Expanded Abstract

Aqueous humour is a clear fluid that nourishes the anterior segment of the eye. It is secreted by the ciliary epithelium and drains from the eye via the conventional, uveoscleral pathway, and lymphatics. The imbalance between secretion and drainage of this fluid results in increased intraocular pressure, a major risk factor for glaucoma, a leading cause of blindness. Aqueous dynamics are regulated by the sympathetic and parasympathetic nervous system, via adrenergic and cholinergic systems, respectively. It is well established that the sympathetic system modulates the lymphatic function in other organs. However, lymphatics from the eye remain to be explored. Currently, all glaucoma medications aim to reduce IOP by decreasing aqueous production or increasing outflow via conventional and uveoscleral pathways. However, the effects of glaucoma medications on the lymphatic pathway are not yet known. Using a non-invasive in vivo photoacoustic imaging approach combined with a near-infrared tracer in mice, the effect of two widely used glaucoma medications, timolol and brimonidine was quantified. Timolol, a nonselective β-adrenergic blocker, significantly reduces lymphatic drainage from the eye. In contrast, brimonidine, an α2-adrenergic agonist significantly increases lymphatic drainage from the eye. Finally, lymphatic channels positive for podoplanin in the ciliary body and conjunctiva were also positive for the α2A-, β1- and β2-adrenergic receptors. These findings provide the first evidence for adrenergic control of lymphatics in the eye. Since both timolol and brimonidine are widely used to treat glaucoma, the observations that timolol reduces lymphatic drainage from the eye and that brimonidine increases it may be relevant to understanding glaucoma care to prevent blindness.