Bunazosin, a Selective $\alpha_1$-Adrenoceptor Antagonist, as an Anti-glaucoma Drug: Effects on Ocular Circulation and Retinal Neuronal Damage

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ABSTRACT

Bunazosin hydrochloride is a potent and selective $\alpha_1$-adrenoceptor antagonist that has been clinically used both as a systemic antihypertensive as well as an ocular hypotensive drug. In a number of studies, we have examined some effects of bunazosin hydrochloride that might indicate its potential as an anti-glaucoma drug. In normal rabbit eyes, topically instilled bunazosin hydrochloride reached the posterior retina by local penetration at concentrations sufficient to attenuate the phenylephrine- or endothelin-1 (ET-1)-induced constriction of retinal arteries. Furthermore, bunazosin hydrochloride improved the impairment of optic nerve head (ONH) blood flow, the prolongation of visual-evoked potentials (VEP) implicit time, the enlargement of the optic disk cup, and the decrease in the number of retinal ganglion cell layer cells induced by repeated injections of ET-1 in rabbits. Topically instilled bunazosin hydrochloride improved the reductions in ONH capillary blood flow and VEP amplitude induced in rabbit eyes by nitric oxide synthase inhibition. In rat primary retinal cultures, bunazosin hydrochloride reduced glutamate-induced neuronal cell death, presumably through a Na$^+$ channel blocking effect. In healthy humans, topically instilled bunazosin hydrochloride reportedly increases blood velocity in the ONH, retina and choroid, without significantly altering either blood pressure or heart
rate. These results indicate that bunazosin hydrochloride exerts both an improvement effect within the ocular circulation and a direct neuroprotective effect. Hence, bunazosin hydrochloride may be useful as a therapeutic drug against ischemic retinal diseases (such as glaucoma and retinal vascular occlusive diseases) that are associated with disturbances of the ocular circulation.