A Useful Mouse Model of Glucocorticoid-Induced Ocular Hypertension

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Glucocorticoid (GC)-induced ocular hypertension and iatrogenic glaucoma still are a major side effect associated with GC therapy, especially with the increased use of intravitreally administered GCs for a variety of retinal conditions. In this issue, Overby and colleagues¹ investigated GC-induced ocular hypertension in mice. They built on the success of Whitlock and coworkers,² who previously reported GC-induced ocular hypertension in mice by systemic delivery of the potent GC dexamethasone (DEX) using osmotic minipumps. Overby et al.¹ showed that systemic DEX delivery significantly elevated IOP (by approximately 3 mm Hg), which correlated with a 52% reduction in the aqueous outflow facility. They also showed DEX-induced changes in the extracellular matrix of the trabecular meshwork (TM) that were very similar to the histologic changes observed in humans with steroid-induced ocular hypertension and POAG, including increased fibrillar material in juxtacanalicular tissue, plaque-like sheath material surrounding elastic fibers in the TM, and myofibroblasts on the outer wall of Schlemm's canal. It should be noted that an important side effect of this route of DEX administration was considerable weight loss in a significant percentage of animals during the 4 weeks of systemic exposure. This will be an extremely useful animal model to study the molecular mechanisms responsible for GC-induced ocular hypertension as well as POAG. The power of mouse genetics will allow determination of the involvement of specific genes and signaling pathways in this model. In addition, there are significant differences in human responsiveness to GC-induced ocular hypertension, so a mouse strain survey may help uncover the mechanisms responsible for these differences in GC sensitivity.

References

1. Overby DR, Bertrand J, Tektas O-Y, et al. Ultrastructural changes associated with dexamethasone-induced ocular hypertension in mice. *Invest Ophthalmol Vis Sci.* 2014;55:4922–4933.
2. Whitlock NA, McKnight B, Corcoran KN, Rodriguez LA, Rice DS. Increased intraocular pressure in mice treated with dexamethasone. *Invest Ophthalmol Vis Sci.* 2010;51:6496–6503.