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Evaluation of blood flow in the ophthalmic artery and central retinal artery in children with retinopathy of prematurity

Ocena przepływu krwi w tętnicy ocznej i w tętnicy środkowej siatkówki u dzieci z retinopatią wcześniaków

Anna Niwald¹, Mirosława Gratek²

¹ Department of Paediatric Ophthalmology, Chair of Paediatrics, Medical University of Łódź, University Hospital No 4 in Łódź
Head of Department: Anna Niwald, MD, PhD

² Department of Ophthalmology, Children's Memorial Health Institute in Warsaw
Head of Department: prof. Mirosława Gratek, MD, PhD

Summary:

Purpose: To evaluate blood flow parameters in the ophthalmic artery and central retinal artery in children with retinopathy of prematurity (ROP).

Material and methods: The study comprised 57 premature children born between 24 and 33 weeks of gestation, with birth weight from 600g to 1660g, including 42 preterm children with retinopathy in stage 1, 2, 3 and 3 „plus” and 15 preterm children without retinopathy. Color Doppler ultrasonography (USG-CD) was used to measure in the studied vessels maximal systolic velocity (Vmax), end-diastolic velocity (Vmin) and resistance index (RI).

Results: Statistically significantly ($p < 0.05$) higher values of Vmax were seen in the ophthalmic artery and central retinal artery in preterm children with retinopathy in stage 2 and 3, as compared with other children. In preterms with dilation and tortuosity of posterior blood vessels in stage 3 „plus” ROP, Vmax in both studied vessels was lower and was comparable to that in stage 1 ROP and in children without retinopathy. RI in the ophthalmic artery in children with ROP in stage 2 and 3 was statistically significantly higher ($p < 0.05$) from its values seen in other groups, and for the central retinal artery RI did not differ statistically significantly.

Conclusions: The conducted USG-CD measurements revealed that in children with retinopathy of prematurity haemodynamic parameters of blood flow in the ophthalmic artery and central retinal artery differ in relation to disease stage of advancement, and in relation to the status of blood vessels in the eye fundus. The clinical implications of these results, however, need to be confirmed in long term studies, in order to determine the sensitivity, specificity and repeatability of this method, as well as to establish the diagnostic standards.

Słowa kluczowe:

retinopatia wcześniaków, kolorowa ultrasonografia dopplerowska, przepływ krwi w tętnicy ocznej, przepływ krwi w tętnicy środkowej siatkówki.

Key words:

retinopathy of prematurity, color Doppler ultrasonography, blood flow in the ophthalmic artery, blood flow in the central retinal artery.

Color Doppler ultrasonography (USG-CD) has been playing an increasing role in the diagnostics of a number of ophthalmic diseases. It is useful in understanding the pathomechanism of these diseases and monitoring treatment results. The application of USG-CD has enabled registering changes in the blood flow in orbital arteries in the course of glaucoma, ischaemic neuropathy, central retinal artery occlusions, thrombotic lesions in retinal veins, neoplastic tumours, diseases of the orbit of vascular origin, and systemic disease such as diabetes and hyperthyroidism (1, 2, 3, 4).

The current knowledge on haemodynamics of the eye vessels in the course of retinopathy of prematurity (ROP) is relatively small. The stages of the disease and changes in the retina characteristic for particular stages determine the treatment. Extraretinal neovascularization, dilation and tortuosity of posterior retinal vessels („plus” disease) and development of the pre-

threshold or threshold retinopathy of prematurity are indications for intervention (5, 6). However, our knowledge on changes in haemodynamic parameters in the orbital vessels that accompany these changes is limited.

The aim of study was evaluation of blood flow parameters in the ophthalmic artery and central retinal artery in children with retinopathy of prematurity. Color Doppler ultrasonography was used to measure in the studied blood vessels systolic and end-diastolic velocity and resistance index in stage 1, 2, 3 and 3 „plus” of the disease. Basing on the results, we determined whether there are significant differences in the haemodynamic parameters values in the ophthalmic artery and central retinal artery in preterm children with various stages of retinopathy.

The study had been approved by the Bioethical Committee of the Medical University of Łódź.

Material and methods

USG – CD measurements were performed in 57 premature children born between 24 and 33 weeks of gestation (hbd), with birth weight from 600g to 1660g, treated in the Intensive Care Unit and Outpatient Clinic of Ophthalmology, University Hospital No 4 in Łódź, Medical University of Łódź, between January 2003 and May 2005. Ophthalmic examination of preterm children was conducted according to current standards. If active stage of retinopathy of prematurity was detected, the stage of advancement of retinal lesions and presence of the "plus" sign were established according to the International Committee for the Classification of ROP criteria (7). USG-CD was performed in 42 preterm children with retinopathy born between 24 and 32 weeks of gestation with birth weight from 600g to 1500g. In all children symmetrical advancement of ROP in both eyes was seen. In 13 children (mean gestational age 28.6 ± 2.72 hbd, mean birth weight 1018.5 ± 269.6 g) ultrasound examination was done in stage 1 of ROP. In 14 preterm children (mean gestational age 27.1 ± 1.46 hbd, mean birth weight 927 ± 257.2 g) USG-CD was performed in stage 2 of ROP. In 9 children (mean gestational age 27.0 ± 1.7 hbd, mean birth weight 878.1 ± 223.3 g) ultrasound examination was done in stage 3 of ROP, where development of extraretinal neovascularization within the ridge was not accompanied by the "plus" sign (in 4 cases blood vessels in the posterior fundus were distorted). In the remaining 6 preterm children with retinopathy (mean gestational age 26.9 ± 1.9 hbd, mean birth weight 890.0 ± 1.9 g) ultrasound imaging was done in stage 3 "plus" („plus" disease), with the presence of dilation and tortuosity of the posterior retinal vessels. USG-CD measurements were also performed in 15 preterms without ROP, born between 24 and 33 hbd (mean gestational age 28.4 ± 2.35 hbd) with birth weight between 600 and 1660 g (mean birth weight 1113.0 ± 2817 g), in whom ophthalmoscopy revealed only peripheral area of immature avascular retina.

In children with retinopathy in stage from 1 to 3 „plus", USG-CD examination was performed in 34.4 ± 2.29 , 35.3 ± 2.09 , 36.1 ± 1.64 i 37.3 ± 1.78 weeks of corrected age (corrected age = gestational age + postnatal age) respectively,

Preterm children Wcześnieki	Vmax (cm/s)	Vmin (cm/s)	RI
stage 1 ROP stadium 1 ROP	26.76 ± 1.27	5.3 ± 0.49	0.81 ± 0.01
stage 2 ROP stadium 2 ROP	29.71 ± 1.61	5.19 ± 0.91	0.83 ± 0.03
stage 3 ROP stadium 3 ROP	30.97 ± 2.14	5.38 ± 0.46	0.83 ± 0.03
stage 3 „plus" ROP stadium 3 „plus" ROP	27.5 ± 1.22	5.06 ± 0.66	0.80 ± 0.03
No ROP Wcześnieki bez ROP	27.4 ± 2.66	5.04 ± 0.74	0.80 ± 0.04

Tab. I. Blood flow parameters in the ophthalmic artery in the examined preterm children.

Tab. I. Parametry przepływu krwi w tętnicy ocznej u badanych wcześniaków.

and in preterms without retinopathy in 34.6 ± 1.88 week of corrected age.

USG-CD measurements were performed using the apparatus ATL 3500 HDI, with a wide-range linear ultrasound probe operating within the frequencies 7-12 MHz. Premature children were examined during normal sleep, through closed lids, using emission medium and typical technique. Ultrasound measurements were performed before ophthalmic examination of the eye fundus, and in preterms with retinopathy qualified for laser therapy before the procedure, to eliminate the effect of the eye ball compression on the blood flow in vessels. The blood flow spectrum in the ophthalmic artery was registered 8-10 mm from the posterior pole of the eye. In the central retinal artery the blood flow was evaluated within the optic nerve, 1-3 mm from its head. The measurements included maximal systolic velocity (Vmax), end-diastolic velocity (Vmin) and resistance index (RI). USG-CD measurements were repeated three times in each preterm child in both eyes. Further analysis was done on the means of the measured parameters.

Statistical analysis was performed using computer programme Statgraphics Plus. The studied values were presented as means \pm standard deviation. The normality of distribution was checked with the Shapiro-Wilk test. Means were compared using univariate variance analysis (ANOVA), and t-Student test was used for unpaired groups.

Results

The analysis of blood flow parameters in the ophthalmic artery showed statistically significantly higher ($p < 0.05$) values of Vmax in children in stage 2 and 3 ROP, as compared with other studied groups. In stage 3 „plus" ROP Vmax was similar to that seen in preterm children in stage 1 ROP and without retinopathy. Resistance index was highest in stage 2 and 3 ROP and differed statistically significantly ($p < 0.05$) from the values obtained in other preterm children. The values of Vmin were similar in all the analysed groups (tab. I).

In the central retinal artery, similarly to the ophthalmic artery, Vmax in stage 2 and 3 ROP was statistically significantly higher ($p < 0.05$) than in other groups of examined children. In preterm

Preterm children Wcześnieki	Vmax (cm/s)	Vmin (cm/s)	RI
stage 1 ROP stadium 1 ROP	7.73 ± 0.37	2.55 ± 0.15	0.67 ± 0.04
stage 2 ROP stadium 2 ROP	8.84 ± 0.52	2.70 ± 0.45	0.68 ± 0.02
stage 3 ROP stadium 3 ROP	8.94 ± 0.82	2.90 ± 0.28	0.67 ± 0.05
stage 3 „plus" ROP stadium 3 „plus" ROP	8.0 ± 0.68	2.71 ± 0.34	0.66 ± 0.02
No ROP Wcześnieki bez ROP	7.84 ± 0.45	2.56 ± 0.26	0.66 ± 0.03

Tab. II. Blood flow parameters in the central retinal artery in the examined preterm children.

Tab. II. Parametry przepływu krwi w tętnicy środkowej siatkówki u badanych wcześniaków.

children with dilation and tortuosity of the retinal vessels in stage 3 „plus” ROP Vmax decreased to the values comparable with that in children without retinopathy and in stage 1 ROP. Vmin was similar in all analysed children, and only in stage 3 ROP was statistically significantly higher ($p < 0.05$) as compared with stage 1 ROP and with preterms without ROP. The value of RI was highest in children with stage 2 ROP, but the differences between the studied groups were not statistically significant (tab. II).

Discussion

USG-CD allowed for safe evaluation of blood flow parameters in the ophthalmic artery and central retinal artery in children in the course of retinopathy of prematurity. There were no side effects during the examination or afterwards. USG-CD was conducted during normal sleep, and the examination was discontinued when the child's movements became too rapid. It made the time of examination much longer, but eliminated possible influence of general anaesthesia on the haemodynamics of orbital vessels (8). We are aware of the fact that conclusions based on quantitative analysis of the blood flow spectrum in orbital vessels in preterm children should be drawn carefully, due to possible physiological variability of the studied parameters, depending on the maturity of the child. Also, general clinical condition of the preterm child and hypoxia may affect the haemodynamics of small blood vessels (9,10,11). Similar effect may be due to administration of some drugs (12). In our study we attempted to limit the effects of potential additional factors on blood flow in orbital arteries, conducting USG-CD in preterm children in stable clinical condition.

Evaluation of the haemodynamic status of the orbital blood vessels in children with retinopathy of prematurity revealed statistically significant differences in Vmax in various stages of advancement of the disease, both in the ophthalmic artery and in the central retinal artery. Interpreting these results, however, requires taking into account the retinal vessels pattern in various stages of ROP, and in particular their diameter.

USG-CD does not enable measurements of the cross-section of the studied vessels, however obtained haemodynamic parameters of the central retinal artery may be correlated with ophthalmoscopic picture.

We found statistically significantly higher values of Vmax in central retinal artery in preterm children with retinopathy in stage 2 and 3, as compared with children in stage 1 and children without retinopathy. Assuming that the diameter of vessels was comparable, it may be stated that in stage 2 and 3 ROP blood flow is significantly increased. In stage 3 „plus” ROP Vmax was statistically significantly lower than in stage 2 and 3, but the diameter of vessels significantly increased, which affected blood flow.

RI in the ophthalmic artery in children with ROP in stage 2 and 3 was statistically significantly higher ($p < 0.05$) from its values seen in other groups, and for the central retinal artery RI did not differ statistically significantly. USG-CD measurements in the ophthalmic artery showed that Vmax was highest in stage 2 and 3 of ROP, similarly as for the central retinal artery, but resistance index in those stages also increased. It may have been due to changes of the diameter of the ophthalmic artery.

The results of Holland et al. (13) of USG-CD measurements in the central retinal artery of preterms (similar to our results,

but not differing in a statistically significant way) indicate that both the eyes with retinopathy in the absence of „plus” disease, and with „plus” disease, show increased blood flow. The authors claim that in children with any degree of ROP excluding „plus” disease Vmax values are higher than in children without retinopathy. In preterms with ROP stage 3 „plus” the values of Vmax are lower and comparable to those in children without ROP, but the diameter of blood vessels is higher. Thus, blood flow to the eye, which depends on mean velocity of blood flow and vessel cross-section area, will be increased in all children with ROP, as compared with preterms without retinopathy.

The studies conducted in preterm children by Harris et al. (14) did not show statistically significant differences in maximum blood flow in the central retinal artery. The authors, however, similarly to Holland et al. (13), evaluated blood flow parameters in two groups of children with ROP differing by the presence or absence of „plus” disease. In our study the stage of advancement was also taken into account, as statistically significant increase of Vmax was not seen in all children with ROP without the „plus” sign, but only in children with stage 2 and 3 ROP. In stage 3 „plus” ROP we found decrease of Vmax, which was also demonstrated by Harris et al. (14) and Holland et al. (13).

Conclusions

Color Doppler ultrasound is a non-invasive technique allowing evaluation of haemodynamic parameters of blood flow in the orbital vessels in children with retinopathy of prematurity in various stages of disease advancement. The clinical implications of these results, however, need to be confirmed in long term studies, in order to determine the sensitivity, specificity and repeatability of this method, as well as to establish the diagnostic standards.

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Adres do korespondencji (Reprint requests to):
Dr n. med. Anna Niwald
Klinika Okulistyki Dziecięcej KP UM,
ul. Sporna 36/50,
91-738 Łódź

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