Austin Journal of Clinical Ophthalmology

Austin Publishing Group

Open Access Full Text Article

Editorial

Modulation of Aqueous Humor Secretion

Chi-wai Do*

School of Optometry, The Hong Kong Polytechnic University, Hong Kong

***Corresponding author:** Chi-wai Do, School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong

Received: March 05, 2014; **Accepted:** March 10, 2014; **Published:** March 13, 2014

Glaucoma is a severe ocular disease that ranks as the second leading cause of blindness in the world. Glaucoma is typically characterized by a progressive loss of retinal ganglion cells, leading to irreversible optic neuropathy. Because of the absence of noticeable symptoms at the early stages of disease, glaucoma often results in substantial vision loss prior to diagnosis and treatment. Frequently, elevated intraocular pressure (IOP) is a major risk factor for glaucoma and perhaps the only treatable risk factor. Thus far, lowering IOP is the only treatment regimen documented to be effective in delaying the onset and progression of glaucomatous blindness. The ocular hypotensive therapy can be achieved primarily by pharmacological agents and if the prognosis is not satisfactory, surgical intervention will be required.

The level of IOP is governed by a dynamic balance between aqueous humor production (inflow) and aqueous drainage (outflow). Most of the anti-glaucoma pharmacological agents act by lowering IOP through suppression of aqueous inflow or facilitation of aqueous outflow. Currently, no pharmacological treatment is proven to be effective in preventing glaucomatous optic neuropathy other than lowering IOP. Physiologically, aqueous humor is secreted by a dual-layered ciliary epithelium comprising the pigment ciliary epithelium (PE) and non-pigmented ciliary epithelium (NPE). Many ion transporters and channels present in this epithelium are involved in driving a net chloride secretion across the ciliary epithelium which has been recognized as a major force for driving aqueous humor production. At least three major transport steps are involved in the transepithelial transport, namely chloride uptake by the PE cells, chloride diffusion from PE to NPE cells and finally chloride release from the NPE cells to posterior chamber of the eye. It has been suggested that gap junctions linking PE and NPE cells, as well as chloride efflux by NPE cells limit the rate of aqueous humor formation. Despite the success of identifying the basic ion transport mechanisms across the ciliary epithelium, the precise cellular pathway(s) for regulating aqueous humor secretion are still elusive. My research has been trying to unravel the signaling cascades and regulatory mechanisms for controlling the rate of aqueous inflow and IOP.

Cyclic adenosine monophosphate (cAMP) is an intracellular second messenger that modulates aqueous humor secretion, however, its precise physiologic significance remains controversial. For example, beta-adrenergic agonists which stimulate endogenous cAMP production as well as beta-adrenergic antagonists cause parallel hypotensive effect in both experimental animals and human. Clinically, beta-adrenergic antagonists have been commonly used to treat patients with glaucoma. Whether or not the effects of these antagonists are mediated through a cAMP-dependent pathway is unknown. The complexity of the responses reported in the literatures can be due to variations among animal species, as well as multiple effects elicited by agonists and antagonists on the aqueous humor dynamics. Given the confounding role of species variation in aqueous humor secretion that may hinder efforts to relate experimental findings to the human, it is crucial to compare data obtained from different mammalian species. In our research, we use porcine eyes as pig is considered a good animal model to mimic human physiology and diseases. We have adopted a comprehensive and integrated approach to study the effects of beta-adrenergic modulators and cAMP-stimulating agents on several parameters of aqueous humor dynamics using ciliary epithelial cells, excised ciliary epithelia and arterially-perfused eyes. The use of isolated ciliary epithelial cells and excised ciliary epithelia can exclude the possible influences from outflow pathway. Simultaneous measurements of the aqueous human formation and IOP using whole-eye perfusion model allow for a better understanding of how these drugs affect the rate of aqueous humor formation and its relationship to IOP. We also compare the effects of drugs (e.g. beta-adrenergic agonists and antagonists) as well as hormones that have been shown to be associated with cAMP signaling cascades to determine whether the hypotensive responses are mediated by cAMP- or non-cAMP-mediated pathways. Furthermore, the time course of the responses among the cell couplet, intact epithelium, and whole-eye preparations will be compared so that we can determine the sequential cascades. Our recent results show that cAMP, when added to the aqueous side, induces a significant increase in short-circuit current. The cAMP-triggered responses can be abolished by the pretreatment of either heptanol or bathing chloride substitution, indicating that gap junctions linking PE and NPE cells as well as NPE-cell chloride channels are the possible sites of action exerted by cAMP. Consistent with these results, cAMP triggers a sustained increase in gap junction permeability across porcine PE-NPE cell couplets. Moreover, cAMP stimulates whole-cell chloride currents in native NPE cells. These results suggest that cAMP increases the net chloride secretion across the ciliary epithelium by increasing the gap junction permeability between PE and NPE cells, as well as stimulating the chloride channels at the basolateral surface of NPE cells. The elucidation of these signaling cascades will not only advance our understanding of the regulation of aqueous inflow, but also shed light on the development of new anti-glaucoma agents.

Citation: Do C. Modulation of Aqueous Humor Secretion. Austin J Clin Ophthalmol. 2014;1(3): 1013.