ANNOTATION

of Phd thesis by Zhumageldiyeva Farida Erkulovna on the topic: **«Pathogenetic-oriented method of treatment of phacomorphic glaucoma»,** submitted for the degree of Doctor Philosophy (PhD) in the specialty 8D10103 – «Medicine»

Relevance of the research subject.

Glaucoma and age-related cataracts are the leading causes of blindness and low vision worldwide. While glaucoma reduces visual function to irreversible blindness, cataracts restore vision after appropriate treatment (*Global causes of blindness and distance vision impairment 1990–2020: a systematic review and meta-analysis / S. R. Flaxman, R. R. A. Bourne, S. Resnikoff [et al.] // The Lancet Global Health. – 2017. – Vol. 5. – № 12.*). Glaucoma is a large group of eye diseases characterized by elevated intraocular pressure that can lead to optic nerve atrophy (*Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis / Y. C. Tham, X. Li, T. Y. Wong [et al.]. // Ophthalmology. – 2014. – Vol. 121. – № 11. – P. 2081-2090*). It is divided into two groups: primary and secondary glaucoma. Phacomorphic glaucoma is one of the main types of secondary glaucoma, which develops due to a sharp swelling of the cortical layers of the lens in immature age-related cataracts (*Potop V. et al. Ultrasound biomicroscopy as a vital tool in occult phacomorphic glaucoma //Romanian Journal of Ophthalmology. – 2019. – T. 63. – №. 4. – C. 311.*). Age-related cataracts can progress from immature to mature, and can sometimes lead to the development of phacomorphic glaucoma. In a mature cataract, the lens is cloudy, therefore, there is no red reflex from the ocular fundus and is accompanied by a decrease in visual acuity to reversible blindness and low vision (*Егоров, Е.А. Национальное руководство по глаукоме / Е.А. Егоров. – М. 2019.: Геотар - Медиа, – С.75-78*). In immature cataracts, due to watering of the cortical layers, the thickness of the lens increases, creating closer contact between the iris and the anterior surface of the lens, which in turn leads to the development of pupillary block, which is accompanied by a sharp increase in intraocular pressure (*Keleş A. Evaluation of biometric parameters in phacomorphic glaucoma and mature cataracts / A. Keleş, E. Şen, U. Elgin // European Journal of Ophthalmology. – 2021. – Vol. 31. – № 3. – P. 1101-1106*).

Data on the worldwide prevalence of phacomorphic glaucoma are sparse, although it is more common in Asian countries. In India, for example, phacomorphic glaucoma is a serious problem, accounting for approximately 3.91% of all cataract surgeries (*Angra SK P. R. and G. S. Cataract induced glaucoma-an insight into management / P. R. and G. S. Angra SK // Indian J Ophthalmol. – 1991. – Vol. 39(3). – № 97. – P. 101*). Phacomorphic glaucoma is often associated with a lower socioeconomic class, perhaps because of unequal access to ophthalmic care and cataract surgery (*Ayub R. et al. Outcomes and Reasons for Late Presentation of Lens Induced Glaucoma: A Prospective Study //Ophthalmology Glaucoma. – 2021. – T. 4.*

– №. 5. – C. 504-511. Shrestha R., Godar M. S., Gurung S., et al. Lens induced glaucoma in a tertiary eye care centre in Western Nepal // Nepalese Journal of Ophthalmology. – 2019. – Vol. 11. – №. 2. – P. 145-151.).

Timely swollen lens extraction is the definitive treatment for phacomorphic glaucoma, which reduces intraocular pressure before the onset of acute glaucomatous optic neuropathy (*Moraru A. et al. Functional results of cataract surgery in the treatment of phacomorphic glaucoma //Romanian Journal of Ophthalmology. – 2017. – T. 61. – №. 3. – C. 202*). The prognosis of visual acuity in phacomorphic glaucoma depends on the duration of the disease and the level of intraocular pressure before surgery (*Khambati A., Syeda S., Tannir J. Expected vs. Actual Refractive Error in Patients Presenting with Phacomorphic Glaucoma //Investigative Ophthalmology & Visual Science. – 2019. – T. 60. – №. 9. – C. 1114-1114*)**.**

Nowadays the main risk factors for phacomorphic glaucoma are short axial length of the eye, shallower anterior chamber depth, and female gender in persons over 60 years of age (*Zhang N. et al. Prevalence of primary angle closure glaucoma in the last 20 years: a meta-analysis and systematic review //Frontiers in medicine. – 2021. – T. 7. – C. 624179*). However, the results of previous studies have been inconsistent and inconclusive. For this reason, there is currently no defined eye parameter on which to rely for the prediction of phacomorphic glaucoma. In addition, there are ethnic differences in eye parameters, making it difficult to generalize results across populations (*Kawamorita T. et al. Evaluation of ocular biometry in the Japanese population using a multicenter approach: Prospective observational study //Plos one. – 2022. – T. 17. – №. 7. – C. e0271814*). Generally, studies on this problem have been performed on small individual samples. Most studies have not noted the role of baseline lens size as a risk factor for phacomorphic glaucoma.

Biometric studies of eyes with phacomorphic glaucoma may explain why not all cases of age-related cataracts result in increased intraocular pressure and thereby help identify an eye at risk for developing phacomorphic glaucoma. Thus, this study aimed to identify risk factors for phacomorphic glaucoma in Almaty natives and improve surgical management of the disease.

The aim of the dissertation research is to determine the average bioparameters of the eyeball and risk factors for phacomorphic glaucoma in the native inhabitants of Almaty.

Research objectives.

1. To conduct a retrospective analysis of archival data of patients with phacomorphic glaucoma of the Central City Clinical Hospital of Almaty for five years (2015-2019).
2. To establish risk factors for the development of phacomorphic glaucoma in the native inhabitants of Almaty.
3. To determine the average bioparameter of eyeball in the natives of Almaty at the age of 40 years and older without ocular pathology.

4. To optimize the surgical treatment of phacomorphic glaucoma with intraoperative complications.

Object and subject of research.

The study was conducted in the eye department and outpatient clinic of the Central Clinical City Hospital in Almaty, Kazakhstan. This study was approved by the local ethical committee of the Kazakh National Medical University named after S.D. Asfendiyarov (Minutes of LEC meeting №12 (123) dated 22.12.2021.

The study was conducted in accordance with the international rules "Good clinical practice" (National Institute on Drug Abuse, 2017), as well as in accordance with the principles of the Declaration of Helsinki (Ethnic Principles of Medical Research with Human Subjects: approved by the 18th General Assembly of the WMA in Helsinki, Finland, June 1964 (last amended at the 64th General Assembly of the WMA in Fortaleza, Brazil, October 2013). 18th WMA General Assembly, Helsinki, Finland, June 1964 (last amended at the 64th WMA General Assembly, Fortaleza, Brazil, October 2013).

The study used archived medical records of patients diagnosed with phacomorphic glaucoma - 233, as well as 864 natives over 40 years of age, 15 patients with phacomorphic glaucoma.

The study consisted of four steps:

Step 1 - Retrospective analysis of patients diagnosed with phacomorphic glaucoma (n=233);

Step 2 - Retrospective case-control study to identify risk of phacomorphic glaucoma (main group n=71, control group n=311);

Step 3 - Cross-sectional study to establish mean ocular bioparameters in natives over 40 years of age without ophthalmopathology (n=864);

Step 4 - Optimization of surgical treatment of phacomorphic glaucoma (n=15).

At the first step the results of treatment of 233 patients with phacomorphic glaucoma, who received surgical treatment in the ophthalmology department of the Central City Clinical Hospital of Almaty from January 2015 to December 2019 were analyzed. Age, gender, ethnicity, duration of disease, comorbidities, preoperative and postoperative intraocular pressure, visual acuity before and after treatment, anterior and posterior eyeball size, anterior chamber depth, lens thickness, and surgery were recorded in all cases. Patients were divided by ethnicity into Kazakhs, Caucasians and other Asians. The total number of patients with phacomorphic glaucoma was 233. Of the total number of patients with phacomorphic glaucoma, Kazakhs made up 72.1% (168), Caucasians 15.9% (37), and other Asians 12% (28).

The second step used data scanned from the Medical Records of inpatients with phacomorphic glaucoma for five years: from 2015 to 2019 and age-related cataract for 2019. Patients with age-related cataracts were chosen as a control group because phacomorphic glaucoma always develops in eyes with age-related cataracts; therefore, choosing healthy control groups was not appropriate.

The final number of patients with facomorphic glaucoma included in this study was 71. From all cases with age-related cataract, 311 patients with complete medical record data were selected.

The inclusion criteria were patients with phacomorphic glaucoma in one eye and unilateral age-related cataract, of Kazakh ethnicity and with completed medical records indicating age, sex, preoperative intraocular pressure, anterior-posterior size, anterior chamber depth, and lens thickness. Patients with other eye diseases such as uveitis, retinal detachment, primary glaucoma, secondary glaucoma (except phacomorphic glaucoma), eye trauma, pseudophakic eye, anisometropia, and early ophthalmic surgery were excluded.

Facomorphic glaucoma was diagnosed when the following criteria were present: increased intraocular pressure above 30 mmHg, eyeball injection, corneal epithelial edema, shallow anterior chamber, moderately dilated pupil, and a swollen lens. Phacomorphic glaucoma differs from an acute attack of primary closed angle glaucoma in several characteristics. Patients with phacomorphic glaucoma mostly have a unilateral case, the presence of a swollen lens in the diseased eye, (as in an acute attack in the other eye) a shallow anterior chamber, and an open anterior chamber angle. In contrast, in an acute attack of occult-angle glaucoma, the anterior chamber angle is also closed in the paired eye. The main cause of phacomorphic glaucoma is pupillary block in the thickened opaque lens, and in acute angle-closed glaucoma, pupillary block occurs in the pre-existing narrow anterior chamber angle.

In this case intraocular pressure was measured using a Maklakov applanation tonometer (model NGM-2, 10 mg, Ocular Instruments Inc., Moscow, Russia). Gonioscopy was not performed due to corneal epithelium edema. The anterior-posterior eyeball size, anterior chamber depth, and lens thickness were measured 10 times using a 10 megahertz (MHz) A-scan biometric probe (A-scan plus, Accutome, USA) with aplanation after instilling 0.5% proparacaine hydrochloride (Alcaine Alcon-Couvreur, Puurs, Belgium); mean values were then estimated. These measurements were performed before cataract surgery and were determined from the medical records of an inpatient.

The eyes were divided into three groups. The first group (G1): patients with phacomorphic glaucoma (71 eyes), G2: control group of patients with age-related cataract (311 eyes) and G3: paired eyes of patients with phacomorphic glaucoma (71 eyes). A-scan eye parameters were compared between groups using binary logistic regression.

Third step: the cross-sectional study was conducted from October 2021 to May 2022 in the outpatient clinic of the Central City Clinical Hospital of Almaty. This study is a prospective study.

We sent out advertisements throughout the city of Almaty to conduct the study. We did not provide any financial incentives for participants. Almaty is a city of two million people, 70% of whom are ethnic Kazakhs, so our sample can be generalized to the entire Kazakh population.

The inclusion criteria were natives aged 40 or more without ophthalmopathology, living in the city of Almaty, Republic of Kazakhstan. Questions about maternal and paternal ancestral ethnicity were included in the screening questionnaire. Patients with other eye diseases such as uveitis, retinal detachment, glaucoma, high myopia, eye trauma, eye tumor, macular edema, epiretinal membrane, pseudophakic eye, pterygium, corneal opacity, contact lens wear, eye trauma and early ophthalmic surgery were excluded.

The original study protocol included assessment of anterior-posterior eye length, anterior chamber depth, and lens thickness, as well as age and gender questions. During the study, we modified the protocol to include other parameters: vitreous chamber length (VCD), keratometry (K), corneal curvature (CC), intraocular pressure (IOP), body weight, and height.

After informed consent was obtained, these patients underwent A-scan ultrasound of the eyeball (anterior-posterior eyeball size, anterior chamber depth, lens thickness, and vitreal cavity depth) were measured 10 times with a 10 MHz A-scan biometric probe (A-scan plus, Accutome, USA) with applanation after instilling 0.5% proparacaine hydrochloride (Alcaine Alcon-Couvreur, Puurs, Belgium), then mean values were estimated.

Keratometry values were measured using an autokeratometer (Topcon, Japan, 2020). The keratometry value was evaluated using two meridians, the largest and smallest radii of curvature (K1, K2), and the average of these two values was taken as the keratometry value. Corneal curvature and noncycloplegic refraction were assessed using autokeratometry (Topcon, Japan, 2020). The device recorded up to eight separate estimates of corneal curvature along two meridians spaced 90° apart. The average value for each meridian was recorded, and the average corneal curvature was calculated as the average of the greater and lesser curvatures.

Intraocular pressure was measured using non-contact tonometry (ST-80 Topcon, Japan, 2019).

A-scan ultrasound, intraocular pressure assessment, and autorefractokeratometry were performed by two experienced ophthalmologists.

Height and body weight were measured during the clinical examination using standard scales and a stediometer by one nurse.

Because the biometric data of the right and left eyes were the same, we used data from the right eye only (*Refractive errors, axial ocular dimensions, and age-related cataracts: The Tanjong Pagar survey / T. Y. Wong, P. J. Foster, G. J. Johnson, S. K. L. Seah // Investigative Ophthalmology and Visual Science. – 2003. – Vol. 44. – № 4. – P. 1479-1485*).

Step 4: Optimization of surgical treatment of phacomorphic glaucoma with intraoperative complications.

The present study is a prospective study in which transscleral intraocular lens fixation was performed in 15 patients diagnosed with phacomorphic glaucoma. This study complied with the Declaration of Helsinki, and written informed consent was obtained

from all subjects. The study group for this technique included 6 men and 9 women, whose age ranged from 62 to 80 years.

The study was conducted on the basis of the ophthalmology department of the Central City Hospital of Almaty. All the patients were followed up more than six months after the operation, which enabled to estimate adequately the long-term results.

The operation is carried out under the local anesthesia with the use of the operational ophthalmic microscope. Briefly, after retrobulbar anesthesia was administered, the cornea was cleared by mechanically removing the corneal epithelium in the optical zone. Then a conjunctiva incision and a sclera incision at 3 and 9 o'clock at 0.5 to 0.75 mm from the limbus were made. Then corneal paracentesis is made in the same places and viscoelastic (Bausch Lomb, Germany) was injected into the anterior chamber through one of them. Then a needle from an insulin syringe (27G) is bent 900 degrees, then the insulin syringe needle is passed through the corneal paracentesis at 3 o'clock parallel to the posterior iris surfaces and out into the sclera at 0.5-0.75 mm from the limbus at 9 o'clock. He then threads a 9/0 prolene thread onto the needle of an insulin syringe (27G) and pulls the thread into the eye cavity. Exactly the same manipulation is done through the paracentesis at 9 o'clock. Through the main incision, both ends of the 9/0 prolene thread are pulled out to tie to the intraocular lens haptics. An intraocular lens is inserted through the main corneal incision. The lens is implanted with fixation in the ciliary sulcus. Needles are additionally guided through the sclera and sutures are tied. The method provides less traumatic transscleral fixation of the intraocular lens and facilitates its insertion.

Scientific novelty.

1. For the first time, the parameters of the eyeball (anterior-posterior size of the eyeball - 23.2 mm, depth of the anterior chamber - 2.9 mm, thickness of the lens - 4.51 mm) in native residents of Almaty at the age of 40 and older were determined.
2. For the first time in the Republic of Kazakhstan risk factors of phacomorphic glaucoma development in native population have been determined: shallow depth of anterior chamber (2,5 mm) and thick lens (4,75 mm).
3. The way of optimization of the eyeball optical system restoration in case of intraoperative complications of phacomorphytic glaucoma surgery has been developed (Certificate №28290 of 16.08.2022, on record in the state register of rights for objects, protected by copyright).

Provision to be defended.

1. The following risk factors for the development of phacomorphic glaucoma have been identified in the native inhabitants of Almaty city: female gender, short anterior-posterior size and shallow anterior chamber of the eyeball, as well as an increased thickness of the lens.
2. The average bioparameters of the eyeball in the native inhabitants of Almaty city were established.

3. Corneal deepithelialization and IOL luting using a 27 G needle in complicated phacomorphic glaucoma will reduce the time of surgery and rehabilitation in the postoperative period.

Practical significance of the obtained results.

1. Ophthalmotonometry, echobiometry, and ultrasound biomicroscopy are recommended for those over 40 years of age with initial age-related cataracts. In the presence of risk factors for the development of phacomorphic glaucoma (shortening of the anterior and posterior eyeball size, shallow anterior chamber, increased thickness of the lens, and weakness of the cinnamic ligaments), recommend early surgical treatment of cataract.
2. Knowing the normal average parameters of the eyeball in natives, a group with risk factors for phacomorphic glaucoma should be singled out and taken on a dispensary record.
3. In the complicated course of phacomorphic glaucoma (disturbance of the integrity of the posterior capsule of the lens and persistent edema of the corneal epithelium due to uncompensated intraocular pressure) the method of transscleral fixation of intraocular lens with corneal de-epithelization is recommended.

Conclusions.

1. It has been established that Kazakhs accounted for 72.1% (168), other Asians for 15.9% and Caucasians for 12% of the total number of patients treated in inpatients with phacomorphic glaucoma. The total number of operations for age-related cataract during this period was 12008, of which phacomorphytic glaucoma was 233 (1.95%).
2. The main risk factors for the development of phacomorphic glaucoma in Almaty natives were identified: eyeballs with anterior chamber depth $\leq$ 2,5 mm had a higher risk of developing phacomorphic glaucoma compared to those with anterior chamber depth >2,5 mm (Risk Ratio 3,113; 95% Confidence Interval 1,562-6,204, p = 0,001). Eyes with a lens thickness of $\geqslant$4.75 mm had a high risk of developing phacomorphic glaucoma (Risk Ratio 26.368; 95% Confidence Interval 9.130-76.158, p < 0.001).
3. The average bioparameters of the eyeball among the native inhabitants of the city of Almaty were determined. Their average anterior-posterior eye size was 23,2 mm (IQR 22,74 - 23,65), anterior chamber depth was 2,9 mm (IQR 2,63 - 3,2) and lens thickness was 4,51 mm (IQR 4,19 - 4,77) at the age of 40 and older.
4. The method of transscleral intraocular lens fixation using a 27G needle is effective in complicated phacomorphy glaucoma (violation of the integrity of the posterior capsule of the lens), and also reduces operation time and rehabilitation in the postoperative period.

Approbation of the results of the dissertaion.

The main provisions of the thesis were reported and discussed at the meetings of the Scientific Council of KazNMU named after S.D. Asfendiyarov (Protocol №5 from 13.12.2022).

Personal contribution of a doctoral candidate.

The author was directly involved in all stages of the study: from setting the goal and objectives, developing the research design, to theoretical and practical implementation. Practical implementation of the study consisted in the recruitment of material, namely, conversation with patients to obtain informed consent, collection of anamnesis, instrumental study, interpretation of instrumental data. The author conducted a literature search on the problem of research, compiled a database, performed statistical processing of the obtained data, interpretation of the results.

Implementation of research results into practice.

The main scientific statements and conclusions of the present study are implemented in the work of the ophthalmology department of the CCP at the PCV of the Central City Clinical Hospital of Almaty and the at the City Polyclinic № 6.

2 security documents were obtained from them:

1 There is a positive result of formal examination for 1 invention: patent for invention Republic of KZ 0495.1 of 15.08.2022. "Method of transscleral fixation of the posterior chamber intraocular lens in complicated swollen cataract".

2 Author's certificate № 28290 dated August 16, 2022. "Evaluation of a method to improve surgical treatment of swollen cataract with persistent corneal edema and instability of the posterior lens capsule.

Publications.

According to the results of the study, 7 scientific papers were published: 4 - in journals recommended by the Committee on Quality Assurance in Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan; 1 in the journal included in the international database Web of Science Core Collection (Clarivate Analytics) Q3, (WJOS); received 2 protective documents of them: 1 patent for invention of the Republic of Kazakhstan, 1 - utility model, 3- implementation act.

The scope and structure of the thesis.

The thesis is written on 117 pages of typewritten text and consists of a list of abbreviations and designations, introduction, literature review, description of materials and methods, results of the research, conclusion, conclusions and practical recommendations. The list of references contains 164 items in English and Russian. The work is illustrated with 24 tables and 32 figures; there are 5 appendices.