

POSSIBILITY OF EARLY DIAGNOSIS OF COMPLICATIONS OF OPTIC NERVE NEURITIS IN PATIENTS WITH ANTERIOR UVEITIS ACCORDING TO COHERENT TOMOGRAPHY OF THE EYE ORBIT

A.V. Kovtun^{1*}, L.V. Venger², N.I. Khramenko³

¹Department of Radiation Diagnostics, Therapy and Oncology Odessa National Medical University by N.I. Pirogov, Odessa, Ukraine

²Department of Ophthalmology Odessa National Medical University by N.I. Pirogov, Odessa, Ukraine

³Department of Visual Function Research Methods, PhD MD: SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine", Odessa, Ukraine

Abstract. *The aim of the study was to determine the possibility of early diagnosis of optic neuritis in patients with anterior uveitis by determining the diameter of the optic nerve using computed tomography of the orbit. The examination and treatment included 114 patients with anterior uveitis and 36 patients with anterior uveitis complicated by optic neuritis. A standard ophthalmological examination was performed and also ocular electrical impedance studies (relative ocular pulse blood filling and ocular blood flow velocity, determination of the diameter of the optic nerve by coherence tomography) were performed. An increase in the diameter of the optic nerve in eyes with anterior uveitis complicated by neuritis by 7.2, 11.5 and 18.3% was shown relative to paired eyes when measured retrobulbar, in the middle section and in the orbital region. An increase in volumetric pulse blood filling was found in anterior uveitis in the diseased eye relative to the paired eye, especially pronounced in the presence of neuritis (65.4%). The obtained data indicate the possibility of predicting the development of neuritis against the background of anterior uveitis with an increase in the diameter of the optic nerve (according to computed tomography) and the presence of a vascular reaction in the focus of inflammation (according to the results of ocular electrical impedance studies).*

Keywords: Anterior uveitis, computer tomography of the orbit, hemodynamics of the eye, optic nerve neuritis

1. INTRODUCTION

Reduced vision and blindness in inflammatory diseases of the choroid develop more often in young people of working age, which determines the social and economic significance of this problem [1]. According to B. Trusko, up to 30 thousand new cases of blindness due to uveitis are registered annually, which ranks fifth or sixth among all causes of blindness in the United States [2]. As a result of epidemiological studies, which characterize, of the pathological process, it was found that anterior uveitis is 61%, intermediate – 12.2%, posterior – 14.6%, panuveitis, 9.4%; [3]. It is not possible to establish the etiology of uveitis in 38–40% of cases, diagnostic tests carried out for this purpose, which defines these cases as idiopathic uveitis [4]. Early diagnosis of the development of the inflammatory process in anterior uveitis is extremely important for the timely treatment and prevention of possible complications arising as a result of concomitant optic neuritis. However, the diagnosis of optic nerve damage in patients with anterior uveitis is complicated by such manifestations of inflammation as exudate in the anterior chamber, vitreous humor, in the pupil area, as well as posterior synechiae, making it

difficult to study the fundus [5]. In cases where fundus examination is not possible due to the opacity of the orbit can assist in the diagnosis of neuritis in anterior uveitis. Based on our earlier data, we believe that a comparative assessment of the diameter of the optic nerve retrobulbar and at the entrance to the orbit based on the results of computer tomography (CT) of the orbit in the diseased and healthy eye may be promising in this case, as well as features of local blood circulation in the choroid of a diseased and healthy eye [6, 7]. The aim of this study was to determine the possibility of early diagnosis of optic neuritis in patients with anterior uveitis by determining of the diameter of the optic nerve using CT of the orbit.

2. MATERIAL AND METHODS

The study involved 150 patients with idiopathic anterior uveitis who were undergoing research and treatment in the Department of inflammatory Eye Pathology The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine: 94 men and 56 women, 300 eyes, age from 18 (1 patient) to 83 (1 patient) with the value of median 36.5 years in all patients, the process was

* khramenkon@gmail.com, kvnkonovalova@gmail.com

monolateral. The studies were carried out with informed consent of patients in accordance with the Declaration of Helsinki. Anterior uveitis was diagnosed according to the International classification of the 43-rd World Health Assembly 1990-2020 based on recommendation Standardization of Uveitis Nomenclature Working Group, what classifies according to anatomical localization, in which the primary site of inflammation occurs, pathomorphology, type of uveitis course, activity of inflammation [8]. On the basis of a comprehensive diagnosis, the patients were divided into 2 groups: anterior uveitis and anterior uveitis, complicated by optic neuritis. Visual acuity of patients was determined by the classical method of measuring acuity in subjects with letters optotypes of Russian alphabet or Landolt Cs symbols, like Snellen acuity chart, performance at 6 meters. Best-corrected visual acuity was used. Patients underwent ophthalmoscopy, biomicroscopy, intraocular pressure, perimetry (Visual Field Examination manual kinetic testing using a Goldman perimeter) and automated static perimetry (Humphrey). In addition, they underwent electrical impedance studies: ophthalmic rheography (ORG), with Reocom, the computerized impedance device, included measurements of relative ocular pulse blood filling (OPBF, expressed as RQ, ‰ - rheographic coefficient), vascular tone (expressed as α/T (%) percentage index) and ocular blood flow velocity (V, Ohm/sec) - change in the impedance of the eye per unit of time. Electrical impedance studies were carried out in Visual Function Research Laboratory of the Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine. Orbital CT was done on a 16 channel multislice tomograph Philips Brilliance. We relied on the data of article about the possibilities of CT in studying the optic nerve diameter in traumatic brain injury [9]. CT was chosen because some patients had metal foreign bodies in the form of implants and stents, claustrophobia and diagnosis by MRT is impossible in such cases. According to CT data, the difference in the diameter of the patient's healthy and diseased eyes was determined. Study eyes were treated as per the methodology protocol approved by the ethical committee of the Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine in 2012 and by the National Academy of Medical Science of Ukraine. The basic protocol for the diagnosis and treatment of patients with anterior uveitis is based on the joint guidelines of the Infectious Diseases Society of America and on Society for Health care Epidemiology of America on the management of patients of various age groups with infection (published in March 2018). As a treatment, patients received antibiotics, non-steroid anti-inflammatory drugs, immunosuppressants, corticosteroids, biological modulators of the immune response. The inclusion criteria for the study were: patients with monolateral anterior uveitis (men and women aged 18 and over). Exclusion criteria were history of patients with diabetes mellitus, acute infectious, viral, cardiovascular diseases, circulatory disorders in the main vessels of the eye, with previous eye surgeries, pregnant women. Statistical analyses were conducted using Statistic 10.0 (Stat Soft, Tulsa, OK, USA) software. The parametric Student test was

used for unpaired samples. The level of significance $p \leq 0.05$ was assumed. Data are presented as mean (with standard deviation (SD) in parentheses).

3. RESULTS

Analyzing the clinical date of patients taking into account the group of persons with complications of the course of anterior uveitis with optic neuritis, the following was revealed. Optic neuritis against the background of anterior uveitis occurred in 24% of cases in the observed group (that is, in 36 people out of 150). At the same time the peripheral form of optic neuritis was in 2 people (5.6% of all patients with neuritis), axial - in 3 people (8.3%), transversal - in 31 people (86.1%). In all 114 patients with uveitis without signs of neuritis, the course of the disease was characterized as acute (less than 3 months). When uveitis was complicated by neuritis in 23 cases (63.9%), the process was chronic (lasting more than 12 months). The visual acuity in the healthy eye in the entire group of patients was quite high (from 0.6 to 1.0). On the diseased eye in individuals with uncomplicated uveitis, the same visual acuity was in 89 people, and 25 cases in fell within the range from 0.3 to 0.5. With the complication of anterior uveitis by neuritis, high visual acuity was observed in one patient, a decrease in this indicator to 0.3 to 0.5 occurred in 22 people, in the remaining 13 patients, the visual acuity values were reduced to 0.12 to 0.25 (36.1%). Intraocular pressure in all cases was within the normal range, constituting 18.0 – 21.0 mm Hg. Based on the data of the study of the hemodynamics of the eyeball, an increase in both the indicator of volumetric pulse blood filling and the rate of volumetric blood filling of the diseased eye in patients with optic neuritis on the background of anterior uveitis, compared with uncomplicated uveitis, was revealed. Thus, the revealed changes for the indicator of volumetric pulse blood filling are 63.4%, 5.38 (0.51)‰ with uveitis complicated by neuritis and 3.29 (0.19)‰ with uncomplicated uveitis respectively (Fig. 1).

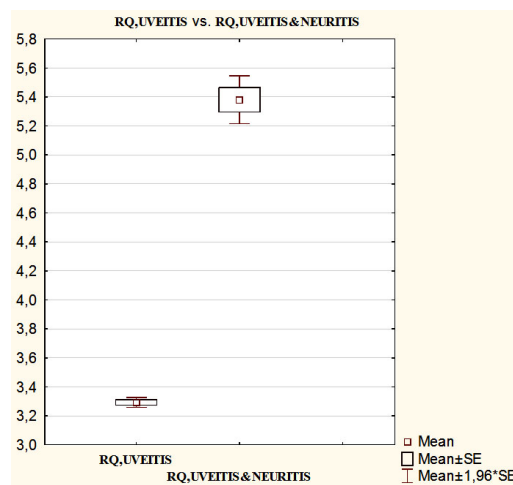


Figure 1. Indicators of volumetric pulse blood filling of the diseased eye of patients with anterior uveitis without and complicated neuritis (RQ presented in ‰)

As for the rate of volumetric blood filling, in this case the differences are less pronounced (36.0%), amounting to 2.18 (0.30) Ohm/sec in uveitis complicated by neuritis and 1.60 (0.11) Ohm/sec in uncomplicated uveitis, respectively, but also significantly ($p=0.000$ in both cases) authentically (Fig. 2).

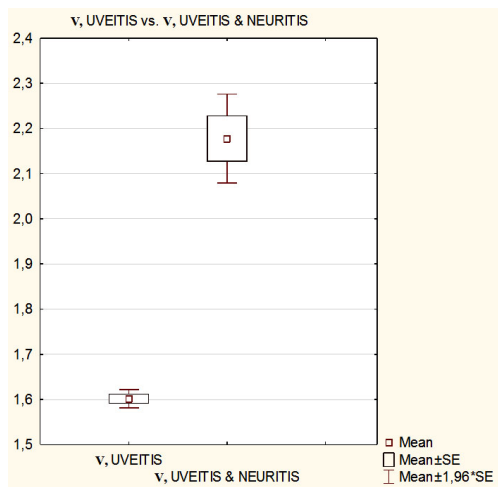


Figure 2. Indicators of the rate of volumetric blood filling of the diseased eye of patients with anterior uveitis without and complicated neuritis (V presented in Ohm/s)

Clinically, the course of anterior uveitis was accompanied by a mixed injection of conjunctival vessels, the presence of precipitates on the corneal endothelium, exudate in the anterior chamber, the formation of posterior synechiae, intense opacities in the vitreous body in the form of fibrosis. Fundus ophthalmoscopy in the acute period was difficult. Analysis of CT in determining the diameter of the optic nerve in the retrobulbar region, the middle section and at the entrance to the orbit showed that the values obtained are higher in the group of patients with neuritis against the background of anterior uveitis than in uncomplicated uveitis at all measurement points (Table 1).

Table 1. Changes in the size of the optic nerve diameter in patients with anterior uveitis complicated by neuritis, M (SD)

Diagnosis	Optic nerve diameter (mm)		
	retrobulbar	middle department	at the entrance to orbit
Anterior uveitis, n=114	6.13 (0.25)	4.33 (0.20)	4.22 (0.15)
Anterior uveitis, complicated by neuritis, n=36	6.43 (0.21)	4.60 (0.33)	4.95 (0.28)

The revealed changes are significant and are most pronounced at the entrance to the orbit, accounting for 17.1%.

We have also carried out a comparative analysis of indicators characterizing the blood filling of the eyes and the data for determining the diameter of the healthy and diseased eyes in the above groups. The data obtained indicate that the indices of blood circulation in the healthy eye in patients with neuritis against the background of anterior uveitis are significantly higher than those in those with uncomplicated uveitis. For volumetric pulse blood filling, these values are 3.25 (0.14) and 3.17 (0.18)%, respectively ($p=0.011$). Comparison of these indications in sick and healthy eyes in each of the studied groups revealed an increase in this indicator in the eyes involved in the pathological process. The differences were especially pronounced in the presents with anterior uveitis, amounting to 65.4%, while in uncomplicated uveitis – 3.9% ($p=0.000$ in both cases). A similar direction of changes was revealed for the rate of volumetric pulse blood filling. In healthy eyes, in the case of anterior uveitis complicated by neuritis, this indicator was significantly higher than in individuals with uncomplicated uveitis, amounting to 1.58 (0.05) and 1.52 (0.04) Ohm/sec ($p=0.000$). In diseased eyes this indicator was significantly higher than those in paired healthy eyes, while the difference was much more pronounced in the case of a complicated course of anterior uveitis, amounting to 37.8%, while in uncomplicated uveitis it was – 5.5% ($p=0.000$ in both cases). Comparative analysis of the data of measuring the diameter of the optic nerve in sick and patients with anterior uveitis without and with concomitant optic neuritis showed the following. The values of the corresponding indicators in paired eyes with uveitis without and with neuritis do not fluctuate significantly, amounting to 2.2, 4.8 and 0.8% when measured retrobulbar, in the middle section and in the orbital region respectively. As for the diameter of the optic nerve in patients on a diseased and healthy eye, in the presence of anterior uveitis without a confirmed diagnosis of neuritis, there are practically no differences between the corresponding values at any point of measurement. In patients with anterior uveitis complicated by neuritis, the diameter of the optic nerve is larger in diseased eyes by 7.2, 11.5 and 18.3% when measured retrobulbar, in the middle section and in the orbital region, making up 6.43 (0.21) mm, 4.60 (0.33) mm and 4.95 (0.28) mm. The differences between the diseased and the healthy eye in patients with complicated uveitis are significant ($p=0.000$ in all cases).

The study made it possible to assess the possibility of optic neuritis in patients with anterior uveitis by the difference in the diameter of the optic nerve in the paired and diseased eye when measured retrobulbar, in the middle section and at the entrance to the orbit with an increase in the studied indicator on the diseased eye. Our results are consistent with the data obtained during ultrasound examination of optic neuritis in elective and urgent cases, including in children [10-12]. In addition, the established fact of an increase in the volumetric pulse blood filling in patients with anterior uveitis in the diseased eye relative to a paired healthy eye, especially pronounced in the presence of neuritis, indicates the presence of a vascular reaction in the inflammation focus at the stage of vasospasm, arterial and venous stasis, which is confirmed by computer

data orbital tomography in relation to an increase in the diameter of the optic nerve and can be considered as one of the mechanisms of edema and the development of optic neuritis. Considering that in recent decades there has been a tendency to change the dynamics and outcomes of inflammatory diseases of the choroid, often leading to loss of visual acuity and disability of patients, this line of research is currently relevant and has an important social and economic significance.

5. CONCLUSION

1. The method of coherent tomography showed an increase in the diameter of the optic nerve in diseased eyes in persons with anterior uveitis complicated by optic neuritis by 7.2, 11.5 and 18.3% relative to paired (healthy) eyes when measured retrobulbar, in the middle section and in the orbital region, respectively, while in patients with anterior uveitis without complication, these changes were not detected. The data obtained suggest the possibility of predicting the development of neuritis as a complication in anterior uveitis by detecting an increase in the size of the optic nerve diameter in the diseased eye relative to those in the healthy one.

2. An increase in the indicator of volumetric pulse blood filling in patients with anterior uveitis in the diseased eye relative to the paired healthy eye, especially pronounced in the presence of neuritis, was found, amounting in this case to 65.4%.

3. The fact of the presence of a vascular reaction in the focus of inflammation at the stage of vasospasm, arterial and venous stasis can be considered as a mechanism for the occurrence of edema of the optic nerve, which is confirmed by the data of computed tomography of the orbit regarding the increase in the diameter of the optic nerve.

4. The importance of searching for ways of early detection of optic neuritis in patients with anterior uveitis lies in the possibility of timely treatment, as well as prevention of optic atrophy and chronicity of the pathological process.

Acknowledgements: *The paper is a part of the research done within the project "Optimization of diagnosis, treatment and prophylaxis of the development of degenerative and inflammatory diseases of the organ of vision. 0119U003575".*

The authors have no conflicts of interest to declare.

REFERENCES

1. I. F. Gutteridge, A. J. Hall, "Acute anterior uveitis in primary care," *Clin. Exp. Optom.*, vol. 90, no. 2, pp. 70–82, Mar., 2007.
<https://doi.org/10.1111/j.1444-0938.2006.00128.x>
PMID: 17311570
2. B. Trusko et al., "The Standardization of Uveitis Nomenclature (SUN) Project. Development of clinical evidence base utilizing informatics tools and techniques," *Methods Inf. Med.*, vol. 52, no. 3, pp. 259–265, 2013.

3. C. A. McCannel et al., "Causes of uveitis in the general practice of ophthalmology. UCLA Community-Based Uveitis Study Group", *Am J. Ophthalmol.*, vol. 121, no. 1, pp. 35–46, 1996.
[https://doi.org/10.1016/s0002-9394\(14\)70532-x](https://doi.org/10.1016/s0002-9394(14)70532-x)
4. T. Tsirouki et al., "A Focus on the Epidemiology of Uveitis", *Ocul. Immunol. Inflamm.*, vol. 26, no. 1, pp. 2–16, 2018.
<https://doi.org/10.1080/09273948.2016.1196713>
PMID: 27467180
5. D. Jee, K. S. Kim, W. K. Lee, S. Jeon "Clinical features of ocular toxocarasis in adult Korean patients," *Ocular Immunology and Inflammation*, vol. 24, no. 2, pp. 207–216, 2016.
<https://doi.org/10.3109/09273948.2014.994783>
PMID: 25564736
6. N. I. Khramenko, N. V. Konovalova, "The state of hemodynamics of the eye with optic neuritis" in *Abstracts of the Scientific and Practical Conference with International Participation "Filatov Memorial Lectures - 2019"*, Odessa, Ukraine, p. 128, 2019.
7. Н. И. Храменко, Н. В. Коновалова, Л. Н. Величко, А. В. Богданова, "Состояние гемодинамики глаза и иммунной системы при неврите зрительного нерва," *Точка зрения Восток-Запад*, вып. 2, стр. 91-93, 2019. (N. I. Khramenko, N. V. Konovalova, L. N. Velichko, A. V. Bogdanova "The state of the eye hemodynamics and the immune system in optic neuritis", *Point of View: East-West*, no. 2, pp. 91-93, 2019).
<https://doi.org/10.25276/2410-1257-2019-2-91-93>
8. D. A. Jabs, R. B. Nussenblatt, J. T. Rosenbaum, "Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop", *Am. J. Ophthalmol.*, vol. 140, no. 3, pp. 509-16, Sep. 2005.
<https://doi.org/10.1016/j.ajo.2005.03.057>
PMID: 16196117
9. А. В. Семенов, Н. В. Монаков, Е. И. Балханова, А. А. Разнобарский, Т. А. Мамонова, «Многослойная и компьютерная томография в диагностике смешанной травматической травмы мозга», *Журнал радиологии и ядерной медицины*, вып. 99 (3), стр. 119-124, 2018. (A. V. Semenov, N. V. Monakov, E. I. Balkhanova, A. A. Raznobarski, T. A. Mamonova, "Multislice computed tomography in the diagnosis of mixed traumatic brain injury", *Journal of Radiology and Nuclear Medicine*, vol. 99, no. 3, pp. 119-124, 2018).
<https://doi.org/10.20862/004676-2018-99-3-119-124>
10. P. Lochner, M. A. Leone, L. Coppo et al., "B-mode transorbital ultrasonography for the diagnosis of acute optic neuritis. A systematic review", *Clin Neurophysiol.*, vol. 127, no. 1, pp. 803-809, Jan. 2016.
<https://doi.org/10.1016/j.clinph.2015.05.005>
PMID: 26024983
11. P. Lochner, R. Cantello, F. Brigo et al., "Transorbital sonography in acute optic neuritis: a case-control study", *AJNR Am. J. Neuroradiol.*, vol. 35, no. 12, pp. 2371-2375, Dec 2014.
<https://doi.org/10.3174/ajnr.A4051>
PMID: 25034772
12. J. Badron, G. Y. Ong, "Bedside Transorbital Ultrasound in the Clinical Evaluation of Pediatric Optic Neuritis in the Emergency Department", *J Emerg Med.*, vol. 56, no. 4, pp. 417-420, Apr. 2019.
<https://doi.org/10.1016/j.jemermed.2018.12.042>
PMID: 30745196