

SURVIVAL RATE OF CORNEAL ENDOTHELIAL CELLS AFTER CATARACT SURGERY WITH A BACKGROUND OF GLAUCOMA

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ABSTRACT

Glaucoma is one of the main causes of irreversible blindness worldwide. Up to 76% of the glaucoma cases are accompanied with complicated cataract. The issue of cataract treatment in glaucoma patients is a difficult task for any surgeon, for the surgical procedure itself can result in a number of complications. One of them is the loss of endothelial cells in the cornea. A decrease in the endothelial cell density in such patients occurs due to long-term use of various hypotensive drops, due to variations of intraocular pressure, as well as due to the surgical interventions themselves. Up to 16.9% of cataract removal cases with a background of glaucoma are accompanied by pronounced post-operative corneal swelling, which leads to an increased risk of losing corneal endothelial cells. The perspective branch of surgical treatment for cataract and glaucoma is the development of a unified algorithm taking into account the individual characteristics of the patient, such as the eye lens clouding, the glaucoma stage, the intraocular pressure, the past surgeries, the hypotensive therapy and the density of corneal endothelial cells.

Keywords: open-angle glaucoma; cataract; surgical treatment of cataracts; endothelial cells.

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BACKGROUND

Glaucoma in Russia, as well as worldwide, is one of the main reasons of incurable blindness and vision-related disability [1]. According to data from the Ministry of Health of the Russian Federation, the number of glaucoma patients in Russia is more than 1.3 mln people. During the 6 years period (2013–2019), the number of glaucoma cases in the country has increased by 10.7% (from 823.8 to 911.7 per 100 thous. of population) [2]. Y.C. Tham et al. [3] are predicting that, by the year of 2040, the number of glaucoma patients worldwide shall reach up to 111.8 mln people.

Glaucoma is a chronic eye disorder, which can be considered as a multifactorial neurodegenerative disease. Glaucoma is characterized by progressive optic neuropathy, pathological changes affecting the fields of view, by death of ganglionic cells in the retina, as well as by the loss of corneal endothelial cells [4]. Absence of complaints in patients, primary diagnostic problems, gradual and progressive visual deterioration, resulting in a decrease in working capacity and disability along with significant expenses both for individual patients and for the whole society — all of

these allows for considering glaucoma as being also a social-economical disease [5].

The percentage of primary open-angle glaucoma is up to 72.3–96.1% of all the glaucoma forms [5]. The incidence of glaucoma combined with cataract varies over a wide range — from 14.6 to 76% [6–10], however, in case of pseudoexfoliative syndrome, the number of such cases increases up to 85% [7, 9, 11–14]. In glaucoma patients, a significantly elevated risk of developing complicated cataract is shown, for both conditions are involution-dependent diseases [11, 15, 16]. In persons aged over 55 years old with the diagnosis of glaucoma and cataract, the probability of developing such a combination is 3 times higher than in persons from the same age group with no ocular diseases [17–20].

GLAUCOMA AS A MULTIFACTORIAL NEURODEGENERATIVE DISEASE

In the development of primary open-angle glaucoma, two mechanisms are involved: the first one affects the anterior segment of the eye, in particular, the structure of the anterior angle, increasing the intraocular pressure,

ВЫЖИВАЕМОСТЬ ЭНДОТЕЛИАЛЬНЫХ КЛЕТОК РОГОВИЦЫ ПОСЛЕ ХИРУРГИИ КАТАРАКТЫ НА ФОНЕ ГЛАУКОМЫ

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АННОТАЦИЯ

Глаукома во всём мире является одной из основных причин необратимой слепоты. До 76% случаев глаукома встречается в сочетании с осложнённой катарактой. Проблема лечения катаракты у пациентов с глаукомой является сложной задачей для любого хирурга, поскольку операция может привести к ряду осложнений. Одним из них является потеря эндотелиальных клеток роговицы. Снижение плотности эндотелиальных клеток у таких пациентов происходит из-за длительного использования гипотензивных капель различных групп, колебания внутриглазного давления, а также в результате хирургических вмешательств. До 16,9% случаев удаления катаракты на фоне глаукомы сопровождается более выраженным послеоперационным отёком роговицы, что приводит к увеличению риска потери эндотелиальных клеток роговицы. Перспективным направлением хирургического лечения катаракты и глаукомы является разработка единого алгоритма, учитывающего индивидуальные характеристики пациента, такие как помутнение хрусталика, стадия глаукомы, внутриглазное давление, хирургический анамнез, гипотензивная терапия, плотность эндотелиальных клеток роговицы.

Ключевые слова: открытоугольная глаукома; катаракта; хирургическое лечение катаракты; эндотелиальные клетки.

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while the other occurs in the posterior segment of the eye, resulting in the development of glaucoma-related optic neuropathy [5].

Ophthalmologists suppose that the progression of cataract in glaucoma is being affected by various factors, which may include the close location of the eye lens, the ligaments, the ciliary body and the eye's draining system, which form the posterior and the anterior ocular chambers. Besides, a certain role belongs to impaired hydrodynamics, blood microcirculation and dystrophic/immunological changes in the ocular tissues [21, 22]. Variations of intraocular pressure, changes in the content of the aqueous humour in the chamber and the associated metabolic changes within the eye structures additionally promote cataract progression, negatively affecting the course of glaucoma and, ultimately, resulting in permanent loss of visual functions [11].

Currently, the attention of the majority of ophthalmologists is attracted by the loss of corneal

endothelial cells associated with glaucoma. The dystrophy of the endothelial layer in the cornea can be also caused by long-term use of glaucoma eye drops, by variations of intraocular pressure and by surgical interventions [23]. As for practical application, the majority of physicians are concerned about the levels of intraocular pressure, for it is the most controllable parameter, which can be effectively modified using medicinal and surgical correction. T. Olsen [24] in 1980 has first reported a mean cell density decrease by 23.1% in case of acute glaucoma comparing to the unaffected eye.

Investigators Y.C. Ko et al. [25] in 2007 have found that the loss of corneal endothelial cells after phacoemulsification surgery is associated with shorter anterior-posterior axis and with the elevation of intraocular pressure within the first 24 hours after surgery, which results in the loss of corneal endothelial cells in 14.5% of the cases. In order to

minimize the damage in corneal endothelial cells, it is of utmost importance to avoid sudden increases of intraocular pressure at the early post-surgery period and to exercise special caution when operating the eyes with the anterior-posterior axis being shorter than 22.6 mm.

Already in the year of 1997, M. Gagnon et al. [26] suggested a hypothesis that the mechanism of damaging the corneal endothelium, just like the damage of the optic nerve, depends on pressure. Glaucoma patients had significantly lower numbers of corneal endothelial cells (2.154 ± 419 cells/mm²) comparing to the control group with no glaucoma (2.560 ± 360 cells/mm²). The authors have demonstrated that the density of corneal endothelial cells is inversely proportional to the mean intraocular pressure. In patients receiving 3–4 glaucoma medications, the number of cells was lower comparing to those undergoing the treatment that employed only 1–2 medications. The number of cells was significantly lower both for primary closed-angle and for primary open-angle glaucoma.

In 2011, the research work by S. Ranno et al. [27] has evaluated the effects of glaucoma eye drops (β -blockers or prostaglandin analogues) on the corneal endothelium. Initially, in glaucoma patients, the density of corneal endothelial cells was 3187 ± 312 cells/mm², however, after two years of using hypotensive drops, the cell density has decreased to 2925 ± 313 cells/mm², including a decrease in the number of nerve fibers in the cornea along with a decrease in the reflectivity of the sub-basal plexus.

S.A. Kandarakis et al. in their descriptive review came to the conclusion that it is preferable to avoid the intake of β -adrenergic blockers Betaxolol and Carteolol at high dosages [28, 29], while patients with Fuchs endothelial dystrophy shall prefer rho-kinase inhibitors [30]. Rho-kinase stimulates the progression of cellular cycle, increasing cell migration, increasing the barrier and pumping functions, also preventing mesenchymal transformation of corneal endothelial cells in patients with Fuchs endothelial dystrophy [31, 32].

Some investigators suggested that the changes in the endothelial cell density were not related to high intraocular pressure [33, 34]. So, Japanese researchers [35] have found that, in patients with primary open-angle glaucoma, a significant decrease was found in the density of corneal endothelial cells, which was not reported in cases of glaucoma with normal pressure. The authors have explained this as being caused by a decrease in the effects of elevated intraocular

pressure. Belorussian investigators P.N. Marchenko and Yu.I. Rozhko [36] have reported a decrease in the density of corneal endothelial cells comparing to the control group of the same age at all the stages of glaucoma, with the statistically significant differences being found at stages II–IV. In 2012 L.A. Deyev et al. [37] have found a direct correlation between the changes in corneal structure and the disease stage. Besides, in 2022 D. Kang et al. [38] have published the results of a research work on the inter-relation between the corneal endothelium parameters and the severity of primary glaucoma. The number of corneal endothelial cells has decreased along with the increase of severity, for in patients with early glaucoma, the density of endothelial cells was 2284 cells/mm², in case of moderate severity disease — 2261 cells/mm², while the severe disease cases were showing the values of 2086 cells/mm² and the difference was statistically significant.

A growing number of surgeons prefer combined interventions performed in one step [39–45]. This approach is attractive, for it allows for simultaneously normalizing the intraocular pressure and improving the vision acuity. At the same time, there are analysis data on the density of corneal endothelial cells in patients with cataract combined with glaucoma. According to the opinion from a number of authors, comparing to single-step combined treatment including the glaucoma surgery and cataract phacoemulsification, two-stage surgery significantly decreases the number of endothelial cells [46–49].

There are research works showing the results of combined surgery for glaucoma using drainages and cataract phacoemulsification [50–53], with the loss of endothelial cell density being more than 30% within 5 years was reported in 27.2% of the patients. In patients undergoing cataract removal and implantation of the CyPass Micro-Stent (Alcon, USA), an epithelial-endothelial dystrophy was found, that was caused by the damage of corneal endothelium. This condition has occurred as a result of the effects caused by the intraocular end of the draining tube, which resulted in cessation of its production [54]. In the research work by E.H. Fang et al. [55], limited reliable evidences were obtained showing that glaucoma surgery associated with the use of long-term implants results in a greater loss of endothelial cell density comparing to cases without using prosthetic appliances.

In patients with glaucoma combined with cataract, the decrease in endothelial cell density results in an increased inflammatory reaction after cataract phacoemulsification [56, 57], which imposes a risk

of corneal swelling and descemetitis of various severity degree. According to data from a number of research works, 16.9% of the patients after cataract extraction had corneal swelling [58, 59]. It is important to note that postoperative swelling is significantly less frequently found in patients with uncomplicated senile cataract (2.7% of the cases). At the same time, mature eye lens clouding was found in 19.3% of all the study patients [13].

T. Dada et al. [60] have arranged a research work on phacoemulsification in patients, focusing on factors which may impair surgical intervention. These factors include a narrow pupil caused by various conditions, such as posterior synechias, atrophy of iris, pseudoexfoliative syndrome, the use of miotics and past history of acute glaucoma onsets. In such cases, additional measure are necessary, in particular, iris retractors or pupil expansion [61]. The cataract removal surgery in glaucoma patients along with such precipitating factors represents a higher risk of damaging the endothelial cells. The research works show that from 17.8 to 51.6% of such surgeries end with intra- or post-operative complications [62].

The acute onset of closed-angle glaucoma plays one of the key roles in changing the number of corneal endothelial cells. M. Chen et al. [63] have found that the density of corneal endothelial cells was inversely related to the duration of an acute onset, but it was not related to demographic and biometric characteristics. The loss of endothelial cell density up to 2271 cells/mm² was reported in patients with a past medical history of acute glaucoma onset comparing to paired eyes, where the cell density was 2458 cells/mm². In patients with diagnosed closed-angle glaucoma with no history of onsets, the density of endothelial cells was 2559±45 cells/mm². The central thickness of cornea and the curvature radius of cornea were not related to earlier acute onset of closed-angle glaucoma. The postoperative corneal swelling was found in 22.85% of the closed-angle glaucoma cases [63].

In 2021, the data were published on the factors affecting the corneal endothelium after selective laser-assisted trabeculoplasty in cases of primary open-angle and closed-angle glaucoma. Based on the research results, the main factors of losing the endothelial cell density after selective laser trabeculoplasty are the age, the initial number of endothelial cells and the shallow anterior chamber for closed-angle glaucoma. It is worth noting that corneal endothelium in cases of primary open-angle glaucoma was recovering within one month, while in closed-angle glaucoma its

damage was persisting for the whole follow-up period. The importance of the research is that it confirms that the obtained data should be taken into account when selecting the algorithm of glaucoma treatment, especially in case of alternative therapy (eye lens/ cataract extraction) for closed-angle glaucoma [64].

The main risk factor for losing the endothelial cell density is more long-term phacoemulsification time. High phacoemulsification energy and high vacuum positively correlate with nuclear density, which defines for the surgeon the correct selection of the viscoelastic gel (solution) and the surgery technique. In 2023, I.A. Loskutov et al. [65] have developed a scale for optimal combining the content of the viscoelastic gel depending on the number of corneal endothelial cells in patients with various stages of cataract. The scale is based on matching various types of viscoelastic gels, which have their own characteristics, specific features, benefits and drawbacks that can significantly affect the surgery results and facilitate the work of the surgeon. With correctly selected viscoelastic gel, the decrease in the number of corneal endothelial cells during the postoperative period is less than 3% regardless of the stage of cataract.

CONCLUSION

The progression of primary open-angle glaucoma negatively affects the structure of cornea and aggravates the age-related conditions, especially in persons aged 55 and older. These factors shall be taken into account when monitoring the patient status and selecting the treatment strategy.

The combination of glaucoma and cataract represents a wide-spread and topical issue in ophthalmology. The development of a unified algorithm of managing the patients with cataract and glaucoma is a promising direction of surgical treatment. Such an approach requires an individual treatment plan taking into account various factors, including the degree of eye lens clouding, the glaucoma stage, the levels of intraocular pressure, the past surgeries, the glaucoma therapy and the density of corneal endothelial cells.

The absence of effective protection method for corneal endothelial cells is a serious problem in developed countries, which results in a significant decrease in the quality of life for the patients. Developing an algorithm of managing the patients with cataract and with a background of glaucoma is the most important task for modern ophthalmology, solving which can improve not only the quality of life for the patients, but also the whole economical aspect worldwide.

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