UVEITIS COMPLICATED BY PHTHISIS BULBI: HEMODYNAMIC PARAMETERS IN THE PREDICTION OF ANTERIOR-POSTERIOR EYE SIZE REDUCTION

Panchenko M.V.[1], Khramova T.O.[2], Pavlyuchenko O.S.[3], Muzhychuk O.P.[3], Honchar O.M.[1], Panchenko H.Y.[1], Kitchenko I.V.[1]

[1]Kharkiv National Medical University, Kharkiv, Ukraine
[2]V.N. Karazin Kharkiv National University, Kharkiv, Ukraine
[3]Prof. L.L. Hirschman City Clinical Hospital No.14, Kharkiv, Ukraine

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ABSTRACT

Background. Phthisis bulbi is a serious complication of uveitis, causing vision loss and esthetic defects. Hemodynamic disorders can play an important role in the formation of this complication as a result of uveitis. We did not find data on predicting the progression of phthisis bulbi with a reduction in anterior-posterior size in the available literature.

Aim. To analyze the possibility of predicting the reduction in the anterior-posterior size of the eye with uveitis, complicated by phthisis bulbi, based on hemodynamic parameters

Materials and Methods. 33 patients aged 5–84 years, of them 19 male and 14 female patients, with unilateral endogenous uveitis, complicated by phthisis bulbi, were examined. 15 patients with uveitis complicated by phthisis bulbi, who had not received any treatment during this time, were examined in dynamics (for at least 1 year). All patients underwent Doppler ultrasound examination of the ophthalmic artery and short posterior ciliary arteries. In addition, all patients underwent biomicroscopic and tonometric examinations, ultrasound biomicroscopy, rheoophthalmography of eyeballs, A-scan and B-scan ultrasonography. The results of the examination of eyes with uveitis complicated by phthisis bulbi were compared with the results of the examination of paired (healthy) eyes of the same patients.

Results. We have developed a multiple regression model that allows us to predict a reduction in the anterior-posterior size of the eye with phthisis bulbi due to uveitis. The dynamics of the disease in 15 patients not taking any treatment for uveitis, has been monitored for more than a year. The prediction of phthisis bulbi progression was confirmed in 13 patients, which amounts to 86.7% ($p<0.05$).

Conclusions. We have proposed a model that allows predicting the progressive or stationary course of phthisis bulbi due to uveitis based on hemodynamic parameters.

Keywords: *infectious uveitis, noninfectious uveitis, phthisis bulbi hemodynamic disorders, anterior-posterior size of the eyeball.*

INTRODUCTION

Uveitis is an inflammatory disease of the uveal tract, in the pathogenesis of which the leading role is played by immunologic disorders [1–7]. Most uveitis (56.0% to 86.3%) causes complications [8–13]. Phthisis bulbi is one such serious complication of uveitis, causing vision loss and cosmetic defects.

Corresponding Author:
Panchenko Mykola Volodymyrovych – MD, MedSc, Professor; Professor at the Department of Ophthalmology, Kharkiv National Medical University.
Postal address: Ukraine, 61204, Kharkiv, Peremohy ave., 70, ap. 161.
E-mail: panchenko0802@gmail.com

The frequency of phthisis bulbi among all eye diseases according to the data of the tertiary center is 0.4% [14], and among patients with uveitis – 1.6% [15]. At the same time, among uveitis leading to significant visual impairment (0.1 or less) the frequency of phthisis bulbi is 19.0% [15].

Among patients blinded due to disease or injury, phthisis bulbi is diagnosed in 4.0–19.0% of cases [16–20].

Uveitis is the cause of 13.9–28.0% of phthisis bulbi [14; 15]; another 21.5–23.0% of cases are caused by infectious diseases [14; 15], and another 17.0% of patients are diagnosed with sympathetic ophthalmia [15].

In general, the proportion of phthisis bulbi as a cause of eyeball removal according to various

authors ranges from 11.7% to 27.0% [21–24]. After penetrating wounds, the proportion of phthisis bulbi as a cause of eyeball removal is 6.1–45.2% [25–27]. At the same time, according to Kaliki S. et al. (2019), phthisis bulbi and atrophy were an indication for enucleation in patients of working age (20–60 years) in 39.0% of cases [28].

The main factors in the pathogenesis of phthisis bulbi, according to researchers, are hypotonia, blood-ophthalmic barrier disorders and inflammation [29].

Hemodynamic disorders can play an important role in formation of this complication as a result of uveitis. It has been shown that ischemia of the anterior segment of the eye is a factor in the development of phthisis bulbi [30].

Researchers have studied the factors contributing to the development of phthisis bulbi after penetrating wounds [25]. We did not find any data on predicting the progression of phthisis bulbi with a reduction in anterior-posterior size in the available literature.

The aim of this work was to analyze the possibility of predicting the reduction in the anterior-posterior size of the eye with uveitis, complicated by phthisis bulbi, based on hemodynamic parameters.

Materials and Methods

33 patients with unilateral endogenous uveitis, complicated by phthisis bulbi, of them 19 male and 14 female patients, aged 5–84 years were examined. 15 patients with uveitis complicated by phthisis bulbi, who had not received any treatment during this time, were examined in dynamics (for at least 1 year).

All patients underwent Doppler ultrasound examination of the ophthalmic artery and short posterior ciliary arteries. Using this method, the maximum blood flow Velocity (V_{max}), minimum blood flow velocity, and Resistance index (R_i) are determined (compared with fellow eye and healthy subjects).

Becides, all of them were examined by rheoophthalmography of eyeballs (using the "Reo-Com" device). Using this method, the rheoophthalmography ratio, pulse volume blood flow, and minute volume blood flow were determined.

The Anterior-Posterior Size (APS) of the eyeball was determined by A-scan ultrasonography. In addition, all the patients underwent biomicroscopic and tonometric examinations, ultrasound biomicroscopy, and B-scan ultrasonography.

The results of the examination of eyes with uveitis complicated by phthisis bulbi were compared with the results of the examination of paired (healthy) eyes of the same patients.

Informed consent to participate in the study was obtained from all patients.

Results

We selected prognostically significant parameters, which can be used to determine the progression of phthisis bulbi in patients' eyes with uveitis.

Statistical processing of blood flow indices during Doppler ultrasound examination of the ocular artery, short posterior ciliary arteries (compared to the paired eye) was performed, such as:

- maximum blood flow velocity,
- minimum blood flow velocity,
- resistance index.

Statistical processing of rheophthalmologic parameters of blood flow (in comparison with the paired eye) was also performed:

- rheoophthalmography ratio,
- pulse volume blood flow,
- minute volume blood flow.

To build a multiple regression model, it is necessary to get rid of the effect of multicollinearity, i.e. to remove interdependent variables from the list of predictors. To do this, we first analyzed the correlations within the list of predictors, and then built and examined a linear multiple regression model.

According to the Pearson's correlation matrix, we determined relevant correlations that characterize the strong interdependence of predictors in the list of variables.

The results were confirmed by considering Spearman's correlations.

After that, regression results were calculated for the variable "anterior-posterior size in comparison with the paired eye".

It is shown that the obtained coefficients are insignificant, which indicates that simple linear regression is not applicable to describe these parameters.

Therefore, we applied a piecewise linear model. We used the quasi-Newtonian method of error minimization. The loss function was estimated by the least squares method.

Numerical test of independence of the residuals was performed using the Durbin-Watson test.

Several methods were applied to the multiple linear regression model: Standard with simultaneous inclusion of all variables in the model, Backward stepwise with exclusion and Forward stepwise with inclusion.

The presented model is the most statistically valid representation of the data and allows predic-

ting the development of anterior-posterior size change compared to the paired eye in uveitis.

The most significant of the analyzed hemodynamic parameters in progression of phthisis bulbi in patients with uveitis were minute volume blood flow, maximum blood flow velocity in the short posterior ciliary arteries and resistance index in the short posterior ciliary arteries.

Using these data, we developed a multiple regression model, which provides the possibility to predict the reduction in the APS of an eye with phthisis bulbi as a result of uveitis in comparison with the fellow eye. This mathematical model is described by the following equation:

$$y=A+0.00354\times x_1+0.015\times x_2+4.674\times x_3 \quad (1),$$

where:

y – is the estimated amount of reduction in the APS of the eye;

A – is a constant which presented formula represents the "initial" average reduction in the APS of the eye with phthisis bulbi due to uveitis, in the group of patients examined by us. It's equal to 4.64;

x_1 – is the disparity between the minute volume blood flow of fellow and diseased eyes

x_2 – is the disparity between maximum blood flow velocity in the short posterior ciliary arteries of fellow and diseased eye;

x_3 – is the disparity between resistance index in the short posterior ciliary arteries of fellow and diseased eyes.

The coefficient (k) represents progression of phthisis bulbi due to uveitis (in terms of the APS reduction compared to the paired eye) and is calculated by formula:

$$k=y/A \quad (1),$$

where:

y – is the estimated amount of reduction in the APS of the eye with phthisis bulbi due to uveitis (determined by the formula, mentioned above);

A – is a constant calculated from the average reduction in APS of the eye with phthisis bulbi due to uveitis in the cases under investigation (4.64).

If the value of the coefficient k=2.0 or more, we can predict a progressive course of phthisis bulbi (with a reduction in the APS of the eye by more than 1 mm per year), and if the value of the coefficient k is less than 2.0, a stable course of the disease is predicted (with a change in the APS of the eye by no more than 1 mm per year).

The dynamics of the disease in 15 patients with uveitis, complicated by phthisis bulbi has been monitored for more than a year. The prediction of phthisis bulbi progression was confirmed in 13 patients, which amounts to 86.7% ($p<0.05$). Patients did not receive treatment during the observation period.

The obtained data is illustrated by the following cases:

Case No.1.

A 61-year old patient was on inpatient treatment in the adult ophthalmologic department of Kharkiv Regional Clinical Hospital with the diagnosis of chronic recurrent uveitis in acute stage, phthisis bulbi OD. His examination results:

APS OD=20 mm,
OS=26 mm;
minute volume blood flow OD=543 mm³/min,
OS=2031 mm³/min;
V_{max} in short posterior ciliary arteries
OD=8 cm/s,
OS=13 cm/s;
R_i in short posterior ciliary arteries OD=0.57,
OS=0.60.

According to the proposed model, we calculated the reduction in APS of the eye in patient K.

Regression equation (1):

$y=4.64+0.00354\times x_1+0.015\times x_2+4.674\times x_3$

$y=4.64+0.00354\times 1488+0.015\times 5+4.674\times 0.03=$
$=10.12$ mm

$k=10.12/4.64=2.19$

Thus, the coefficient k=2,19 and k>2, which predicts a progressive course of phthisis bulbi of the eye in the patient.

The patient was offered a course of conservative therapy. However, due to family circumstances, the patient refused treatment.

This patient was examined a year later. Measurement of the eye APS was performed, and the following parameters were obtained:

OD APS=16.6 mm, OS APS=26.0 mm. Thus, the eye with phthisis bulbi decreased in size by 3.4 mm per year, which confirms the correctness of the prognosis.

Case No.2.

A 35-year-old patient was treated as an inpatient in the adult ophthalmologic department of Kharkiv Regional Clinical Hospital with the diagnosis of chronic recurrent uveitis in the acute stage, phthisis bulbi OD. His examination results:

APS OD=20.1 mm, OS=24.2 mm;
minute volume blood flow
OD=850.1 mm³/min,
OS=808 mm³/min;

V_{max} in short posterior ciliary arteries
OD=9.9 cm/s,
OS=14.7 cm/s;
R_i in short posterior ciliary arteries OD=0.69,
OS=0.69.

According to the proposed model, we calculated the reduction in APS of the eye in patient L.

Regression equation (1):

$y=4.64+0.00354\times x_1+0.015\times x_2+4.674\times x_3$

$y=4.64+0.00354\times(-42.1)+0.015\times 4.6+$
$+4.674\times 0=4.56$ mm

$k=4.56/4.64=0.98$

Thus, the coefficient k=0.98 and k<2, which predicts a stationary course of phthisis bulbi of the eye in this patient.

The patient was examined one year later. The eye APS was measured, and the following parameters were obtained: OD APS=20.0 mm, OS APS=24.2 mm.

The eye with phthisis bulbi decreased only by 0.1 mm during the year, which confirms the correctness of the prognosis.

Discussion

In terms of discussion of the obtained results, it should be noted that the pathogenetic factors of the occurrence of phthisis bulbi according to the researchers are hypotony, deranged blood-ocular barriers, and inflammation [29].

Coskun M. et al. [25], studying the factors that influence the development of phthisis bulbi after penetrating ocular wounds, concluded that the significant factors are the anatomical localization and size of the wound, concomitant pathologies of the anterior or posterior segment of the eye, as well as endophthalmitis due to trauma. However, those results cannot be extrapolated to patients with uveitis.

The development of phthisis bulbi due to severe ischemia of the anterior segment of the eye of various etiologies described in the literature [30; 31] indicates an important role of hemodynamic disorders in the pathogenesis of phthisis bulbi and indirectly corresponds with our results.

In the literature, we did not find a description of prediction models for progression of phthisis bulbi due to uveitis and reduction in APS.

Si S. et al. (2023) proposed a prognostic model for the development of phthisis bulbi after cosmetic injection of hyaluronic acid [30], based on the determination of the severity of anterior segment ischemia. According to the authors, anterior segment ischemia occurs as a complication of hyaluronic acid injection due to thrombosis of the terminal branches of the ocular artery. A prognostic model [30] can predict the long-term prognosis and the likelihood of subsequent development of phthisis bulbi through several dynamic assessments over a 6-month period. The authors state that patients with ophthalmoplegia at 1-month follow-up and persistent hypotony for 6 months are extremely likely to develop phthisis bulbi.

Our model allows predicting the progressive or stationary course of phthisis bulbi due to uveitis based on the ratio of minute volume blood flow, maximum blood flow velocity in the short posterior ciliary arteries and resistance index in the short posterior ciliary arteries of fellow and diseased eyes with the probability of correct prognosis 86.7%.

Limitations

We did not study the accuracy of the prediction in patients who underwent conservative treatment or surgical intervention.

The mathematical model was developed on the basis of 33 patients and shows a fairly high frequency of correct prognosis (86.7%), however, the constant A can be refined with an increase in the number of patients.

In this way, we have developed a mathematical model that provides the possibility to predict the reduction in the anterior-posterior size of the eye with uveitis, complicated by phthisis bulbi.

Conclusions

We have proposed a model that allows predicting the progressive or stationary course of phthisis bulbi due to uveitis based on hemodynamic parameters.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

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Consent for publication

All authors give their consent to publication.

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