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Steroid Induced Glaucoma

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1. Introduction

Increased intraocular pressure and glaucoma following corticosteroid therapy are well known issues for the ophthalmologist for more than 50 years. Corticosteroids use has gained popularity in ophthalmology as anti-inflammatory and anti-allergic agents but can have important consequences and should be used only with judicious monitoring. The therapeutic use of corticosteroids can lead to the development of ocular hypertension and iatrogenic open-angle glaucoma in susceptible individuals. It can occur in any age group, either gender and from steroid therapy for any ocular or systemic disease and by any route of administration: topical, systemic or inhaled.

2. Epidemiology

About one in every three people is considered a potential "steroid responder", but only a small percentage will have a clinically significant elevation in intraocular pressure. 5-6% of the normal population develops a marked increase in intraocular pressure of more than 31 mmHg after 4-6 weeks of topical corticosteroids therapy. 33% are moderate responders (elevation of 6-15 mmHg) and the remaining are considered non responreds (less than 6mmHg of elevation in intraocular pressure). Although approximately 30%–40% of the normal population are “steroid responders” (i.e., develop reversible steroid-induced ocular hypertension), most of primary open angle glaucoma patients or with a family history are steroid responders. Normal individuals who are steroid responders are at higher risk for subsequently developing primary open angle glaucoma. In one study, high corticosteroid responders (intraocular pressure greater than 31 mm Hg during dexamethasone administration qid for 6 weeks), 13.0% developed glaucomatous visual field loss during the follow-up period of 5 years. In steroid induced glaucoma patients, glaucoma is triggered by steroid treatment, and intraocular pressure will not decrease after cessation of steroid application. Thus, steroid induced glaucoma patients necessitate anti-glaucoma medications to control intraocular pressure. Steroid responsiveness appears to be heritable, however low concordance of pressure response in monozygotic twins to topical testing may indicate a limited role for a genetic basis. In addition highly myopic patients and diabetic patients have a higher rate of elevated intraocular pressure response to topical steroids.
Age is also an important factor. In pediatric patients taking oral prednisone for inflammatory bowel disease 32% were steroid responders. When children younger than 10 years of age where treated with topical instillation of dexamethasone, marked elevation in

intraocular pressure was noted. A dose-dependent hypertensive pressure response occurs more frequently, more severely and more rapidly in children than in adults.

3. Pathophysiology

There have been reports suggesting that endogenous cortisol may play a role in the pathogenesis of primary open angle glaucoma. Excess endogenous production of glucocorticosteroids (Cushing's syndrome) can also cause increase in intraocular pressure.
Glucocorticosteroids alter several trabecular meshwork cellular functions including inhibition of cellular proliferation, migration, phagocytosis, and increased cell and nucleus size. Glucocorticosteroids also increase extracellular matrix synthesis and decrease its turnover.
Many mechanisms have been proposed to explain the elevated intraocular pressure in response to glucocorticosteroids. One hypothesis is that glucocorticosteroids protect the lysosomal membrane and thus inhibit release of hydrolases responsible of depolimerization of glycosaminoglycans. Accumulated glycosaminoglycans in the ground substance of the outflow pathways retain water and narrow the trabecular spaces, causing increase in outflow resistance. In steroid-induced glaucoma there is also an increase in fine fibrillar material in the subendothelial region of Schlemm's cannal. These fibrils are deposited underneath the inner wall endothelium. The main finding in steroid-induced glaucoma is an accumulation of basement membrane-like material staining for type IV collagen. These accumulations are found throughout all layers of the trabecular meshwork.
There are multiple isoforms of the glucocorticoid receptor (GR) a ligand-dependent transcriptional factor that activates or represses gene transcription. GRα is the ligand binding form of the receptor that is responsible for the physiologic and pharmacological effects of glucocorticosteroids. Most of the physiological and pharmacological effects of glucocorticosteroids are directly mediated by GRα. GRα resides predominantly in the cytoplasm in the absence of ligand as a multiprotein heterocomplex that contains Hsp 90, Hsp 70 and other proteins. Steroid binding to GRα causes a conformation change and activation of the receptor. Activated GRα can alter gene expression via GRE-dependent (classical) and GRE-independent (nonclassical) mechanisms. In the GRE-dependent pathway activated GRα translocates to the nucleus along microtubules. GRα bind to specific palindromic DNA sequence (GRE) as a homodimer on the promoter region of target genes to induce transcription. In addition, GRα functions as a negative regulator of transcription in a specific subset of genes that contains a negative GRE. The GRE-independent pathway is an additional way to inhibit gene expression. GRα physically interacts with other transcription factors to prevent them from binding to their response elements of genes that encode for proinflammatory cytokines. The anti-inflammatory and immune suppression are mediated via this GRE-independent pathway. GRβ is an alternatively spliced form of the receptor, that resides in the nucleus, which lacks the conventional ligand binding domain, does not bind glucocorticosteroids, and acts as a dominant negative regulator of glucocorticosteroids activity. Increased expression of GRβ appears to be responsible for unresponsiveness to anti-inflammatory therapy for asthma, inflammatory bowel disease rheumatoid arthritis and ulcerative colitis. Recent work has shown that glaucomatous trabecular meshwork cells have lower levels of GRβ compared with normal trabecular meshwork cells, and this appears to be responsible for increased glucocorticosteroids sensitivity in the glaucomatous trabecular meshwork cells. In primary open angle glaucoma

an abnormal accumulation of dihydrocortisol may potentiate exogenous glucocorticosteroids activity and increased intraocular pressure.

Changes in protein synthesis have also been implicated in steroid induced glaucoma. *MYOC* gene, located on chromosome 1, encodes a secretory glycoprotein of 504 amino acids named Myocilin, and is the first gene to be linked to juvenile open-angle glaucoma and some forms of adult-onset primary open-angle glaucoma. The gene was identified as an up regulated molecule in cultured trabecular meshwork cells after treatment with dexamethasone and was originally referred to as trabecular meshwork-inducible glucocorticoid response (*TIGR*). Interestingly, the profile of *MYOC* up regulation by dexamethasone is in a dose- and time-dependent manner very similar to the course of development of steroid induced glaucoma. This led many investigators to believe that an increased *MYOC* level is a cause of glaucoma. However, a putative association between *MYOC* induction and primary open angle glaucoma has not been firmly established.

Glucocorticosteroids inhibit prostaglandin synthesis by trabecular cells. Prostaglandins E_2 and F_{2a} normal function is to lower the intraocular pressure by increasing the outflow facility. Endothelial cells of the trabecular meshwork can act as phagocytes of debris. Glucocorticosteroids can suppress phagocytic activity causing accumulation of debris in the trabecular meshwork and decrease in outflow facility.

In a study on rabbit eyes, after topical treatment with dexamethasone, Transmission electron microscopy showed increased abnormality of nucleus of the trabecular meshwork cells, microfilament and microtubules among interstitial cells also increased, cytoplasmic vacuolation, rough endoplasmic reticulum expansion, as well as an increase in intercellular amorphous material. The mechanism of elevated intraocular pressure is thought to be increased aqueous outflow resistance owing to an accumulation of extracellular matrix material in the trabecular meshwork (fig 1).

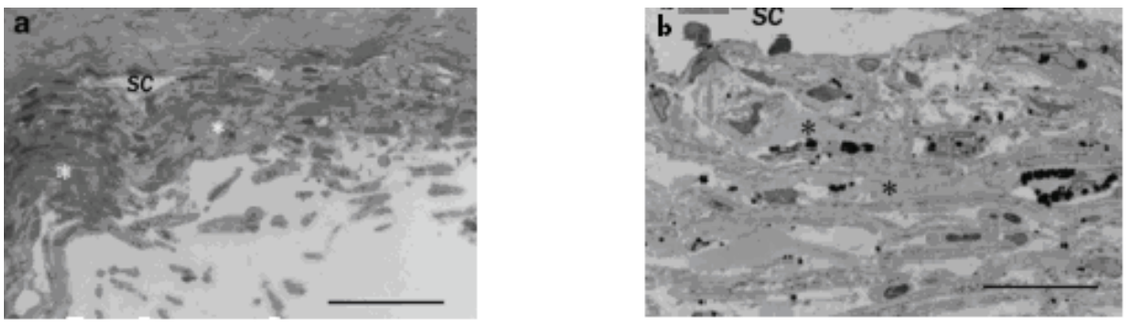


Fig. 1. Light microscopic pictures of the trabecular meshwork from steroid-induced glaucoma (SG). a) (Right eye in case 1), b) (Case 2): Schlemm's canal (SC) is open. The intertrabescular spaces in the outer part of the TM are filled with the homogeneous extracellular matrix (ECM) (asterisks). Azure II staining. Scale bars indicate 50 µm for a) and 20 µm for b)

Effects of Glucocorticosteroids are mediated by the Glucocorticosteroids receptor, which is a ligand-dependent transcription factor altering the expression of trabecular meshwork genes. Glucocorticosteroids increase the expression of extracellular matrix (collagen, fibronectin, laminin), proteinase inhibitor genes (Serpina3) and decreased expression of proteinase genes (MMP1, TPA). Altered expression of cytoskeletal genes (ACTA2, FLNB, and NEBL) may be associated with Glucocorticosteroids mediated reorganization of trabecular meshwork cell

microfibrils and microtubules. Glucocorticosteroids reorganizes the actin cytoskeleton to form cross-linked actin networks (CLANs) in cultured trabecular meshwork cells, and is reversible after Glucocorticosteroids withdrawel. In addition Glucocorticosteroids alters microtubules to form microtubule tangles.

4. Routes of corticosteroid administration

4.1 Topical route

Topical route includes ocular drops and ointments. Of various routes of administration, topical therapy most commonly induces elevated intraocular pressure and correlates with the duration and frequency of administration. Dexamethasone and prednisolone increase intraocular pressure more frequently than loteprendol (Lotemax), fluorometholone (FML), rimexolone (Vexol) or hydrocortisone. Fluorometholone (FML) in particular is less likely to increase intraocular pressure but is also a less potent steroid (table 1). Rimexolone has a low intraocular pressure elevating potential comparable to that of fluorometholone in adults. The chemical structure is responsible to the lower propensity to increase intraocular pressure of some steroids. Loteprendol is a site-active steroid that contains an ester rather than a ketone group at the C-20 position, rendering de-esterification to an inactive metabolite. It is highly lipid-soluble, with enhanced penetration into cells. Loteprendol appears to have an improved safety profile compared with ketone corticosteroids. Fluorometholone is deoxygenized at the C-21 position. Rimexolone lacks a hydroxyl substituent at the C-21 position. It has lower aqueous solubility and increased lipophilicity. It appears that the potency of topical steroids is directly correlated with the propensity to elevate intraocular pressure. Intraocular pressure elevation almost never occurs in less than 5 days and rarely in less than 2 weeks of steroid treatment. However, late rise in ocular pressure is not uncommon, even if intraocular pressure has been within normal limits during a treatment course of 6 weeks.

4.2 Intraocular route

Before the advent of anti VEGF, intravitreal steroid injections have been used largely in the treatment of exudative age related macular degeneration, chronic cystoid macular edema, proliferative diabetic vitreoretinopathy, retinal vascular occlusion and chronic uveitis. Rise in intraocular pressure is dependent on dose, presence of aphakia or pseudophkaia and a history of vitrectomy, facilitating penetration of the drug into the anterior segment. Intraocular pressure may rise in 30-50 % of patients as soon as 1-4 weeks after intravitreal injection of triamcinolone acetonide (Kenalog) and often returns to baseline several months after injection. It is advisable to perform a trial of topical prednisolone acetate before intravitreal triamcinolone acetonide injection is performed.

Fluocinolone acetonide intravitreal implants are an effective therapy for non-infectious posterior uveitis. However, patients receiving this treatment are at high risk for development of vision-threatening increased intraocular pressure. Therefore, patients treated with these implants should have frequent intraocular pressure monitoring. Intractable glaucoma may necessitate removal of the depot by pars plana vitrectomy to lower intraoculare pressure. In the SCORE study grid photocoagulation and repeated injections of triamcinolone acetonide 1 or 4 mg seemed to be equally effective in producing improvements in best corrected visual acuity in patients with macular edema due to branch retinal vein occlusion. 41% of patients treated with triamcinolone acetonide 4 mg initiated

intraocular pressure lowering medications during the 12 months study. In patient with central retinal vein occlusion 35% of the patients receiving 4 mg triamcinolone acetonide initiated glaucoma medications. Ozurdex is a slow release intravitreal implant of dexamethasone currently under clinical trials for the treatment of macular edema in retinal vein occlusion disease. It appears that the dexamethasone implant is well tolerated, producing transient, moderate and readily managed increase in intraocular pressure in less than 16% of eyes.

4.3 Periocular route

Subconjunctival, sub-Tenon and retrobulbar injections of triamcinolone acetonide may cause dangerous and prolonged elevation of intraocular pressure because of their long duration of action. Surgical excision of sub-Tenon triamcinolone acetonide deposit should be considered if the primary treatment for steroid-induced glaucoma is refractory to medical treatment.
The application of topical corticosteroids to the eyelids and periorbital region, in the treatment of atopic dermatitis, even over long periods of time, was not related to the development of glaucoma or cataracts.

4.4 Systemic route

Systemic administration includes ingestion, inhalation and nasal spray. It is less likely to cause intraocular elevation. However, intraocular pressure may rise weeks to years after treatment. When administrated concurrently with topical steroids it may have an additive effect and higher intraocular pressure than a single route.
Intranasal corticosteroids have become a gold standard in therapy for allergic rhinoconjunctivitis and recent evidence indicates that may be effective at alleviating ocular symptoms as well. Intranasal corticosteroids are absorbed systemically in small measurable amounts. Some studies suggest a relationship between intranasal steroids and increased intraocular pressure.
Aerosolized drugs delivered with a facemask may inadvertently deposit in the eyes, raising concerns about ocular side effects. Inhaled corticosteroids have been associated with an increased risk of skin thinning, bruising, cataracts and possibly glaucoma in adults. The risks increase with advanced age, higher doses, and longer duration of use. In children, the risks of cataracts and glaucoma were negligible with inhaled corticosteroids, whether a mouthpiece or a mask interface was used. It is not known whether exposed children will have increased risks from inhaled corticosteroids later in life. Therefore, it is wise to avoid face and eye deposition when possible, to use the minimally effective dose and a regular follow up of intraocular pressure.

4.5 Endogenous route

Elevated blood levels of corticosteroids of endogenous production, as seen in adrenal hyperplasia or neoplasia (Cushing syndrome) can also cause increase in the intraocular pressure. After adrenalectomy, increased intraocular pressure may retune to normal values

5. Clinical course

An increase in intraocular pressure may occur days to weeks and even months after the administration of steroids. The increase in intraocular pressure depends on potency, penetration, frequency and route of administration. Individual susceptibility, older age and

ocular disease are also important factors. An acute presentation may occur after intense systemic steroid therapy. Patient may complain on pain, decreased vision and conjunctival hyperemia. In infants the clinical picture may resemble that of congenital glaucoma. Signs are tearing, Descement's membrane breaks, corneal edema, enlarged corneal diameter, elevated intraocular pressure and optic disc cupping. Unlike congenital glaucoma, the anterior chamber angle is normal.

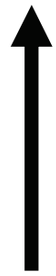
Potency	Steroid	Glaucoma risk
High	Betamethasone Clobetasol propionate Dexamethasone Flucinonide	
Medium	Triamcinolone acetonide Loteprendole etabonate Dexamethasone sodium phosphate Fluormethalone	
Low	Hydrocortisone Rimexolone Medrisone	

Table 1. Comparison of anti-inflamatory and intraocular pressure elevating potencies

Additional ocular findings from topical steroids include corneal ulcers, exacerbation of bacterial and viral infections, posterior subcapsular cataracts, mydriasis, delayed wound healing, scleral melting ptosis and skin atrophy and depigmentation of the eyelids. Systemic steroids side effects are suppression of the pituitary-adrenal axis, Cushinoid facies, buffalo hump, truncal obesity, hirsutism, cutaneous striae, easy bruisability, delayed wound healing, osteoporosis, aseptic necrosis of the hip, peptic ulcers, diabetes, hypertension, insomnia and psychiatric disorders.

6. Management

This secondary glaucoma clinically mimics many features of primary open angle glaucoma. Currently, the propensity to develop steroid-induced ocular hypertension must be determined empirically. Therefore, all patients on protracted steroid therapy should have their intraocular pressure monitored periodically.

Steroid induced glaucoma usually responds to cessation of steroid therapy and to topical anti-glaucoma medication. In steroid responders the intraocular pressure generally returns to normal within few days to weeks after discontinuation of steroids. Rarely, intraocular pressure remains elevated despite steroid cessation and may result from damage to outflow channels. In these cases management is similar to that of open angle glaucoma patients.

If anti-inflammatory therapy is needed in known steroid responders or glaucoma patients, treatment with FML 0.1% or medrisone (MHS) are possible options. Loteprendol (Lotemax) and Rimexolone (Velox) are potent anti-inflammatory corticosteroids with reduced propensity to raise intraocular pressure.

Alternative topical anti-inflammatory agents are the nonsteroidal anti-inflammatory agents (NSAIDs), such as diclofenac (Voltaren), ketorolac tromethamine (Acular LS) and bromfenac (Xibrom). NSAIDs do not induce increase in intraocular pressure but their anti-inflammatory potential is lower than that of corticosteroids.

When indicated, topical anti-glaucoma medications should be used. Prostaglandins should be used with caution as they may have pro-inflammatory effect. If intraocular pressure remains intractable despite maximal tolerated medical therapy, Argon laser trabeculoplasty and Nd:YAG laser selective trabeculoplasty (SLT) have variable success and patients required additional surgical procedures. Repeat SLT treatments may be necessary. SLT is a temporizing procedure to consider in patients with steroid-induced elevated IOP.

A possible new treatment under investigation is anecortave acetate injection into the anterior sub-Tenon space in eye with uncontrolled steroid-related ocular hypertension following intravitreal or sub-Tenon injections of triamcinolone acetonide. Anecortave acetate is a synthetic molecule derived from cortisol. The resulting molecule is referred to as a cortisene. The modification renders the molecule free of all glucocorticoid and mineralocorticoid activity. Anecortave acetate possesses antiangiogenic activity via inhibition of the proteases necessary for vascular endothelial cell migration and has been evaluated as a potential therapy for neovascular age-related macular degeneration. In one preliminary, uncontrolled study a rapid and sustained reduction of intraocular pressure was noted as soon as 1 week after treatment. The mechanism by which anecortave acetate lowers intraocular pressure in eyes with steroid-related ocular hypertension is unknown. With glucocorticoid treatment, trabecular meshwork cells increases the expression of plasminogen activator inhibitor–1, a protein that inhibits activation of extracellular proteinases and leads to enhanced extracellular matrix deposition. Recent studies have shown that anecortave acetate blocks glucocorticoid induction of plasminogen activator inhibitor–1, which may be partially responsible for anecortave acetate's intraocular pressure lowering activity.

Surgical treatments include filtration surgery, tube shunt, excision of the sub-Tenon steroid depot, explantation of steroid implant and pars plana vitrectomyfor the removal of the intravitreal depot.

7. References

Armaly MF. The heritable nature of dexamethasone-induced ocular hypertension. Arch Ophthalmol. 1966; 75:32–5.

Bamberger CM, Bamberger AM, de Castro M, Chrousos GP. Glucocorticoid receptor beta, a potential endogenous inhibitor of glucocorticoid action in humans. J Clin Invest. 1995; 95:2435–41.

Bartlett JD, Woolley TW, Adams CM. Identification of high intraocular pressure responders to topical ophthalmic corticosteroids. J Ocul Pharmacol. 1993; 9:35–45.

Becker B, Chevrette L. Topical corticosteroid testing in glaucoma siblings. Arch Ophthalmol. 1966; 76:484–7.

Becker B. Diabetes mellitus and and primary open angle glaucoma. Am J Opphthalmol. 1971; 71:1.

Bregmann J, Witmer MT, Slonim CB. The relationship of intranasal steroids to intraocular pressure. Curr Allergy Asthma Rep. 2009 Jul; 9(4):311-5.

Duma D, Jewell CM, Cidlowski JA. Multiple glucocorticoid receptor isoforms and mechanisms of post-translational modification. J Steroid Biochem Mol Biol. 2006; 102:11–21.

Fautsch MP, Bahler CK, Jewison DJ, et al. Recombinant TIGR/MYOC increases outflow resistance in the human anterior segment. Invest Ophthalmol Vis Sci 2000; 41:4163–8.

Gould DB, Miceli-Libby L, Savinova OV, et al. Genetically increasing MYOC expression supports a necessary pathologic role of abnormal proteins in glaucoma. Mol Cell Biol 2004; 24:9019–25.

Haeck IM, Rouwen TJ, Timmer-de Mik L, de Bruin-Weller MS, Bruijnzeel-Koomen CA. Topical corticosteroids in atopic dermatitis and the risk of glaucoma and cataracts. J Am Acad Dermatol. 2011 Feb; 64(2):275-81.

Haller JA et al. for the OZURDEX GENEVA Study Group. Randomized, sham controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology 2010;117:1134-46.

Hass JS, NootensRH: Glaucoma secondary to benigne adrenal adenoma. Am J Ophthalmol 1974; 78:497.

Jilani FA, Khan AM, Kesharwani RK: Study of topical corticosteroid response in glaucoma suspects and family members of established glaucoma patients. Indian J Ophthalmol 1987; 35:141.

Jonas JB, Degenring RF, Kreissig I, Akkoyun I, Kamppeter BA. Intraocular pressure elevation after intravitreal triamcinolone acetonide injection. Ophthalmology. 2005;112(4):593-598.

Jonas JB. Intravitreal triamcinolone acetonide: a change in a paradigm. Ophthalmic Res. 2006;38(4):218-245.

Jones R 3rd, Rhee DJ. Corticosteroid-induced ocular hypertension and glaucoma: a brief review and update of the literature. . Curr Opin Ophthalmol. 2006 Apr; 17(2):163-7.

Kitazawa Y, Horie T. The prognosis of corticosteroid-responsive individuals. Arch Ophthalmol. 1981; 99:819–23.

Kwok AK, Lam DS, Fan DS, et al. Ocular hypertensive response totopical steroids in children. Ophthalmol1997; 104:2112.

Lewis JM, Priddy T, Judd J, Gordon MO, Kass MA, Kolker AE, Becker B. Intraocular pressure response to topical dexamethasone as a predictor for the development of primary open-angle glaucoma. Am J Ophthalmol. 1988; 106:607–12.

Lutjen-Drecoll E, May CA, Polansky JR, et al. Localization of the stress proteins alpha B-crystallin and trabecular meshwork inducible glucocorticoid response protein in normal and glaucomatous trabecular meshwork. Invest Ophthalmol Vis Sci 1998; 39:517–25.

McCarty GR, Schwartz B. Increased plasma noncortisol glucocorticoid activity in open-angle glaucoma. Invest Ophthalmol Vis Sci. 1991; 32:1600–8.

Mindel JS, Tavitian HO, Smith H, Jr, et al. Comparative ocular pressure elevation by medrysone, fluorometholone, and dexamethasone phosphate. Arch Ophthalmol 1980; 98:1577–8.

NG JS, Fan DS, young AL et al,Ocular hypertensive response to topical dexamethasone in children: a dose-dependent phenomenon. Ophthalmol 2000; 107:2097.

Nguyen TD, Chen P, Huang WD, et al. Gene structure and properties of TIGR, an olfactomedin-related glycoprotein cloned from glucocorticoid-induced trabecular meshwork cells. J Biol Chem 1998; 273:6341–50.

Oakley RH, Sar M, Cidlowski JA. The human glucocorticoid receptor beta isoform. Expression, biochemical properties, and putative function. J Biol Chem. 1996; 271:9550–9.

Ohji M, Kinoshita S, Ohmi E, Kuwayama Y. marked intraocular response to instillation of corticosteroids in children. Am J Ophthalmol 1191; 112:450.

Okka M, Bozkurt B, Kerimoglu H, Ozturk BT, Gunduz K, Yılmaz M, Okudan S. Control of steroid-induced glaucoma with surgical excision of sub-Tenon triamcinolone acetonide deposits: a clinical and biochemical approach. Can J Ophthalmol. 2010 Dec; 45(6):621-6.

Robin AL, Suan EP, Sjaarda RN, Callanan DG, Defaller J; Alcon Anecortave Acetate for IOP Research Team. Reduction of intraocular pressure with anecortave acetate in eyes with ocular steroid injection-related glaucoma. Arch Ophthalmol. 2009 Feb; 127(2):173-8.

Rozsival P, Hampl R, Obenberger J, Starka L, Rehak S. Aqueous humour and plasma cortisol levels in glaucoma and cataract patients. Curr Eye Res. 1981; 1:391–6.

Rubin B, Taglienti A, Rothman RF, Marcus CH, Serle JB. The effect of selective laser trabeculoplasty on intraocular pressure in patients with intravitreal steroid-induced elevated intraocular pressure. J Glaucoma. 2008 Jun-Jul;17(4):287-92.

Schwartz JT, Reuling FH, Feinleib M et al. Twin study on ocular pressure after topical dexamethasone. I. frequency distribution of pressure response. Am J Ophthalmol 1973; 76:126.

Schwartz JT, Reuling FH, Feinleib M et al. Twin study on ocular pressure folloing topically applied dexamethasone. II. Inheritance of variation in pressure response. Arch Ophthalmol 1973; 90:281.

SCORE Study Research Group. A randomiezed trial compering the efficacy and safety of intravitreal triamcinolone with standard care to treat vision loss associated with macular edema secondary to central retinal vein occlution: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) Study report 5. Arch Ophthalmol 2009;127:1101-14.

SCORE Study Research Group. A randomiezed trial compering the efficacy and safety of intravitreal triamcinolone with standard care to treat vision loss associated with macular edema secondary to branch retinal vein occlution: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) Study report 6. Arch Ophthalmol 2009;127:1115-28.

Smithen LM, Ober MD, Maranan L, Spaide RF. Intravitreal triamcinolone acetonide and intraocular pressure. Am J Ophthalmol. 2004;138(5):740-743.

Southren AL, Gordon GG, Weinstein BI. Genetic defect in cortisol metabolism in primary open angle glaucoma. Trans Assoc Am Physicians. 1985; 98:361–9.

Stone EM, Fingert JH, Alward WL, et al. Identification of a gene that causes primary open angle glaucoma. Science 1997; 275:668–70.

Tawara A, Tou N, Kubota T, Harada Y, Yokota K. Immunohistochemical evaluation of the extracellular matrix in trabecular meshwork in steroid-induced glaucoma. Graefes Arch Clin Exp Ophthalmol. 2008 Jul;246(7):1021-8.

Tektas OY, Lütjen-Drecoll E. Structural changes of the trabecular meshwork in different kinds of glaucoma. Exp Eye Res. 2009 Apr;88(4):769-75.

Tripathi RC, Kirschner BS. Kipp M. et al. corticosteroid treatment for inflammatory bowel disease in pediatric patients increases intraocular pressure. Gastroenterology 1992; 102:1957.

Wang RF, Guo BK. Steroid-induced ocular hypertention in high myopia. Chin Med J 1984; 97:24.

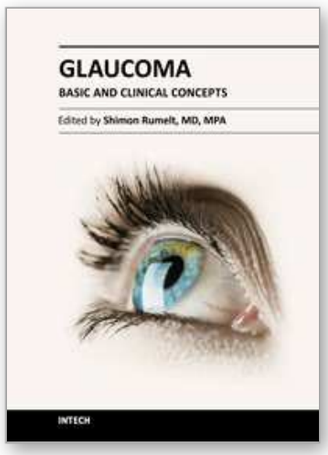
Wang X, Johnson DH. mRNA in situ hybridization of TIGR/MYOC in human trabecular meshwork. Invest Ophthalmol Vis Sci 2000; 41:1724–9.

Zhang X, Clark AF, Yorio T. Regulation of glucocorticoid responsiveness in glaucomatous trabecular meshwork cells by glucocorticoid receptor-beta. Invest Ophthalmol Vis Sci. 2005; 46:4607–16.

Zhang X, Ognibene CM, Clark AF, Yorio T. Dexamethasone inhibition of trabecular meshwork cell phagocytosis and its modulation by glucocorticoid receptor beta. Exp Eye Res. 2007;84(2):275-284.

Zhao J, Zhang Q. Ultrastructural changes of the trabecular meshwork in glucocorticoid induced glaucoma. Yan Ke Xue Bao. 2010 Nov; 25(2):119-124.

Zillig M, Wurm A, Grehn FJ, et al. Overexpression and properties of wild-type and Tyr437His mutated myocilin in the eyes of transgenic mice. Invest Ophthalmol Vis Sci 2005; 46:223–34.



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This book addresses the basic and clinical science of glaucomas, a group of diseases that affect the optic nerve and visual fields and is usually accompanied by increased intraocular pressure. The book incorporates the latest development as well as future perspectives in glaucoma, since it has expedited publication. It is aimed for specialists in glaucoma, researchers, general ophthalmologists and trainees to increase knowledge and encourage further progress in understanding and managing these complicated diseases.

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