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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

CATARACT SURGERY OPTIMIZATION DURING PSEUDOEXFOLIATIVE SYNDROME

Speciality**:**	3219.01 – Eye diseases
Field of science:	Medicine
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Baku – 2024

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GENERAL DESCRIPTION OF THE WORK

Relevance of the theme. The changing demographic situation in the world sets new tasks and priorities for science and healthcare. So, due to the increase in the average life expectancy, 1.3 billion people are older than 60 years old, and globally cataract and glaucoma are the dominant causes of eye pathologies [1, 2]. For this reason, cataract and glaucoma are in the center of attention in Azerbaijan [3,4, 5].

Along with pseudoexfoliative syndrome (PES), the presence of cataract and glaucoma among age-related pathologies is one of the urgent problems in ophthalmology, as it is a high risk factor. The worldwide prevalence of PES varies widely (1.5–40.9%), indicating a lack of consensus in epidemiologic studies [6,7,8].

For the first time, PES was detected in intraocular structures by Lindbergh in 1911, and later it was identified in extraocular tissues, which

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established PES as a systemic pathology of the organism[6, 8,9].

Modern technologies of cataract surgery (CS), phacoemulsification (PHE), which is considered the "gold standard", have significantly increased confidence due to the high results obtained[10]. But despite the high results of phacoemulsification, a meta-analysis of 22 studies revealed a doubling of complications during PES[11,12]. However, a 50% incidence of delayed intraocular lens (IOL) dislocation after uncomplicated phacoemulsification is observed during PES [10, 11, 12].

Cases of high intraocular pressure (IOP) and pseudoexfoliative glaucoma (PEG) during PES are debated, but the view that it can prevent the development of CS-related PEG is controversial. There are opinions that IOP significantly decreases after KC during more cataracts and PEQ [13,14].

However, the proposed classifications vary from two stages to five stages in terms of different factors related to the development of PES[7,11,12]. A high risk of complications such as bullous keratopathy of the cornea, intraocular inflammation, phimosis of the crystalline capsule, “contracture syndrome” after phacoemulsification is noted in

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connection with PES [15,16].

The role of hemato-ophthalmic barrier disruption, subclinical inflammation, and ischemic process related to PES is specially emphasized[17]. Although there is a lot of literature devoted to the increased risk of complications associated with CS, there is a lack of information on prognostic factors[7,17].

When choosing the most optimal approaches of CS in eyes with PES, priority should be given to the evaluation of all clinical manifestations[18,19,20,21,22].

Thus, the important stages of research on solving the problem are: 1) the early detection of PES and the incidence of cataracts; 2) a comprehensive study of changes in clinical manifestations related to the development of the syndrome, posible risk factors, and inflammatory complications; 3) the detailed assessment of the development of the syndrome, associated with crystal nuclear hardness and surgical risk factors; the development of adequate preventive measures, the choice of optimal surgical tactics, techniques are of high attention and importance.

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Based on the listed factors, taking into account the relevance of the problem, the purpose and tasks of the research were determined.

The purpose of the study. In order to improve the results of cataract surgery (phacoemulsification) in eyes with pseudoexfoliative syndrome, to comprehensively assess possible risk factors related to the stages of development of the syndrome, to ensure the selection of optimal surgical tactics and techniques.

Research objectives:

1. To estimate the incidence of age-related PES among eye pathologies in the Shirvan-Salyan economic region of Azerbaijan based on population referral data.
2. To comprehensively investigate and evaluate the clinical manifestations of PES in terms of potential risk factors associated with surgery.
3. To study the level of pre-inflammatory cytokines-Interleukin 1-beta (IL-1β) and Tumor Necrosis Factor (TNFa) in the anterior chamber aqueous humor, blood serum in terms of possible inflammatory complications associated with surgery against the background of PES.
4. To analyze possible relationship with pre-inflammatory cytokines in the anterior chamber aqueous humor by studying changes in the posterior corneal epithelium in the eyes with cataracts with PES.
5. To ensure the choice of optimal tactics, surgical techniques, IOL by analysing specific surgical risk factors associated with the development of PES, its complications, from the point of view of the stages of development of the syndrome.

Main provisions submitted for defense:

- The frequency of occurrence of PES in the older generation, including its association with cataracts and glaucoma, its early detection, and its influence on the outcome of cataract surgery are important.
- A complex assessment of the clinical manifestations of PES, the direct dependence of surgical risk factors on the stages of their development is determined.
- Taking into account the risk factors associated with the development of PES, there is an opportunity to optimize surgical intervention and the choice of preventive measures.
- Against the background of PES, the imbalance of cytokines

IL-1β, TNFα, which regulate inflammation in the anterior chamber aqueous humor and blood serum, can be considered as a risk factor for possible complications in patients with cataracts and glaucoma.

Scientific novelty of the study:

- In the Shirvan-Salyan economic region of Azerbaijan, the frequency of PES among various pathologies, including cataract, glaucoma, was studied.
- As a result of a comprehensive evaluation of the clinical manifestations of PES related to cataract surgery, the superiority of the 3-stage approach has been proven in relation to the evidence of both structural changes of the eye and possible complications.
- The concentration of pro-inflammatory cytokines - IL-1β and TNFα in the anterior chamber aqueous humor and blood serum of the possible inflammatory complications related to cataract surgery was studied, the dependence related to the development of the syndrome was determined with significant differences, it was possible to choose preventive measures based on prognostic factors.
- For the first time in eyes with PES, the correlation of the changes of cytokines in the posterior corneal epithelium and in the anterior chamber aqueous humor, its dependence on the development of the syndrome was determined with significant differences, and it was found to be an important risk factor from a surgical point of view.
- By predicting potential risk factors from the point of view of optimal surgical approach, among the clinical features, it was revealed that the nuclear hardness of the crystal, the weakening of Zinn ligaments is related to the development of the syndrome, and the selection of less traumatic surgical tactics and techniques was ensured.

Theoretical and practical significance of the study:

- A comprehensive evaluation of clinical manifestations during PES, the importance of the development of the syndrome in cataract surgery, identified as potential risk factors and confirmed.
- Optimum surgical tactics, techniques and IOL selection were determined by identifying potential difficulties and complications associated with the development stage of the PES.
- The nature and characteristics of potential complications

associated with a set of chronic, age-related pathologies in patients with cataracts and glaucoma against the background of PES have been determined in advance.

• Preventive measures related to the development of PES have been developed.

Research materials and methods. PES was determined in 150 (75.0%) eyes of 200 patients prepared for CS (PHE). Since 50 (25.0%) patients did not have signs of PES in their eyes, they were included in the control group (CG). In the Shirvan-Salyan economic district, the frequency of PES, cataract and glaucoma, among various pathologies, was studied based on the frequency of eye pathologies of people aged 45 and older (incidences per 1000 people) in 2022 based on the data of treatment and prevention institutions.

Ophthalmological examination methods. Determination of visual acuity (with and without correction), two-stage biomicroscopy (with narrow pupil and then with mydriasis), gonioscopy, ophthalmoscopy, contact, non-contact tonometry (pneumotonometer, Goldman tonometer), ultrasound biomicroscopy (UBM plus, Accutome, USA), specular microscopy (SM EM-3000, TOMEY), biometry (IOL - Master" Zeiss, Germany), which determines the curvature of the cornea and the depth of the anterior chamber, ultrasound (US) examination (A, B scan), optical coherence tomography (Cirrus HDp -OCT 5000) was applied.

Laboratory examination methods. In the Clinical Immunology laboratory of the National Ophthalmology Center named after akad. Zarifa Aliyeva, the concentration of pro-inflammatory cytokines - Interleukin 1 beta (IL-1β), Tumor necrosis factor (TNFα) was determined in the blood serum and anterior chamber aqueous humor with the BioScreen MS-2000 device. Anterior chamber aqueous humor (n=81) and blood serum (n=81) at the general system level, which are informative material for conventional assessment of preoperative local cytokine status, were selected for the study.

Methods of surgical intervention. Cataract surgery was performed by phacoemulsification method under local anesthesia using Ozil Pulse technology and Phacochop technique using "Infiniti Vision System"

and "Laureat" phacoemulsificator (Alcon Laboratories Inc., USA). Combined sinustrabeculectomy (STEK) surgery with phacoemulsification was performed in eyes with glaucoma with PES.

Methods of statistical processing of materials. Comparison of results in independent groups was carried out using one-dimensional statistical methods by calculating Kruskal-Wallis and Mann-Whitney criteria. According to the test results, if the distribution of the data is abnormal, the Wilcoxon (Wilcoxon signed ranks test) statistical method, the dispersion analysis method in the comparison of two or more groups, and the Spearman (Spearmans rank correlation coefficient) method were applied during the correlation analysis between different variable indicators.

PERSONAL RESEARCH

General characteristics of the problem of cataract surgery in eyes with pseudoexfoliative syndrome, study results.

Taking into account the importance given to the frequency and early detection of PES in the world, the incidence of PES among various pathologies such as cataracts and glaucoma, some of their features in persons aged 45 and older were studied on the basis of data from medical institutions of the Shirvan-Salyan economic region of the Republic of Azerbaijan in 2022 (incidences per 1000 people).

Cataract (6.24%) and glaucoma (5.46%) were among the eye pathologies that were the reason for referral to medical institutions. In the 45-49 age interval, the frequency of PES was very low. Although the difference in indicators in this age interval is noticeable, it was not statistically significant ($p>0.05$). In the next age interval (50-54 years), the occurrence of PES increased 3 times in men and 1.5 times in women, but the gender difference was not statistically significant ($p>0.05$). In the 55-59 age interval, the frequency of PES increased, this increase significantly differed from the indicator in the 45-49 age group ($p<0.05$). The frequency of PES in the 60-64 age interval was significantly higher ($p<0.05$) in comparison with all the previous age intervals, it was more noticeable in the 65-69 age interval, and the highest level was observed at the age of 70 and above.

At the time of application, PES was detected as a concomitant pathology in 46.34% of persons with eye pathologies.

Results of the study of clinical manifestations and important risk factors associated with cataract surgery during pseudoexfoliative syndrome.

Taking into account important potential risk criteria related to cataract surgery during PES (pupillary rigidity, changes in lens ligaments), the clinical manifestations detected by biomicroscopy and UBM in eye structures were analyzed.

Based on the previously proposed surgical classification, evaluation criteria included the degree of development of dystrophic changes in eye structures, PEM location, intensity, results of UBM. Based on the surgical risk factors, 3 variants of character manifestations were determined, and the potential risk factors of phacoemulsification were analyzed in relation to the development of the syndrome.

Among them, in 54 (36.0%) eyes, in addition to preservation of the pupil's reaction to light and mydriatics, partial destruction of the pigment border of the pupillary margin, weak removal of the corneal pattern, sclerosis of the trabecular tissue, and mild exogenous pigmentation (I stage of PES) of the anterior chamber angle were characteristic. Gonioscopy of anterior chamber angle revealed Sampaolessi's line, but the degree of pigmentation of anterior chamber angle was more significant in the PEG group. Most importantly, changes in lens fibers were not detected by UBM.

In 58 (38.7%) eyes, the dystrophic component of PES was more pronounced (stage II PES). PEM was observed in the posterior corneal epithelium (PCE) of 10 (50%) eyes. There was a decrease in the pupil's response to mydriatics, but no significant changes were observed in the fibers of the Zinn ligaments. The weak pupil response was more likely due to the development of iridocapsular synechiae, which was confirmed by UBM.

Dystrophic-destructive component was more important in 38 (25.3%) eyes with PES detected (stage III PES). Thus, the changes were more intense and prominent, transillumination of stromal vessels was observed. With UBM, elongation, thinning, adhesion were

determined in the fibers of the Zinn ligament. PEM formed a plaque on the back surface of the mucous membrane. As a result of various degrees of lysis of Zinn ligament fibers, which is characteristic of this stage, the increase in the sphericity of the lens and the equatorial angle was determined. As a result of the violation of field relations, the depth of anterior chamber angle is different in different ways. Adhesions in anterior chamber angle caused by inflammatory complications were also worthy of attention.

The results obtained with UBM were compared with the development stages of control group and PES (Fig. 1 and Fig. 2). A comprehensive assessment of the clinical manifestations of PES, a corresponding comparative analysis of the obtained indicators related to the development of the syndrome was determined in the following UBM dimensions with significant differences. Of them, anterior chamber angle: 39.2±2.8 in control group; 38.3±1.7 in stage I; 28.9±0.8 in stage II; 22.0±1.2 in stage III; anterior chamber depth: 2.63±0.24 mm in control group; 2.58±0.06 mm in stage I; 2.29±0.13 mm in stage II; 1.87±0.10 mm in stage III; lens thickness: 3.78±0.02 mm in control group; 3.80±0.11 in stage I; 3.94±0.08 mm in stage II; 4.74±0.15 mm in stage III, equatorial angle: 14.3±1.0 in control group; 16.2±0.8 in stage I; 25.9±1.2 in stage II; 31.6±1.8 degrees in stage III.

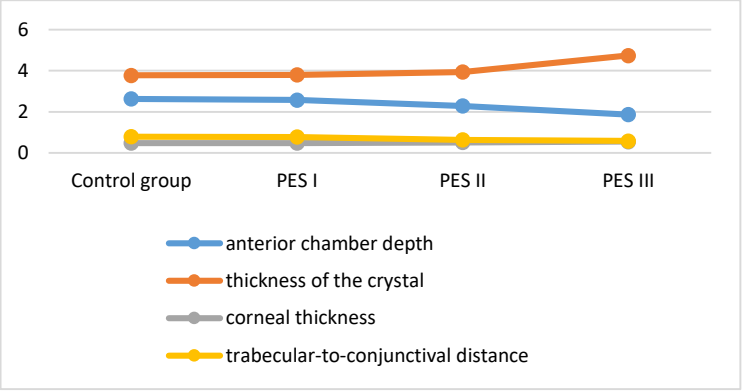

Figure 1. The relationship between the indicators obtained by UBM and the development of PES.

Anterior chamber depth is 1.4 times less in stage III compared to control group ($p< 0.05$); in stage I it was 1.4 times more than in stage III ($p< 0.05$), in stage II it was 1.2 times more than in stage III ($p<0.05$). Anterior chamber angle: compared to control group, it was 1.8 times less in III ($p<0.05$); in stage I was 1.3 times more than in stage II ($p<0.05$); 1.7 times more than in stage III ($p<0.05$); in stage II it was 1.3 times more than in stage III ($p< 0.05$). The thickness of lens was 1.3 times more in stage III than in control group ($p<0.05$); in stage I was 1.2 times less than in stage III ($p<0.05$); in stage II was 1.2 times less than in stage III ($p< 0.05$). The measurements of the equatorial angle were 2.2 times more in the III stage than in the control group ($p< 0.05$); in stage I 1.6 times less than in stage II ($p<0.05$); in stage I were 2 times less than stage III ($p<0.05$); in stage II were 1.2 times less than in stage III ($p<0.05$).

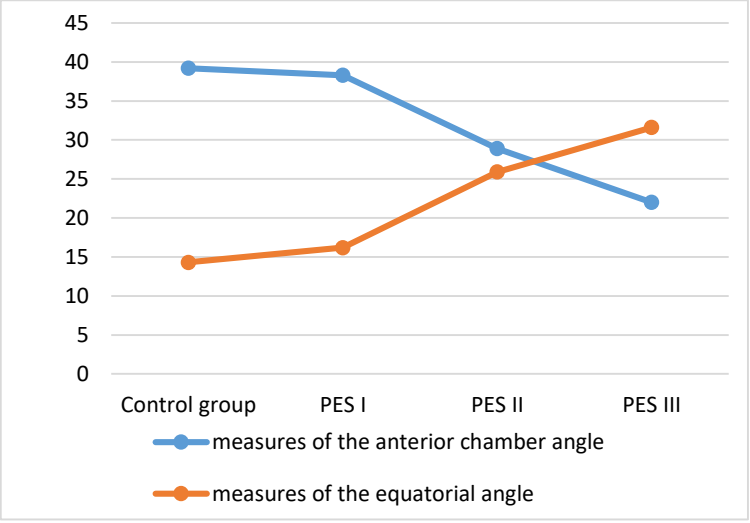

Figure 2. Anterior chamber angle and equatorial angle associated with development of PES according to the results of UBM.

Thus, the decrease in the depth and angle of the anterior chamber associated with the development of PES, the increase in the thickness of the lens, the hardness of the nucleus, and the increase in the equatorial angle are indicators of the damage of the Zinn ligaments, so it helps to accurately assess the condition of the capsule-ligament

apparatus of the crystal in advance, and to develop measures against it. The obtained results, as surgical risk factors, make it difficult to move the phaconeedle in the anterior chamber during phacoemulsification, increasing the risk of corneal damage. The use of US energy in more economical methods ensures less damage to the cornea.

Evaluation of the changes of the posterior corneal epithelium related to the stages of development of pseudoexfoliative syndrome and from the point of view of cataract surgery.

Because the posterior corneal epithelium is a very delicate structure, it is noteworthy that it is associated with possible surgical injury. The results of the posterior corneal epithelium examination were determined with significant differences related to the stages of development of the PES. Thus, the average density of posterior corneal epithelium cells in stage I - 2871.6 ± 57.3; II - 2388.6±55.0; III - 1181.2±97.7 cells/mm² were determined.

Analysing the morphological changes of posterior corneal epithelium associated with the stages of PES, compared to II in I: 1.2 times more cell number-density (CD) in 1 mm² ($p<0.05$); average cell area (AVG) was1.2 times less ($p<0.05$); the mean cell area standard deviation (SD) was 1.3 times less ($p<0.05$). In II compared to III: CD was 2 times more ($p<0.05$); AVG - 2.2 times lower ($p<0.05$); SD was 2.3 times lower ($p<0.05$). In I compared to III: CD was 2.4 times more ($p<0.05$); AVG was 2.7 times lower ($p<0.05$); SD was detected 3 times less ($p<0.05$) with significant differences.

The differences of posterior corneal epithelium indicators between eyes with normal İOP (PES group) and eyes with glaucoma (PEG group) were analyzed. İn stage I: CD was 1.5 times more ($p<0.05$); AVG was 1.6 times less ($p<0.05$); SD was 2 times less ($p<0.05$). In stage II: CD was 3 times more ($p<0.05$); AVG was 1.3 times less ($p<0.05$); SD was 1.6 times less ($p<0.05$). In stage III: CD was 1.6 times less ($p<0.05$); SD was 1.5 times more ($p<0.05$); CV was 1.1 times less ($p>0.05$); AVG was 1.7 times more ($p<0.05$). According to the results of the posterior corneal epithelium study, it was determined that the percentage of polymegatism increased in PEG groups compared to control group ($p<0.01$). During PES, the values

of this indicator did not differ significantly in control group, but were lower than in patients with PEG ($p<0.05$).

Thus, along with the development of pseudoexfoliative syndrome, the presence of glaucoma had a significant impact on the posterior corneal epithelium.

Results of the study of pre-inflammatory cytokines in the anterior chamber aqueous humor of the eye, blood serum in patients identified with pseudoexfoliative syndrome and cataracts.

The study of cytokines, which are associated with inflammatory complications, was analyzed in three stages: ophthalmological, immunological and assessment of the somatic state of patients. Before phacoemulsification, the stage of development of PES is designated. So, in 11 (23.91%) eyes, PES was determined in stage I, in 20 (43.48%) eyes - in stage II, and in 15 (32.61%) eyes - in stage III. Results of immunological studies, mean concentrations of IL-1β and TNFα in serum and anterior chamber aqueous humor were compared between patients with PES and control group (fig.3)

IL-1β in anterior chamber aqueous humor was 7.4 times higher in PES group than in control group ($p<0.05$); 15 times more in I ($p<0.01$); 7.5 times more in II ($p<0.01$); 1.7 times more in III ($p>0.05$). 2 times more in stage I than in stage II ($p>0.05$); 8.8 times more than III ($p\leq0.01$); 4.4 times higher in stage II than in stage III ($p<0.05$).

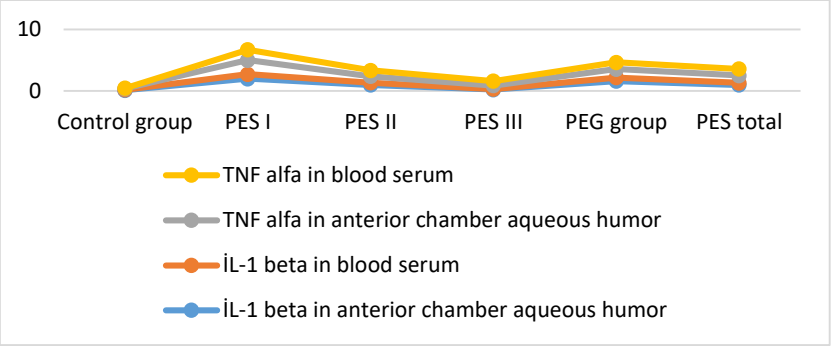

Figure 3. Results of the dynamics of IL-1β and TNFα- cytokines concentration in the anterior chamber aqueous humor and blood serum related to the development of PES.

IL-1β in blood serum was 4.4 times higher during PES than in control group ($p<0.05$); 9 times more in stage I ($p<0.01$); 4.4 times more in II ($p<0.05$); there was practically no difference in stage III ($p>0.05$). 2.1 times more in stage I than in stage II ($p>0.05$); 9 times more than in stage III ($p<0.01$); 4.4 times more ($p<0.05$) in II than in III.

TNFα in the anterior chamber aqueous humor was 6.9 times more in the PES group than in control group ($p<0.01$); 13.2 times more in stage I ($p<0.001$); 6 times more in II ($p<0.01$); 3.4 times ($p<0.001$) more in III; 2.2 times more in I than in II ($p<0.05$) and 3.9 times more ($p<0.01$) than in III; It was 1.8 times more in II than in III ($p>0.05$).

TNFa in blood serum compared to control group in the main group was 11.5 times more ($p<0.001$); in I -18.3 times more ($p<0.001$); in II - 10.6 times more ($p<0.001$); in III - 7.6 times more ($p<0.001$, in I was1.7 times more than in II ($p>0.05$) and 2.4 times more than in III ($p<0.05$); in II was1.4 times more than in III ($P>0.05$).

As a result of the examination of doctors of various specialties, somatic pathology was found in patients with PES about 2 times more often than in control group.

In addition, the results obtained during the study of IL-12β and TNFa cytokines in anterior chamber aqueous humor, blood serum of 12 patients with cataracts and glaucoma during PES were analyzed comparatively. IL-1β in the anterior chamber aqueous humor was 12.1 times more in the PEG group and 5.7 times more in the PES group ($p<0.05$) than in the control group ($p<0.05$); and 2.1 times more in the PEG group than in the PES group ($p>0.05$). In the blood serum, IL-1β was 7 times higher in the PEG group than in the control group ($p<0.05$).

TNFα in anterior chamber aqueous humor was 8.1 times higher in PEG group compared to control group ($p<0.05$); It was 6.4 times higher in the PES group ($p < 0.01$). It was 1.3 times higher in the PEG group than in the PES group ($p>0.05$). Serum TNFα was 11.7 times higher in PEG group compared to control group ($p<0.001$); It was 11.7 times more in the PES group ($p<0.001$).

The fact that inflammatory complications are even more common in stage II of PES can be explained by the presence of a connection with changes in the cytokine network at this stage.

Thus, developmental mechanisms of aging-related PES, disruption of the hemato-ophthalmic barrier, age-related changes in the structures of the eye, reduction of compensatory capabilities form the background of surgical treatment in elderly patients at a certain level[23,24].

Searching for a possible correlation between IL-1β, TNFα cytokines in the anterior chamber aqueous humor and posterior corneal epithelium changes of eyes with pseudoexfoliative syndrome and cataracts.

The study of IL-1β, TNF α cytokines in the anterior chamber aqueous humor and blood serum with the determined changes of posterior corneal epithelium, their correlation analysis showed that between the indicators: positive (when one indicator increases, the other also increases) and negative (when one indicator increases, the other indicator decreases) correlation relationships exist.

Thus, a positive correlation relationship between corneal thickness (CT) indicator and AVG was determined (cor. coefficient is 0.142, $p>0.05$), since the difference is not statistically significant, as a result, it was not possible to determine a significant correlation relationship between CT and other indicators.

However, the IL-1β indicator in anterior chamber aqueous humor had a negative correletion with AVG indicator of posterior corneal epithelium (cor. coefficient is -0.341, $p<0.05$), a positive correletion with TNFα in anterior chamber aqueous humor (cor. coefficient is 0.522, $p<0.05$); a positive correlation with IL-1β in blood serum (cor. coefficient is 0.485, $p<0.05$); a positive correlation with TNFα in blood serum (cor. coefficient is 0.300, $p<0.05$) was determinated.

The TNFα indicator in anterior chamber aqueous humor had a positive correlation with AEQ and HEX (cor. coefficient is 0.322, $p<0.05$);

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a negative correlation with AVG (cor. coefficient is -0.325, $p<0.05$); a positive correlation with IL-1β indicator in blood serum (cor. coefficient is 0.460, $p<0.05$); a positive correlation with the TNFα index in the blood serum (cor. coefficient is 0.603, $p<0.05$), the differences were statistically significant.

IL-1β indicator in blood serum had a negative correlation with AVG (cor. coefficient is -0.345, $p<0.05$); a positive correlation with TNFα in blood serum (cor. coefficient is 0.490, $p<0.05$), the differences were statistically significant.

Thus, in addition to surgical injury to posterior corneal epithelium, the influence of processes associated with cytokines IL-1β, TNFa in the anterior chamber aqueous humor, blood serum, should be considered as a possible risk factor.

Potential risk factors of cataract surgery associated with the development of pseudoexfoliative syndrome and their features.

Surgical risk factors determined by UBM, important risk criteria for phacoemulsification - the degree of rigidity of the pupil and the degree of weakness of the lens ligaments, a comprehensive assessment of the manifestations related to the development of the syndrome, were important in the selection of surgical tactics and techniques.

Preoperative nuclear stiffness according to the stages of PES was evaluated according to the classification of L. Buratto, the analysis of the results showed: in the main group 1 eye (0.7%) – grade 2, in 4 eyes (2.7%) – grade 3, in 63 eyes (42.0%) - grade 4, in 82 eyes (54.7%) - grade 5. In control group, nuclear hardness was determined in grade 3 in 15 eyes (30%), grade 4 in 22 eyes (44.0%), grade 5 in 13 eyes (26.0%).

According to the LOCS III classification, 95 (63.3%) of eyes in the main group had nuclear sclerotic cataract (NSC), 45 (30.0%) cortical spoking cataract (CC), 10 (6.7%) posterior capsular clouding (posterior subcapsular cataract PSC). İn control group 13 (26.0%) eyes had NSC, 22 (44.0%) eyes had CC, 15 (30.0%) eyes had PSC.

In relation to these results, the increase in nuclear hardness of the crystal associated with the development of PES was confirmed as an important predictive factor of posterior corneal epithelium loss during surgery.

During the operation, the anterior chamber was deepened with dispersive viscoelastic (VE) of high molecular weight in stage I of PES and in control group. This VE coats and protects the cornea for a longer period of time, and has the ability to wash out later from the anterior chamber, keeping the depth of the chamber stable [25]. No further manipulation was needed during the course of phacoemulsification in control group.

Synechiolysis was additionally performed in 2 (3.7%) eyes during stage I of PES. In order to minimize the possibility of rupture of the posterior capsule, it was operated with minimal indications using the "Phacochop" technique. Usually, during phacoemulsification, “Burst” mode was used in all cases, because in this mode, US energy was used more economically[26]. The choice of IOL was determined according to UBM. Both multifocal and monofocal IOLs of any type were selected in control group. In stage I of PES, any type of monofocal IOL was selected.

One of the main difficulties in phase II of PES was related to narrow pupils. In narrow pupils, pharmacological dilators were injected into the chamber. Among the surgical methods, synechiolysis was performed in 11 (18.96%) eyes, pupillary membrane cleaning in 3 (5.17%) eyes. In pupils dilated no more than 2 mm, technical means - corneal hook were used in 5 (8.62%), Malyugin's ring in 6 (10.34%) eyes. During phacoemulsification, a capsulorhexis of approximately 5.5 mm was performed, the goal of which was to prevent shrinkage of the lens capsule. At this stage, since inflammatory complications and narrow pupils are the main problems, a plan of actions was prepared in advance.

In order to prevent inflammatory complications, steroidal and non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed before the operation, and were even injected into the chamber during

[25] Monaco G. New ophthalmic dual-viscoelastic device in cataract surgery: a comparative study / G.Monaco, M.Gari, S.Pelizzari // BMJ Open Ophth., 2019, №4, p.e000280.

[26] Kumar S. Vertical chopping preferred over horizontal chopping in phacoemulsification of cataracts in pseudoexfoliation syndrome / S.Kumar, H.Trehan, P.Kumar [et al.] // PARIPEX - Indian journal of research, 2017, v.6(6).

the operation. More than optimal IOL models, monofocal, one-piece lenses were implanted. Considering the development of the syndrome over the years, the risk of shrinkage of the lens capsule and IOL decentralization, it was more appropriate not to use multifocal IOL.

The main features of stage III of PES were the narrowness of the pupil and the weakness of Zinn ligaments. Viscomidriasis was achieved mainly by using viscous VE, when the image of the periphery of the crystal was unsatisfactory, the lens hook - capsule stabilizers were used to both dilate the narrow pupils and ensure stability of the capsule.

The importance of capsulorhexis size in the development of "capsule contracture" syndrome is discussed [25, 27]. In the study carried out by Vasavada, it was proposed to make an initial small capsulorhexis and then increase its size to a standard size (5-5.5 mm in diameter) [23,24,28]. Small-diameter capsulorhexis was considered as a preventive measure in eyes with pre-confirmed Zinn ligament weakness during UBM, and its enlargement was known to be more optimal to prevent capsular contracture after IOL implantation. Weakness of the Zinn ligaments of was confirmed by the wrinkling of the capsule during the operation. The advantage of this tactic has already been mentioned by several authors.The severity of the weakness of the capsule-ligament apparatus of the lens was pre-evaluated according to the UBM indicators. As additional manipulation, synechiolysis was performed in 9 (23.68%), pupillary membrane cleaning in 2 (5.26%) eyes, corneal hook was used in 27 (71.05%), Malyugin's ring in 9 (23.68%) eyes has been done. At this stage, our goal in using the capsule tension ring (CTR) in all eyes is to prevent capsule phimosis, IOL decentralization in the early and late stages. According to the UBM results, the choice of which IOL model was decided in advance. Basically, a less dislocated three-part "AMO Sensar AR40" and "AcrySof MA60AC"

[27] Vasavada A. Cionni Ring and In-the-Bag Intraocular Lens Implantation for Subluxated lenses: a prospective case series / A.Vasavada, M.Praveen, V.Vasavada [et al.] // Am J Ophthalmol., 2012, v.153(6), p.1144-1153.

[28] Chang D. Comments on: Dye-enhanced anterior capsulorhexis: surgical techniques, guidelines, and recommendations for surgeons // Comp. Ophthalmol. Update, 2003, v.4, p.187-188.

from Alcon were implanted into the ciliary furrow.

The analysis performed according to the duration of US use showed that the differences obtained in the comparison of control group with stage I ($p<0.05$), stage II ($p<0.05$), stage III ($p<0.05$) are significant, stage I compared to stage II ($p>0.05$), stage I compared to stage III ($p>0.05$), stage II compared to stage III ($p>0.05$), the differences were not significant.

Thus, the differences were significant, as nuclear stiffness was greater in the PES group than in the control group. According to the time of the operation, there were significant differences in the comparison of control group with stage I ($p<0.05$), II ($p<0.05$), and III ($p<0.05$). Stages I and II did not differ according to the time of the operation ($p>0.05$), the difference between II and III ($p<0.05$), I and III ($p<0.05$) was significant.

CTR was implanted after phacoemulsification to prevent capsular phimosis in 148 (98.7%) eyes in all stages of PES. As a result, prevention of decentralization of the IOL with possible dislocation of the IOL-capsule complex was carried out. CTR was not implanted in 2 (1.3%) eyes due to posterior capsule tear. In the PES group, due to the completeness of the capsule and the weakness of the Zinn ligaments, the IOL was implanted in the ciliary fold in 38 (25.33%) eyes, and in the lens capsule in 112 (74.66%) eyes. 50 (100.0%) IOLs were implanted in the lens capsule in eyes from control group.

Characteristic complications and functional outcomes of cataract surgery in eyes with pseudoexfoliative syndrome.

The possibility of CS related complications in eyes with PES is known to be possible for a variety of reasons, widely discussed in the literature, including those associated with various risk factors [29].

Complications were divided into 2 groups related to intra-operative and post-operative period. At the same time, complications of the postoperative period were divided into 2 groups according to the time of occurrence: early and delayed. Intraoperative complications were

[29] Lee G. Risk Factors for Intraocular Lens Dislocation After Phacoemulsification: A Nationwide Population-Based Cohort Study / G.Lee, D.Lim, S.Chi [et al.] // American journal of ophthalmology, 2020, v.214, p.86-96.

encountered only in stage III of PES. So, at this stage, zonular dialysis was performed in 3 eyes (7.89%); corneal bleeding in 1 eye (2.63%); rupture of the posterior lens capsule in 2 eyes (5.26%); vitreous loss in 2 eyes (5.26%); iridodialysis was found in 1 eye (2.63%).

In the early period (up to 2 weeks), postoperative complications include corneal edema, hypertension, and inflammatory reaction. In the PES group, 8 (5.33%) eyes had an inflammatory reaction (Tyndal's phenomenon in the anterior chamber), 9 (6.0%) eyes had various degrees of edema, and 5 (3.33%) eyes had hypertension. Inflammatory reaction was determined in 6 (10.34%) eyes at II stage, in 2 (5.26%) eyes at III stage. Corneal edema was detected in stage I in 2 eyes (3.70%), stage II in 3 eyes (5.17%), stage III in 4 eyes (10.52%). Elevation of İOP was detected in stage II in 3 (5.17%) eyes, stage III in 2 (5.26%) eyes. No complications were detected during the operation in the control group. The mentioned complications were eliminated by appropriate conservative treatment.

In 8 (5.33%) eyes, during phimosis of the capsule, which is the basis of "contracture syndrome", which belongs to the series of delayed complications of the postoperative period, capsulotomy was performed from several places along the circular edges of the anterior capsule of the crystal with Nd:YAG laser. Posterior capsule opacification was removed by Nd:YAG laser in 38 (25.33%) eyes from the group with PES and 8 (16.0%) eyes from the control group. Phimosis of the crystal capsule and opacification of the posterior capsule, and the fact that inflammatory reactions were more common in the II stage of the syndrome confirmed the inflammatory nature of these complications.

In 3 (2.0%) eyes with IOL dislocation, it was removed together with the IOL-capsule complex, implantation of the "Iris-claw" type of IOL in the retropupillary area was performed.

Among the factors affecting visual acuity after surgery, retinal diseases were investigated. Thus, in the PES group, 66 (44.0%) eyes had various diseases of the retina: 12 (8.0%) eyes had diabetic retinopathy, 17 (11.3%) eyes had glaucoma-related optic neuropathy, 17 (11.3%) had optic neuropathy associated with glaucoma, macular edema in 4 (2.7%) eyes, and maculodystrophy in 16 (10.7%) eyes. Macular edema was detected in stage II, maculodystrophy in stage III. Various retinal diseases were

detected in 16 (32.0%) eyes: diabetic retinopathy in 7 (14.0%) eyes, hypertonic angioretinopathy in 9 (18.0%) eyes.

Although complications were more common during PES, more optimal results could be achieved with an adequate approach. Thus, the visual acuity in PES and control group before surgery (vis.1), visual acuity 1 day after surgery (vis.2), visual acuity 3 days after surgery (vis.3), visual acuity 1 month after surgery (vis.4) compared. In the final result, the results obtained in PES and control group were very close to each other (fig.4).

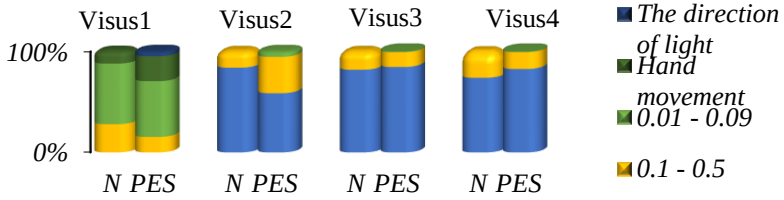

Figure 4. Results of visual acuity in control and PES groups

Thus, a study conducted in order to improve the results of cataract surgery in eyes with pseudoexfoliative syndrome investigated possible risk factors and determined their association with the development of the syndrome. As a result, optimal technique, surgical technique, and IOL selection were provided. So, by determining the important risk factors of surgery, the development of PES in terms of 3 stages, the preparation of preventive measures against possible complications in advance made it possible to obtain more successful results.

As a result, early detection of PES and a detailed and comprehensive assessment of clinical manifestations associated with CS ensure the development of a preventive strategy. So, according to the results of the research, early detection of PES during population appeals and preventive examinations, early determination of CS is of high importance. Important for surgical intervention, a softer lens core and surgery on structures with milder dystrophic changes may result in less surgical damage and milder inflammatory complications.

RESULTS

1. The frequency of occurrence of pseudoexfoliative syndrome in Shirvan-Salyan economic region of Azerbaijan among eye pathologies among the population aged 45 and over was revealed by 46.34% on the basis of appeals, age-related tendency to change and its characteristics were determined. Its highest level was traced at the age of 70 and older.
2. A comprehensive assessment of the clinical manifestations of pseudoexfoliative syndrome (structural, topographo-anatomic changes) in terms of cataract surgery determined the dependence of important surgical risk factors (rigidity of the pupil, weakness of the Zinn ligaments, changes in posterior corneal epithelium) on the development of the syndrome, confirmed the choice of the optimal surgical approach with significant distinctive evidence of three stages of development. Among them, it was determined that factors such as the morphological changes of the posterior epithelial layer of the cornea, the reduction of the indicators of the depth and angle of the anterior chamber ($p<0.05$), the increase of the nuclear hardness of the crystal, the equatorial angle, and the weakening of the Zinn ligaments ($p<0.05$) are significant in the surgical approach, made it possible to choose preventive measures.
3. Inflammatory complications, which are considered extremely important with cataract surgery during pseudoexfoliative syndrome, were confirmed by changes in the cytokine network (in anterior chamber aqueous humor, blood serum) related to the development of the syndrome, including statistically significant results supporting the inflammatory nature of the syndrome. Among them, serum IL-1β was 4.4 times more in the main group compared to control group ($p<0.05$); it was 7.4 times more ($p<0.05$) in anterior chamber aqueous humor. Serum TNF-α was determined 11.5 times more in the main group compared to control group ($p<0.001$); 18.3 times more in stage I ($p<0.001$); 10.6 times more in II ($p<0.001$); 7.6 times more in III ($p<0.001$); Compared with I and III, it was 2.4 times more ($p<0.05$). The concentration of TNFα in the anterior chamber aqueous humor was determined 6.9 times higher in the

main group than in the control group ($p<0.01$); 13.2 times more in stage I ($p<0.001$), 6 times more in stage II ($p<0.01$), 3.4 times more in stage III ($p<0.05$); between stages of development of the syndrome was confirmed by significant differences: in stage I was 2.2 times more than in II ($p<0.05$) and 3.9 times more than in III ($p<0.01$), 1.8 times more in III than in II ($p>0.05$).

4. As a potential risk factor in terms of complications after cataract surgery in the case of pseudoexfoliative syndrome, the presence of correlation relationships between changes in the posterior corneal epithelium and indicators of cytokines IL-1β, TNFa in the anterior chamber aqueous humor was established: a negative correlation relationship between IL-1β in the anterior chamber aqueous humor and the AVG of posterior corneal epithelium (coefficient is -0.341, $p<0.05$); a positive relationship with TNFa (coefficient is 0.522, $p<0.05$); a positive correlation relationship between the TNFa indicator and the CD indicator of posterior corneal epithelium (coefficient is -0.322, $p<0.05$); a negative correlation relationship with the AVG indicator (coefficient-0.325, $p<0.05$), relationships were statistically significant. Thus, possible risk factors directly and inversely related to the development of the additive syndrome were investigated.
5. Cataract surgery was provided based on the evidence of a three-stage approach in terms of optimal intervention selection in eyes with pseudoexfoliative syndrome. Thus, the relationship between potential surgical risk factors and the progression of the syndrome, including the increase in nuclear stiffness, was determined, and the selection of preventive measures against possible character complications was preferred. Advance preparation of measures against surgical complications, optimal tactics, technique, IOL selection were ensured, more successful results were achieved.

PRACTICAL RECOMMENDATIONS

1. It is important to pay high attention to early detection of PES during referrals and preventive examinations of the age-related population.
2. Early determination of cataract surgery in eyes with PES, which is important for surgery, is possible to achieve less tissue damage

by surgery performed on structures with milder dystrophic changes in the softer crystal nucleus.

3. By identifying prognostic factors, the operation performed in the early stages of PES can be observed with less inflammatory processes.
4. A 3-stage surgical approach to optimizing surgical intervention related to the development of the syndrome, it is possible to perform phacoemulsification with more economical US energy and minimal surgical damage to structures, despite the increase in nuclear stiffness as the syndrome progresses.
5. It is important to monitor postoperative complications (intraocular pressure, inflammatory process, decentralization of IOL, cystic macular edema, etc.) and take appropriate measures to eliminate them.

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LIST OF ABBREVIATIONS

WHO – World Health Organization
PES – pseudoexfoliative syndrome
PEM – pseudoexfoliative material
PEG – pseudoexfoliative glaucoma
CS – cataract surgery
PHE – phacoemulsification
ABQ – open-angle glaucoma
IOP – intraocular pressure
STEC – sinustrabeculectomy
CG – control group
ACA – anterior chamber angle
ACD – anterior chamber depth
PCE – posterior corneal epithelium – adopted indicators:
HEX – percentage of hexagonal cells
SD – the standard deviation of the cell area
AVG – average cell area
CD – cellular density
CT – corneal thickness
CV – coefficient of variation
IL-1β – interleukin 1-beta
TNFα – tumor necrosis factor
IOL – intraocular lens
NSAID – non-steroidal anti-inflammatory drug
OCT – optical coherence tomography
UBM – ultrasound biomicroscopy
US – ultrasound
VE – viscoelastic
CTR – capsule tension ring

The defense will be held on 23 October 2024 at 14⁰⁰ at the meeting of the Dissertation council FD 1.03 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the National Ophthalmology Center named after academician Zarifa Aliyeva

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Dissertation is accessible at the National Ophthalmology Center named after academician Zarifa Aliyeva Library

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Abstract was sent to the required addresses on 23 September 2024

Signed for print: 20.09.2024
Paper format: $60\times84^{1/16}$
Volume: 39 892
Number of hard copies: 20 copies