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Review Article: Vegetative regulation of the lens

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Abstract
The literature data about the lens structure and physiology in norm and pathology are presented. The mechanism of protection for the lens internal environments from ultraviolet damage, based on increased oxidative stress is described. The cholinergic, dopamine, serotoninergic and melatoninergic signaling in lens are described. Present-day pharmacologic and surgical treatment methods of lens are shortly outlined.

Keywords: lens, bioamines, regulation

1. Introduction

It is known, that together with the lens, the cornea forms a single morphofunctional system responsible for the transparency and refractive properties of the eye, which are necessary for normal vision. It also provides protection for the lens internal environments from ultraviolet damage, based on increased oxidative stress. Protection of the internal environment of the lens from ultraviolet damage is achieved due to the high content of various antioxidant enzymes in the surface layers of the cornea, including melatonin. To minimize the extent of oxidative damage to the lens, increased expression of corneal crystallins is also important [1].

The lens is a unique structure that is part of the optical system of the eye, the main functions of which are light transmission and focusing the image on the retina. To perform these functions, the lens must for a long time maintain its main property - transparency. It is achieved due to the fact that the lens does not have blood and lymph vessels, nerve trunks, and the lens is fed by diffusion and active transport through a capsule of nutrients and oxygen dissolved in the intraocular fluid [2].

As is known, from all sides the lens is covered with a thin elastic membrane - a capsule. The capsule consists of collagen, laminin and heparin sulfate mucopolysaccharide, which plays an important role in organizing the matrix structure and maintaining the transparency of the capsule. Under the anterior capsule of the lens is the epithelium. Three cell populations are distinguished in the lens epithelium: - the surface layer of cells containing organelles and providing active transport of ions, amino acids, lipid synthesis precursors to the lens, and facilitated glucose diffusion; - differentiating epithelial cells, which, lengthening, provide the growth of the lens and turn into lens fibers in the equator area; - Mature lens fibers, in which most cellular organelles are absent. Young ribbon-like fibers push the older ones to the center and form around the dense nucleus the elastic cortex of the lens, which is the most metabolically active zone. The intracellular lens compartment can be divided into three functionally distinct radial domains: the epithelium (E), which covers the anterior hemisphere; differentiable fibers (DF), which extend from the surface to 15% of the distance in the lens; and mature fibers (MF) that fill the core. There are differences in membrane transport between domains, and within E and DF there are differences in transport with a location around the lens [3].

The lens fibers are hexagonal prismatic elongated cells. In the cytoplasm of the lens fibers there is a transparent protein of three modifications: α-, β- and γ-crystallins. Alpha crystallins consist of a sequence of 80–100 amino acids. J. Horwitz first described α-crystallins as chaperones — a class of proteins whose main function is to restore the correct native tertiary or quaternary structure of proteins, as well as in the formation and dissociation of protein complexes [4]. In animal experiments, it was shown that the appearance of mutations in genes encoding α-crystallins leads to the development of cataracts.

Fluid balance is very important for accommodating the lens and maintaining transparency. Due to the presence of aquaporins in the lens cells (AQPs), a large amount of fluid is rapidly transferred. Aquaporins (AQP) - a family of transport protein channels embedded in the membrane, widely represented in many tissues of the human body. The architecture of the canal is such (a narrow gap in the center and extensions at opposite ends) that water can penetrate only in the form of a thin chain of molecules connected by hydrogen bonds. Such proteins are capable of carrying out 3x109 water molecules per second per each monomer.

Also, AQP0 performs the function of a structural protein by interacting with specific cytoskeletal proteins of the lens cells - facinin and philensin [5].

Changes in water-salt and energy metabolism are important in the process of formation of opacities in the lens. With cataracts, the microelement, amino acid composition of the lens changes, sodium, calcium, zinc and water accumulate in its tissues, and potassium, aluminum, soluble proteins, sulfur-containing amino acids, ascorbic acid, riboflavin, and cytochrome are reduced. The activity of ATPase, pyruvate phosphokinase, carbonic anhydrase, etc., decreases.

Currently, one of the dominant theories of cataractogenesis is the theory of oxidative stress. In the study of the lenses of patients with cataracts, in contrast to normal age-related changes, oxidation of proteins of not only membranes, but

also of cytoplasm, changes in their configuration with exposure of thiol groups that are normally inside the protein structure, oxidation of methionine, cysteine, and lipid oxidation are detected membranes. In addition, cataracts are characterized by the formation of high molecular weight protein complexes covalently linked by disulfide bonds. Such protein aggregation leads to the fact that the light in these areas is scattered, and the transparency of the lens decreases [3].

Lens regulation

Cholinergic system

During neurogenesis, markers of the cholinergic system are present in the eye and visual cortex of vertebrates. In adult vertebrates, the role of these molecules, including muscarinic acetylcholine receptors (mAChR), in non-accommodative regulation of eye growth is also known. To understand the biological mechanisms triggered by the cholinergic system in these events, the effects of the cholinergic agonist (10 (-4) M carbachol) and antagonist (10 (-4) M atropine) muscarinic receptors on the early development of the lens of chickens were evaluated. It has been shown that these drugs affect the known nervous and pre-nerve functions of cholinergic markers, such as cell signaling during primary induction and receptor regulation of lens cell apoptosis [6].

The relative distribution of acetylcholine (ACh) receptors on the surface of an isolated rabbit ophthalmic lens was determined by the induced changes in the translational short circuit current (I (SC)) and the translicular resistance (R (t)) in seven differentiated parallel zones from the anterior to the posterior pole. It is suggested that ACh receptors that are clearly present in the lens epithelium, which covers about two-thirds of the surface area of the rabbit lens, may be absent in the cells of the posterior fiber, and indicate that the calcium-induced Ca (2+) signal does not propagate throughout the epithelial layer [7].

Both NHLEC cells and lens HLE-B3 cells express muscarinic receptors that cause significant changes in cytosolic calcium levels in response to acetylcholine. Both pharmacological data and QRT-PCR data show that although the M1 subtype predominates in NHLEC, M3 is a major contributor to HLE-B3 cells [8].

Serotoninergic system

Neurotransmitters play an important role in the regulation of cell function of the lens [10]. Serotonin receptors were found in the lens of animals [11], an important role of indolamine in regulating the transparency of the lens has been established [12, 13]. Serotonin reuptake inhibitors increase blood serotonin levels by blocking its reabsorption by nerve terminals. A study of a sample of 6024 patients older than 50 years operated on for cataracts showed that the use of serotonin reuptake inhibitors is associated with an increased risk of secondary cataracts [14]. It is also known that the rapid development of bilateral cataracts is also possible in young patients taking serotonin reuptake inhibitors [15].

As noted in the review, Becker R.A., Bykov Yu.V. (2016), Depression in ophthalmology is the cause and effect of eye diseases [16]. Thus, many patients with depression have both lens cataracts and diabetes mellitus [17].

Depressive conditions are accompanied by premature aging of both individual cells and the body as a whole. Accordingly, age-related lens cataract may develop [18]. The frequency of lens cataract development is statistically significantly correlated not only with the frequency of development of depressive states, but also with the frequency of Parkinson's disease, and this association cannot be explained only by the elderly patients and the increased incidence of these disorders in old age [9]. It cannot be ruled out that mitochondrial dysfunction of dopaminergic neurons can cause free radical damage to noradrenergic neurons, free radical damage to the lens - premature development of cataracts,

Accordingly, surgical treatment of the lens cataract helps normalize circadian rhythms and reduce depression. It was also established that the presence and severity of age-related vision problems (age-related cataract of the lens, presbyopia) correlate with both a general decrease in the quality of life and disability, as well as levels of stress, depression and anxiety, and surgical replacement or phacoemulsification of the lens contributes not only to improvement in quality life, but also the normalization of the mental state of an elderly person, a decrease in depression and anxiety [19, 20].

Melatoninergic system

Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous indolamine that is synthesized from the neurotransmitter serotonin mainly in the pineal gland and is an extremely multifunctional molecule. First of all, it plays a key role in the regulation of circadian rhythms, and also takes part in the functioning of the reproductive, cerebrovascular, neuroendocrine, immune and visual systems. The implementation of the numerous biological effects of melatonin is achieved through its production, in addition to the pineal gland, in a number of organs in situ. Functionally, many cells producing melatonin belong to the so-called diffuse neuroendocrine system - a universal system for adapting and maintaining the body's homeostasis. Within this system, two links of melatonin-producing cells are distinguished: the central one (includes the pineal gland and the visual analyzer), in which the rhythm of melatonin secretion coincides with the light-dark rhythm, and the implementation of its functions is receptor-dependent in nature, and the peripheral lens and all the rest of the cells, where the secretion of the hormone does not depend on illumination, and the functioning is receptor-independent in nature. MT is important in regulating the physiology of the lens. Here, it is also capable of being synthesized de novo, judging by the presence in the lens of rats of two key enzymes for the synthesis of MT enzymes - HIOMT and N-acetyltransferase, the latter demonstrating a clear daily rhythm of its activity. MT controls the morphology and functional state of the cellular protein structures of the lens, in particular crystallin. Obviously, this explains the fact that repeated administration of MT to animals in a wide range of doses can, although in different ways, affect the size and weight of the lens. Regular prophylactic administration of MT (5 mg / kg), limiting the manifestations of oxidative stress, prevents such violations and restores the optical properties of the lens [21].

The precursor of serotonin, melatonin, is highly effective in preventing the occurrence of lens degeneration (opacification) resulting from damage to the lens proteins of newborn rats by free radicals. Moreover, the protein-protective effects of melatonin are comparable to those of glutathione (one of the most powerful antioxidants).

Therefore, melatonin also has protective properties with respect to free-radical damage to the lens and other structures of the eye [22].

Melatonin exhibits its properties by interacting with the family of G-protein-binding receptors of M1 and M2 subtypes. These receptors are found in the lens, in all layers of the retina, and are also found in the cornea, ciliary body, choroid and sclera.

The biological membrane of the lens fiber is a barrier that separates the lens proteins from the intercellular substance and maintains a constant medium inside the cell. Damage to the membrane can be associated with various external and internal factors, including aging, as a result, the control of biochemical processes is disrupted, which leads to pathological changes in the cell. Changes in lipids and proteins in the lens with age go parallel and interconnected. It can be assumed that the degradation of membranes, damage to lipids, and then a change in the protein of the fibers primarily lead to the appearance of turbidity.

The ability of the lens to regenerate has been proven, but its usefulness in different species of living organisms is not the same. An example of this process in humans is secondary cataract, which develops even after a successful operation for age-related cataracts. The cause of this postoperative complication is based on a violation of the nervous trophism of the tissues that make up the organ, which causes its cells not to reparative but to pathological regeneration.

Non-Cholinergic system

Dopamine. It was shown that the incidence of crystalline lens cataract and age-related macular degeneration of the retina pairwise statistically significantly correlate not only with the incidence of depressive states, but also with the incidence of Parkinson's disease, and this association cannot be explained only by the elderly patients and the increased incidence of these disorders precisely in advanced age [9]. It cannot be ruled out that mitochondrial dysfunction of dopaminergic neurons can cause free radical damage to noradrenergic neurons, free radical damage to the lens - premature cataract development, and free radical damage to the retina - accelerated age-related macular degeneration [9].

Cells of the central part of the anterior capsule of the lens have less pronounced luminescence (catecholamines - 0.0049 ± 0.0004 mv, serotonin - 0.0193 ± 0.0012 mv) in comparison with cells of its growth zone (catecholamines - 0.0097 ± 0.0007 mv, serotonin - 0.0228 ± 0.0014 mv). With the formation of age-related cortical cataracts, a significant increase in serotonin levels was found. The level of catecholamines and serotonin in the cells of the peripheral part of the anterior lens capsule with a cortical type of cataract is 0.0105 ± 0.0007 mv [10].

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Conclusion

Comparing the neurotransmitter support of the processes of formation of different types of secondary cataract, it was found that the formation of its proliferative species was initiated by a significant increase in the concentration of histamine, catecholamines and serotonin in the epithelium of the lens, to initiate the fibrous type of secondary cataract, a significant increase in the level of serotonin amines in the lens epithelium, a moderate increase and the immutability of normal histamine levels. Thus, the study revealed significant differences in the bioamine supply of lens epithelial cells during the formation of different types of age and secondary cataracts, which confirms the previously put forward assumption that the pathogenetic mechanisms of formation of different types of secondary cataracts in humans in the postoperative period.

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