GUEST EDITORIAL

GLAUCOMA, HYPERTENSION, AND MARIJUANA

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The glaucomas are characterized by increased intraocular pressure resulting in damage to the optic nerve. Concomitant ocular pathology that can frequently result in increased pressures are due to: (1) fibrovascular membranes; (2) inflammatory closure by synechiae; (3) trauma, either social or surgical; (4) trabecular obstruction (blood, macrophages, alpha-chymatrypsin); (5) lens-induced glaucomas; and (6) corneal endotheliopathy-atrophic iris syndromes. The primary glaucomas are either of the open or closed-angle varieties. Primary open-angle glaucoma, the most common variety, is characterized by (1) increased pressures within the eye (increased ocular tension, OT); (2) pressure-related visual field defects[1,2]; and (3) optic nerve pallor and atrophy.

No good epidemiological data exist on the prevalence of open-angle glaucoma. In 1978 a cohort study from Framingham, Massachusetts, suggested that 3 percent of this 99.4 percent Caucasian population has open-angle glaucoma.[3] Although there are no data on blacks, the National Eye Institute suggested that data retrieved from a model reporting area (22 states in 1970) suggested that open-angle glaucoma blinded three to five times more nonwhites than whites.[4]

Open-angle glaucoma treatment traditionally has been medical in the United States. Data gathered over ten years in Cambridge, England, have inferred that primary surgical interventions may be more effective in open-angle glaucoma.[5] The medical therapies include eye drops (miotics, aqueous inflow inhibitors) and systemic carbonic anhydrase inhibitors. Topical beta adrenergic blockers (timolol), epinephrine and its pro-drug (dipivefrin hydrochloride) all lower ocular tension by decreasing aqueous formation. The miotics, however, lower ocular tension by increasing aqueous outflow from the anterior chamber. Blacks respond less favorably to miotics,[6,7] epinephrine[8] and timolol,[9] than whites. Similarly, surgical procedures designed to lower ocular tension by aqueous drainage from the anterior chamber (filtering operations) have significantly higher failure and complication rates among blacks than in whites.[10-12] Therefore, any ocular hypotensive agent should receive clinical trials not only in these various types of glaucomas, but also in various population subsets.

Mexican marijuana, containing 1.8 to 2.8 percent Δ9 tetrahydrocannabinol (Δ9 THC), has consistently been shown to lower both intraocular pressure and blood pressure in both open-angle glaucoma[13] and heterogenous glaucoma.[14,15] The decreased ocular tension results from decreased aqueous production mediated through the pressure-dependent portion of aqueous formation (ultrafiltration). Characteristically, marijuana induces a tachycardia within 5 to 10 minutes, which is invariably followed by decreased blood and intraocular

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pressures. The maximum ocular hypotensive effect of 25 to 30 percent occurs between 60 and 90 minutes.

Cardiovascular changes generally return to baseline with 3½ hours; but ocular hypotensive responses often persist longer.[15] Sudden precipitous falls in systolic blood pressure have occurred in 18 percent of marijuana-naive subjects inhaling Mexican marijuana. These syncopal-like episodes were characterized by sudden falls in blood pressure, lightheadedness, a faint, and thready pulse often accompanied by nausea and bradycardia. Positioning the subject in a reclining position invariably alleviated these signs. This postural hypotension was not related to plasma Δ9 THC levels, previous marijuana experience, or inhalation techniques.[16] A similar episode of postural hypotension and dysphoria occurred 1 hour after the ingestion of 5 mg of oral Δ9 THC in a 52-year-old black woman with both essential hypertension and open-angle glaucoma. Although our studies would indicate that 5 mg of oral Δ9 THC are inactive in heterogenous glaucoma, this case may represent a certain sensitivity of the hypertensive glaucoma patient to the peripheral dilatory effects of Δ9 THC.[17]

Hypertensive subjects have consistently been shown to receive a more substantial lowering of the blood pressure and intraocular pressure when compared to normotensive glaucoma populations.[18,19] Similarly, topical 0.1 percent Δ9 THC in light mineral oil vehicles decreased the systolic blood pressure 12.8 mmHg (in 8 hypertensive glaucoma subjects) after unilateral topical applications.[19] The maximum hypotensive effect in both treated and untreated eyes after unilateral topical Δ9 THC has repeatedly been shown to occur at 6 hours with significant ocular hypotensive effects persisting for 8 to 12 hours in both animal and human studies.[19,20] It is known that the contralateral decrease of ocular tension in fellow untreated eyes after topical Δ9 in light mineral oil vehicle results from decreased aqueous production.[21] Less well demonstrated are the possible cardiac and/or central nervous system mechanisms involved in aqueous dynamics. Systemic Δ9 THC therapies invariably produce a decreased perfusion pressure to the eye. This decreased perfusion to an already damaged optic nerve may not be of long-term benefit to glaucoma victims, although it may well *treat* their concomitant essential hypertension. Therefore, other cannabinoids which may exert a pressure-lowering effect locally within the eye should become the focus of present glaucoma research.

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