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New Prediction Method of the Certain Type of Secondary Cataract

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Abstract: The aim of the research was to investigate the ophthalmologic status and to investigate the influence of dominating part of vegetative nervous system, following the different types of senile and secondary cataract formation in human. Thus, the domination a sympathetic nervous system and correlated systemic dystrophic changes of the tissues in patients with cortical and secondary proliferative cataract have been found for the first time. Moreover, patients with nuclear and secondary fibrous cataract had the domination of parasympathetic nervous system and another character of dystrophic changes. Therefore, the dominating part of vegetative nervous system can be offered as an available clinical marker of character of neurodystrophic process occurring in an eye. The revealed set of changes in the lens with its pathological aging includes violation of certain vagosympathetic balance of the autonomic nervous system and its post-operative complications development following even after a successful surgical treatment of age-related cataract – secondary cataract. The results allow for the first time to put forward a new view of the secondary cataract pathogenesis.

Keywords: Secondary Cataract, Age-Related Cataract, Pathogenesis, Autonomic Nervous System, Prediction, Marker

1. Introduction

Today the significant increase of age-related cataract morbidity is marked out all over the world, it being referred to the main cause of blindness in the world and considered as the 'medico-social problem of national importance' [1, 2].

Secondary cataract – the most common postoperative complication, which causes a repeated, significant visual acuity reduction, even after a successful operation on the lens. The incidence of secondary cataract ranges from 3 to 87% [3]. There is even an opinion that if approaches to diagnosis, prevention and treatment of secondary cataract are not improved, it will become the second leading cause of blindness in the world after age-related cataract.

Clinically two main kinds of age-related cataract of a human being – cortical and nuclear – are distinguished. Clinical manifestations of cortical and nuclear kinds of age-related cataract have no great resemblance. They resemble each other only in the time of origin (at the age over 60) and the progressing decrease of visual acuity due to the gradual transparency loss of the lens. Much number of important clinical distinctions of cortical and nuclear kinds of age-related cataract is of great importance. Modern ophthalmology also distinguishes the whole number of important peculiarities of clinical course and character of possible complications in the given kinds of age-related cataract (pseudoexfoliative syndrome, secondary glaucoma, secondary cataract, loss of the vitreous body, instable position of the intraocular lens et al.) [3-6].

Also clinically we mark out the following varieties of secondary cataract: 1 – the posterior wall thickening of the capsule; 2 – Elscnig's balls formation on the posterior capsule surface; 3 – diffusive and local fibrosis of the lens posterior capsule [3].

The findings of important morphological and functional differences between the processes of age-related cortical and nuclear cataractogenesis suggest that exposure to the human lens of such causal factors as age, can be realized through completely different pathogenetic mechanisms, leading eventually to the certain types formation of complications, including postoperative (secondary cataract types) [1, 7-11]. It is revealed the significant differences in the bioamines

supply of the epithelium and the lens material in the formation of postoperative proliferative and fibrous types of secondary cataract in humans [12, 13, 14]. It is revealed the significant flexibility of the epithelial cells phenotype and the lens substances in a human in normal, at its age-related and secondary opacity. This investigation revealed that the changes in the lens cells phenotype depended on the age-related cataract type. Also it was proven that the lens cells immunohistochemical status differences determined the different pathogenesis mechanisms of secondary dystrophic processes in the human crystalline lens [5, 10, 15-17].

The nervous system trophic function is the most important factor in the stability maintaining of tissue differentiation, morphological aspects of which in the lens cells in its secondary opacity formation is virtually unknown. Meaning of nerve regulatory mechanisms disorders in the pathology development cannot be overestimated. It is known that the influence of the nervous system, directly or indirectly is common to all processes in the body [18, 19]. Modern medicine attaches great importance to age-related changes of the autonomic nervous system, which helped to reveal important mechanisms of many age-related diseases [3, 19, 20]. Taking into account that mechanisms of biological regulating functions of various organs and systems are due to action of neurotransmitter mediated biogenic amines, which are an integral part of the diffuse neuroendocrine system of the body [18, 20], the study of the autonomic nervous system functional state in the postoperative different types formation of secondary cataract is an important step in solving the actual health problems on the study of the secondary cataract pathogenesis in humans.

Thus, taking into account the clinical features of different types of secondary cataract, the functional state of the autonomic nervous system of patients in the different types formation of secondary cataract should be considered as specific practical problems of developing pathogenetic methods of its preclinical diagnosis, prevention and therapy.

Objective

To investigate the ophthalmologic status and to investigate the influence of dominating part of vegetative nervous system, following the different types of senile and secondary cataract formation in human and to propose a new method of pre-clinical prediction.

2. Material and Methods

The observations were carried out on 396 lenses of 198 patients of both sexes aged 60-84 years. The research applied methods focused on the study of clinical features of fibrous and proliferative types formation of secondary cataract in humans. The continuous statistical clinical study of patients successfully operated for age-related cataract and applying to the hospital within one year after surgery with signs of secondary lens opacity was carried out during the ophthalmologic examination and retrospective analysis of outpatient cards' data of called patients was conducted. The studied patients were divided into two groups: group A – patients operated on for the cortical type of age-related cataract (78 people); group B – patients operated on for the nuclear type of age-related cataract (120 people). These groups of patients were studied with the biomicroscopy method of the anterior eye to identify the type of age-related and secondary cataract using a slit lamp SL-3G-06. The compulsory condition for this material inclusion in the study was the secondary cataract development in a patient for one year after the successfully performed surgery for age-related cataract. The standard course of operations, provided in the patient signed informed consent, was not impaired.

The studied patients were studied with the following methods of general ophthalmic clinical diagnosis:

1. The visometry method to determine the severity of a patient's central vision using the standard table of optotypes.
2. The biomicroscopy method of the anterior eye to identify the type of age-related and secondary cataract using a slit lamp SL-3G-06.
3. The reactive hyperemia test on the forearm skin to determine the influence degree of the sympathetic and parasympathetic divisions of the autonomic nervous system of the body.
4. The blood pressure measurement and heart rate determination to determine the body hemodynamic type and the Kerdo vegetative index calculation by the formula: Kerdo index = (1-D/p) ×100, where D – the diastolic pressure level, p – the heart rate per minute.
5. The mathematical results analysis of morphological, clinical and experimental study sections, followed by the statistical processing of the obtained information. The resulting digital data were processed statistically. Statistical significance of the results was determined with nonparametric Wilcoxon-Mann-Whitney test.

3. Results and Discussion

3.1. Features of the Autonomic Nervous System Functional State of Patients with Postoperative Different Types Formation of Secondary Cataract

In making test with reactive hyperemia in the forearm skin in 64 patients from the group with *the proliferative type* of secondary cataract the white dermographism expression (83.2%) was mainly revealed. At that in 13 patients (16.9%) mixed dermographism was detected and only in one patient (1.3%) – red.

In making tests with reactive hyperemia in the forearm skin in patients suffering from postoperative *fibrosis of the posterior lens capsule* in 112 examined (93%) red dermographism was revealed. At the same time cases of white dermographism was not fixed. Mixed dermographism in this group of patients was revealed only in eight clinical cases (6.6%).

Blood pressure measurement and heart rate determination, followed by the calculation of Kerdo's vegetation index also found differences in the effects expressivity on the body of

the sympathetic and parasympathetic divisions of the autonomic nervous system (Table 1).

Table 1. *The Autonomic Nervous System Functional State of Patients with Different Types of Secondary Cataract.*

Type of secondary cataract in a human	Proliferative type of secondary cataract (n=78)	Fibrous type of secondary cataract (n=120)
Test with reactive hyperemia in the forearm skin (dermographism)	White – 64 patients (83.2%) Mixed – 13 patients (16.9%) Red– 1 patient (1.3%)	Red – 112 patients (93%) Mixed – 8 patients (6.6%)
Diastolic blood pressure	78.22±1.05 mm Hg	88.33±0.85 mm Hg
Heart rate (pulse)	80.63±1,15 bpm	71.86±0.7 bpm
Hemodynamics type	Hyperkinetic type – 65 patients (84.5%) Hypokinetic type – 13 patients (16.9%)	Hypokinetic type – 120 patients (100%)
Vegetative index of Kerdo	2.79±1.4	– 23.52±1.28

It was found that in patients with *the proliferative type of secondary cataracts*, the heart rate (on the average 80.63±1.15 bpm, P<0.05) significantly exceeded the diastolic blood pressure level (on the average 78.22±1.05 mm Hg, P<0.05) regardless of the systolic blood pressure level. Therefore, among patients with this type of secondary cataract the most common was the hyperkinetic type of hemodynamics, and vegetative index of Kerdo averaged 2.79±1.4 (P<0.05) with positive values in 64 patients (83.2%).

In patients with *the fibrous type of secondary cataracts*, the heart rate (on the average 71.86±0.7 bpm, P<0.05) was significantly lower than the diastolic blood pressure level (on the average 88.33±0.85 mm Hg, P<0.05), and also didn't depend on the systolic blood pressure. Consequently, for the examined patients with fibrosis of the posterior lens capsule the more characteristic was the hypokinetic type of hemodynamics and the vegetative index of Kerdo averaged -23.52±1.28 (P<0.05) with negative values in all 120 patients (100%).

Thus, the results of this study indicate the effects predominance of the sympathetic division of the autonomic nervous system in patients with proliferative type of secondary cataract, in patients with fibrous type of secondary cataract – the effects of the parasympathetic division.

3.2. Pathogenetic Substantiation of a New High-Risk Prediction Method of the Certain Type Development of Secondary Cataract

During the dynamic observation of the postoperative period in patients with the cortical and nuclear types of age-related cataract using methods of standard ophthalmic diagnostics, general clinical diagnosis and the retrospective analysis of outpatient cards data of 198 patients of both sexes aged 60 to 84 years (average age 72±12 years), having the surgical retreatment of age-related cataract of the paired eye, were studied. *Inclusion criteria:* patients of both sexes over 60 years; diagnosis of age-related cataract of cortical or nuclear types in one eye; the secondary cataract formation in the paired eye during the postoperative period in patients undergoing successful operation for age-related cataract; long-lasting remission of concomitant chronic diseases of internal organs; concomitant eye diseases, and the clinical course and treatment methods, which can not cause the lens opacity. *Exclusion criteria:* the exacerbation phase of concomitant chronic diseases of internal organs, their severe uncompensated course, active drug treatment; concomitant eye diseases, clinical course, and treatment methods that are able to independently initiate the lens opacity formation; simultaneous opacity of the lens cortex and nucleus; severe intoxication in history; professional activities related to work in conditions of harmful physical, chemical and biological factors.

Measurement of blood pressure and heart rate followed by the Kerdo vegetative index calculation differences in the expressivity on the body of the sympathetic and parasympathetic divisions of the autonomic nervous system were revealed. In patients with the cortical type of age-related cataract and the proliferative type of secondary cataract the heart rate was on the average 80.63±1.15 bpm (P<0.05), diastolic pressure averaged 78.22±1.05 mm Hg (P<0.05), therefore, in this group of patients, the most common was the hyperkinetic type of hemodynamics. The vegetative index of Kerdo averaged 2.79±1.4 (P<0.05), having positive values in all examined persons, and indicated the predominance of sympathetic effects of the autonomic nervous system.

In patients with the nuclear type of age-related and the fibrous type of secondary cataract the heart rate was on the average 71.86±0.7 bpm (P<0.05), diastolic pressure averaged 88.33±0.85 mm Hg (P<0.05), in this group of patients, the most common was the hyporkinetic type of hemodynamics. The vegetative index of Kerdo averaged -23.52±1.28 (P<0.05), having negative values in all examined persons, and indicated the predominance of parasympathetic effects of the autonomic nervous system.

The results allowed us to develop accessible, not laborious 'a new risk prediction method of certain type development of secondary cataract', contributing to the optimization and reduction of public funding costs for medical measures (patent of the Russian Federation № 2512744, priority of 19.12.2012). The proposed method makes possible to determine the type of dermographism, hemodynamic type and the vegetative index of Kerdo and, therefore, to establish the autonomic nervous system functional state of a patient over 50 years old, the doctor of any specialty with a probability of more than 84% to predict the formation in the given patient the proliferative or fibrotic type of secondary cataract and to carry out its specific targeted prevention.

The comparative analysis showed that in patients of group

1 at the age of 50 years already there was the predominance of white dermographism manifestation and the hyperkinetic type of hemodynamics, values of the Kerdo vegetative index averaged 2.79±1.4 ($P<0.05$), within a year after surgical treatment of the cortical type of age-related cataract the proliferative type of secondary cataract was formed 22 times more frequently (17 patients). In group 2 patients at the age of 50 years there was already the predominance of red dermographism manifestation and the hypokinetic type of hemodynamics, values of the Kerdo vegetative index averaged -23.52±1.28 ($P <0.05$), within one year after surgical treatment of the nuclear type of age-related cataract the fibrous type development of secondary cataract was revealed 10 times more frequently (14 patients).

Confirming the importance of the nervous system trophic influences, the obtained data can serve as a new evidence of regular manifestations of age-related involution of the various divisions of the autonomic nervous system and indicate the effects' predominance of the sympathetic division of the autonomic nervous system in patients with the proliferative type of secondary cataract; in patients with the fibrous type formation of secondary cataract – parasympathetic effects. Consequently, the functional state of the autonomic nervous system of an elderly patient may serve as a marker of pre-clinical risk of postoperative formation of the proliferative or fibrous type of secondary cataract. The revealed patterns between the forming type of secondary cataract in the postoperative period and the features of the patient's vagosympathetic balance allow to consider secondary cataract as a local manifestation of the age-related neurodystrophic process, which is another evidence of the importance of the nervous system trophic function in the fundamental process of stability maintaining of tissue differentiation and tissue metabolism.

The ability to predict the specific type formation of secondary cataract until it occurrence was confirmed by the following clinical examples.

Example 1

Patient E., 70 years old. Diagnosis: Age-related nuclear cataract of the right eye, pseudophakia of the left eye. She underwent the extracapsular extraction of the age-related nuclear cataract of the left eye 11 months ago. Biomicroscopy: the expressed posterior lens capsule fibrosis of the left eye. Visual acuity of the right eye was $0.2–2.0^{D}$ =0.3. Visual acuity of the left was 0.3 (no correction). General clinical diagnostics revealed: red dermographism, the hypokinetic type of hemodynamics (BP = 160/92 mm Hg; pulse = 59 bpm), vegetative index of Kerdo = –56. While analyzing the outpatient card's data using general clinical diagnosis methods from the age of 49 years, in the patient the parasympathetic effects' predominance of the autonomic nervous system over the sympathetic ones was revealed.

Example 2

Patient I., 71 years old. Diagnosis: pseudophakia of the right eye, age-related cortical cataract of the left eye. Biomicroscopy: the right eye – on the surface of the posterior lens capsule and intraocular lens (IOL) multiple Adamyuk-Elshnig pearls were clearly visualized. Visual acuity of the right eye was 0.3 (no correction). Visual acuity of the left eye was $0.4+0.75^{D}$=0.5. General clinical diagnostics revealed: white dermographism, the hyperkinetic type of hemodynamics (blood pressure = 132/8 mm Hg; pulse = 86 bpm), vegetative index of Kerdo = 7. Outpatient card's data analysis showed that from the age of 49 years general clinical methods of diagnosis recorded the steady effects' predominance of the sympathetic division of the autonomic nervous system over the parasympathetic ones.

Thus, for the first time it was found that the formation of secondary cataract of the proliferative type occurs on the background of predominant sympathetic effects of the patient's autonomic nervous system; the fibrous type of human secondary cataract forms in conditions of predominating parasympathetic effects.

Study findings

1. It was found that in patients with white dermographism, the hyperkinetic type of hemodynamics and the Kerdo vegetative index values $\geq$ 2.79±1.4 ($P<0.05$) in 83.2-84.5% of clinical cases the proliferative type of secondary cataract was formed; with red dermographism, the hypokinetic type of hemodynamics and the Kerdo vegetative index values $\leq$ –23.52±1.28 ($P<0.05$) in 93-100% of cases – the fibrous type.
2. It was noted that the vagosympathetic balance change with the effects' predominance of the sympathetic nervous system was preceded by the proliferative type formation of secondary cataract, and the parasympathetic effects' predominance – the fibrous type.

4. Conclusion

The results of the study allowed to propose to implement into clinical ophthalmology practice the original, not laborious risk prediction method of certain type development of secondary cataract, based on the patient's vagosympathetic imbalance revealing in the preoperative period and allowing the doctor with a high probability to predict in a patient over 50 years the increased risk of secondary cataract of the proliferative or fibrous type.

The results allow us to reaffirm a new concept of the secondary cataract pathogenesis: the nervous trophism disturbance, determining the age-related neuro-degenerative process direction of organs and tissues, causes the lens cells, remaining after surgical excision, to pathologic regeneration in previously formed direction (the sympathetic effects' predominance of the patient's vegetative nervous system initiates the development of the cortical type of age-related cataract and the proliferative type of secondary cataract, the parasympathetic effects' predominance – the nuclear type of age-related cataract and the fibrous type of secondary cataract).

All the above indicates the pathogenetically substantiated possibility of creating in the near future, new methods of

differentiated treatment and prevention of human secondary cataract and sets the following actual scientific task of developing these methods.

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