar space in patients suffering from ophthalmologic ailments of the vascular origin [7, 8, 9]. Available ophthalmologic literature explains amaurosis fugax most often as insufficiency of blood circulation

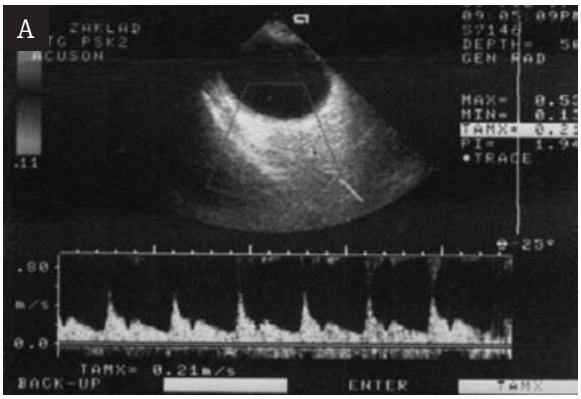

Figure 1 A. Doppler US – normal blood flow in ophthalmic artery (OA).

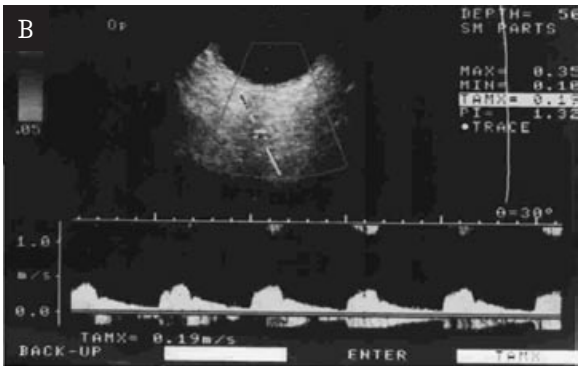

Figure 1 B. Doppler US – blood flow in OA – patient with transient blindness.

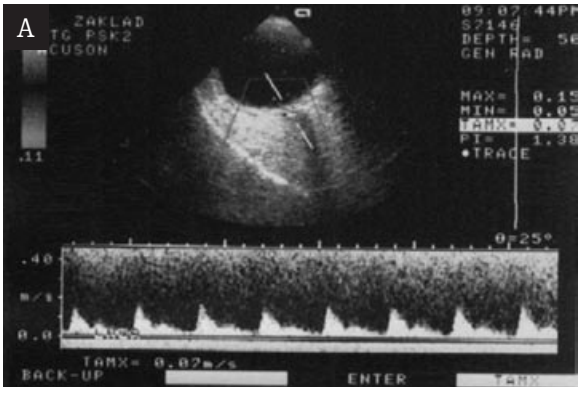

Figure 2 A. Doppler US – normal blood flow in central retinal artery (CRA).

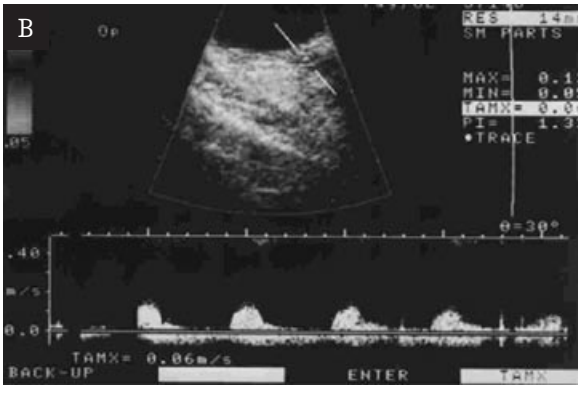

Figure 2 B. Doppler US – blood flow in CRA– patient with transient blindness.

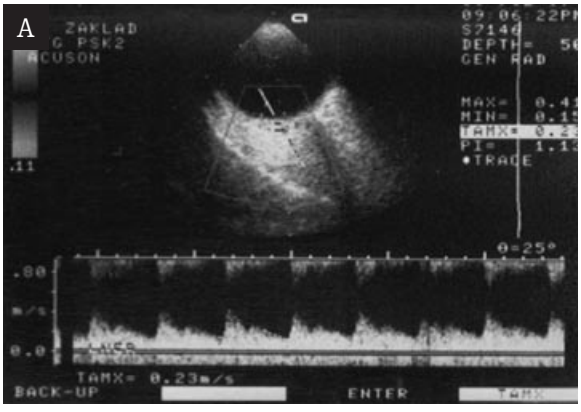

Figure 3 A. Doppler US – normal blood flow in short posterior ciliary artery (SPTCA).

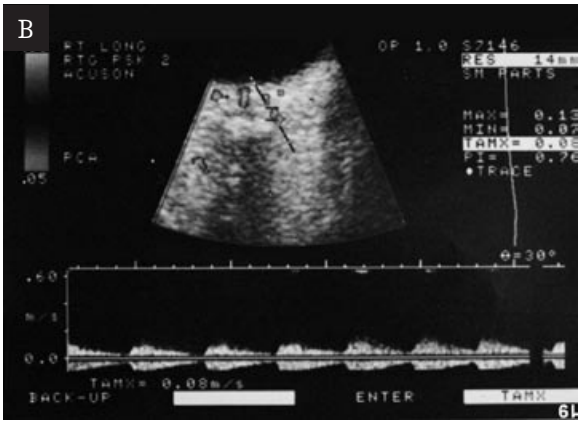

Figure 3 B. Doppler US – blood flow in SPTCA – patient with transient blindness.

in carotid vessels. Blindness is usually described as transient, periodically recurrent, though it might be accompanied by neurological and cardiological symptoms. In patients with amaurosis fugax characteristic pathological lesions of optic nerve and retinal vessels may occur in eye fundus [10, 11].

Unlike amaurosis fugax, transient monocular blindness (TMB) in the course of primary vasospastic syndrome is a frequent ailment in ophthalmic practice. TMB symptoms are recognized in patients generally considered to be healthy, with no morphologic changes in their carotid arteries. Moreover, these patients had neither general nor ocular diseases and their intraocular pressure did not exceed 21 mm Hg. Common features of these patients were: low arterial blood pressure, cold hands, periodic headaches, migraine and asymptomatic ischemic heart disease. The above mentioned symptoms, known as primary vasospastic syndrome, most often occurred in response to cold or emotional stress [12, 13, 14, 15]. Accessible literature mentions that the described symptoms are caused by a vascular spasm, also known as functional, defined as a vasospasm

recurring without a clearly explainable cause [15, 16]. The underlying phenomenon concerns the narrowing of vascular lumen due to the contractions of vascular smooth musculature [17]. Although there are many etiologic factors causing the vasospastic syndrome, its pathogenesis remains uncertain. It is believed that vascular spasm etiology is multi-factorial and the factors of neural, humoral and local nature are at study. The substances responsible for vessel diameter, like endothelin-1, nitric oxide, prostaglandins, serotonin, histamine, and others are suspected to be involved. Secondary vascular spasm may be associated with other disease entities of an inflammatory and autoimmune origin, such as Raynaud syndrome, Prinzmetal angina, multiple sclerosis, systemic lupus erythematosus, antiphospholipid syndrome, rheumatoid arthritis, giant cell arteritis, Behcet's disease, migraine syndrome, anterior ischemic neuropathy, glaucoma etc. [12, 15, 16, 18, 19]. The blood flow in eyeball arteries depends mainly on perfusion pressure. Additional factors affecting the volume of vascular flow are vascular resistance and blood viscosity. Arterial hypotension is associated by the lowering of perfusion pressure. This and other factors responsible for alteration of blood rheological properties cause the slowing down of both ocular blood flow velocity and resistance parameter. As a result of these changes dysregulation response as a constriction following dilatation of the vessel is observable, at the same time autoregulation mechanisms are not disturbed. Similar vascular derangements, despite their different nature, are associated with some ophthalmologic diseases, such as: anterior ischemic optic nerve neuropathy or glaucoma [13, 15, 18, 19].

Some authors imply that patients with primary vasospastic syndrome have an inborn tendency for vascular spasm, as well as lack of vasodilatation response in ocular microcirculation [20]. Additionally, the literature delivers that the vasospasm syndrome occurs more frequently in women than in men and is more common in young and middle-aged people [20]. Subsequently, our studies were similar to the literature data; most of the examined patients were women, 66.3%. The average age of the patients in the study group was 47.31 years. Ophthalmologic clinical symptoms of transient blindness caused by vascular spasm did not differ from the flow disturbances in internal carotid arteries. Blindness episodes were short lived and self limited and they appeared as scotomas or the darkening of the visual field. Clinical symptoms occurred in both eyes, but most frequently only one eye was involved and the symptoms were occasionally accompanied by migraine headaches [20].

In the studied group no thrombosis or microembolic changes in carotid arteries were found [7, 9, 11, 21]. The results of our study confirmed the occurrence of haemodynamic disturbances in the eyeball arteries in patients with past episodes of transient blindness, which were most likely associated with vascular spasms. Arterial hypotension, lack of functional and morphologic changes in carotid arteries, absence of other ophthalmologic or systemic symptoms in the majority of cases confirmed our hypothesis.

The statistically significant decrease of vascular pulsation and resistance indices measured in the ocular arteries, was probably connected to the secondary dilatation of the vessels, following the constriction of precapillary vessels, as an opposite response to low perfusion pressure in blood. On the contrary, in glaucoma a different disturbance mechanism in arterial perfusion of an eye occurs while autoregulation mechanism fails. The statistically significant lowering of parameters of systolic velocity in ocular arteries in our patients is probably a result of inborn propensity to vascular spasm. The changes of velocity were most often visible in the small arteries of retina and choroidea. In transient blindness episodes, the dilatation of the arterial vessels and the widening of ocular vascular bed probably occurs as a consequence of the preexisting narrowing of the vessels and may attest a phenomenon of vascular dysregulation, while autoregulation mechanisms remain intact [12, 16, 18].

The results of this study may indicate that the vital factors causing pathogenesis of transient monocular blindness are due to the disturbances in the haemodynamics of the circulation in eyeball arteries, mainly in CRA and SPTCA. Evaluation of blood flow in the ocular and carotid arteries is a key element in diagnosis of the transient blindness in middle aged patient group with accompanying arterial hypotension.

Conclusions

1. The statistically significant diminishing of systolic blood flow velocity parameters, pulsation and resistance indices in eyeball arteries may indicate disturbances in ocular circulation in patients with transient monocular blindness in primary vasospastic syndrome.

2. Color Doppler ultrasound is an effective and helpful method in the assessment of haemodynamic disturbances in eye circulation in patients with transient blindness symptoms.

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