Drug-Induced Glaucoma

- Author: Douglas J Rhee, MD; Chief Editor: Hampton Roy Sr, MD more...

Updated: Jul 29, 2014

Background

Several different drugs have the potential to cause the elevation of intraocular pressure (IOP), which can occur via an open-angle mechanism or a closed-angle mechanism. Steroid-induced glaucoma is a form of open-angle glaucoma that usually is associated with topical steroid use, but it may develop with inhaled, oral, intravenous, periocular, or intravitreal steroid administration. Medications prescribed for a variety of systemic conditions (eg, depression, allergies, Parkinson disease) can produce pupillary dilation and precipitate an attack of acute angle-closure glaucoma in anatomically predisposed eyes that have narrow angles.[1] Dietary supplements have also been reported to induce acute angle-closure glaucoma.[2]

Open angle

Drug-induced elevation of IOP is more common by an open-angle mechanism. Corticosteroids are a class of drugs that may produce IOP elevation by this mechanism. Not all patients taking corticosteroids will develop elevated IOP. Risk factors include preexisting primary open-angle glaucoma, a family history of glaucoma, high myopia, diabetes mellitus, and history of connective tissue disease (especially rheumatoid arthritis).

Additionally, the number of people responding with an elevated IOP varies with the route of administration. More people respond from topically applied drops (including topically applied creams to the periorbital area) or intravitreal injection. In order of decreasing frequency, incidence of elevated IOP is less with intravenous, parenteral, and inhaled routes of administration. Patients on chronic corticosteroid therapy can remain undiagnosed with an elevated IOP, which can result in glaucomatous optic nerve damage.

Steroid-induced IOP elevation typically occurs within a few weeks of beginning steroid therapy. In most cases, the IOP lowers spontaneously to the baseline within a few weeks to months upon stopping the steroid. In rare instances, the IOP remains elevated. Additionally, there may be some patients whose underlying condition necessitates the continued use of corticosteroids despite the elevated IOP. These patients are treated identically to those with primary open-angle glaucoma.

Closed angle

Most categories of drugs that list glaucoma as a contraindication or adverse effect are concerned with inducing acute angle-closure glaucoma. These medications will incite an attack only in those individuals with occludable angles (ie, very narrow anterior chamber angles). The classes of medications that have the potential to induce angle closure are topical anticholinergic or sympathomimetic dilating drops, tricyclic antidepressants, monoamine oxidase inhibitors, antihistamines, antiparkinsonian drugs, antipsychotic medications, and antispasmolytic agents.[3]

Sulfa containing medications may induce angle-closure glaucoma by a different angle-closure mechanism, involving anterior rotation of the ciliary body. Typically, the angle closure is bilateral and occurs within the first several doses of the sulfonamide-containing medication. Patients with narrow or wide open angles are potentially susceptible to this rare and idiosyncratic reaction.

Pathophysiology

Open angle

Exact pathophysiology of steroid-induced glaucoma is unknown. It is known that steroid-induced IOP elevation is secondary to increased resistance to aqueous outflow. Some evidence indicates that the defect could be increased accumulation of glycosaminoglycans or increased production of trabecular meshwork-inducible glucocorticoid response (TIGR) protein, which could mechanically obstruct outflow. Other evidence points toward corticosteroid-induced cytoskeletal changes that could inhibit pinocytosis of aqueous humor or inhibit the clearing of glycosaminoglycans, resulting in the accumulation of this substance.

Closed angle

The pathophysiology of drug-induced angle-closure glaucoma is usually increased pupillary block (ie, increased iris-lens contact at the pupillary border) from pupillary dilation. Medications have a direct or secondary effect, either to stimulate sympathetic or inhibit parasympathetic activation causing pupillary dilation, which can precipitate acute angle-closure glaucoma in patients with occludable angles. The other possible mechanism is dilation in patients with plateau iris syndrome. See Glaucoma, Angle Closure, Acute.

A notable exception is the angle closure resulting from sulfa containing medications. The mechanism involves anterior rotation of the ciliary body and/or choroidal effusions, resulting in shallowing of the anterior chamber and blockage of the trabecular meshwork by the iris. Pupillary dilation and a preexisting shallow anterior chamber angle are not necessary. The exact defect that causes the ciliary body swelling is unknown.

Epidemiology

Frequency

United States

Open angle

The incidence of steroid-induced IOP elevation in patients on systemic corticosteroids is unknown because most of these patients do not have their IOP checked. These patients may be discovered during a routine eye exam while on their medication, or the glaucoma may have progressed to the point of causing visual symptoms. Patients taking topical steroid drops usually receive follow-up care by an ophthalmologist who monitors IOP.

The risk of developing steroid-induced glaucoma is related to its potency and frequency of administration. People with preexisting primary open-angle glaucoma have a much greater potential to experience an elevated IOP from topical corticosteroids. Patients with primary chronic angle closure and patients with secondary open-angle glaucoma behave similarly to normal eyes with regard to steroid response.

Studies completed by Armaly indicated that approximately one third of normal eyes and more than 90% of patients with primary

open-angle glaucoma respond with greater than 6 mm Hg of IOP elevation after receiving a 4-week course of topical dexamethasone 0.1%.[4, 5] Following intravitreal injection of triamcinolone, over 50% of nonglaucomatous eyes will have an increase in IOP; this increase in IOP can occur as long as 6 months after the injection.

Closed angle

Prevalence of occludable angles in whites from the Framingham study is 3.8%.

Narrow angles are more common in the Asian population. A study of a Vietnamese population estimated a prevalence of occludable angles at 8.5%.

Mortality/Morbidity

Glaucoma is the third leading cause of blindness in the United States. The risk of becoming legally blind in one eye from open-angle glaucoma is approximately 20%, with bilateral blindness occurring in 9%.

Race

No racial predilection exists for steroid-responsive IOP.

Sex

No sexual predilection exists for steroid-responsive IOP.

Age

Steroid-responsive IOP elevations can occur in people of all ages, although children less frequently are reported to have IOP elevation with steroids.

Contributor Information and Disclosures

Author
Douglas J Rhee, MD Chair and Professor, Department of Ophthalmology and Visual Science, University Hospitals Eye Institute, Case Western Reserve University School of Medicine

Douglas J Rhee, MD is a member of the following medical societies: Alpha Omega Alpha, American Academy of Ophthalmology, American Glaucoma Society, American Medical Association, Association for Research in Vision and Ophthalmology, and Phi Beta Kappa

Disclosure: Alcon Grant/research funds Independent contractor; Allergan Grant/research funds Independent contractor; Santen Consulting fee Consulting; Alcon Consulting fee Consulting; Allergan Consulting fee Consulting; Merck Consulting fee Consulting; Merck Independent contractor; Ivantis Grant/research funds Independent contractor; Glaukos Consulting fee Consulting; Ivantis Consulting fee Consulting

Coauthor(s)
Michael D Greenwood, MD Resident Physician, Department of Ophthalmology, University Hospitals Case Medical Center

Michael D Greenwood, MD is a member of the following medical societies: American Academy of Ophthalmology, American Society of Cataract and Refractive Surgery, and International Society of Refractive Surgery

Disclosure: Nothing to disclose.

Steven Gedde, MD Program Director, Assistant Professor, Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami School of Medicine

Steven Gedde, MD is a member of the following medical societies: Alpha Omega Alpha, American Academy of Ophthalmology, American Medical Association, American Society of Cataract and Refractive Surgery, Contact Lens Association of Ophthalmologists, and Phi Beta Kappa

Disclosure: Nothing to disclose.

Specialty Editor Board
Andrew I Rabinowitz, MD Director of Glaucoma Service, Barnet Dulaney Perkins Eye Center

Andrew I Rabinowitz, MD is a member of the following medical societies: Aerospace Medical Association, American Academy of Ophthalmology, and American Medical Association

Disclosure: Nothing to disclose.

Francisco Talavera, PharmD, PhD Adjunct Assistant Professor, University of Nebraska Medical Center College of Pharmacy; Editor-in-Chief, Medscape Drug Reference

Disclosure: Medscape Salary Employment

Martin B Wax, MD Clinical Professor, Department of Ophthalmology, University of Texas Southwestern Medical School; Vice President, Ophthalmology Research and Development, Head, Ophthalmology Discovery Research, Alcon Labs, Inc

Martin B Wax, MD is a member of the following medical societies: American Academy of Ophthalmology, American Glaucoma Society, and Society for Neuroscience

Disclosure: Nothing to disclose.

Lance L Brown, OD, MD Ophthalmologist, Affiliated With Freeman Hospital and St John's Hospital, Regional Eye Center, Joplin, Missouri

Disclosure: Nothing to disclose.

Chief Editor
Hampton Roy Sr, MD Associate Clinical Professor, Department of Ophthalmology, University of Arkansas for Medical Sciences

Hampton Roy Sr, MD is a member of the following medical societies: American Academy of Ophthalmology, American College of Surgeons, and Pan-American Association of Ophthalmology

Disclosure: Nothing to disclose.

References

1. Rudkin AK, Gray TL, Awadalla M, Craig JE. Bilateral simultaneous acute angle closure glaucoma precipitated by non-prescription cold and flu medication. *Emerg Med Australas*. Oct 2010;22(5):477-9. [Medline].
2. Hwang JC, Khine KT, Lee JC, Boyer DS, Francis BA. Methyl-Sulfonyl-Methane (MSM)-induced Acute Angle Closure. *J Glaucoma*. Nov 14 2013;[Epub ahead of print].
3. Razeghinejad MR, Pro MJ, Katz LJ. Non-steroidal drug-induced glaucoma. *Eye (Lond)*. Aug 2011;25(8):971-80. [Medline]. [Full Text].
4. Armaly MF. Effect of corticosteroids on intraocular pressure and fluid dynamics. I. The effect of dexamethasone in the normal eye. *Arch Ophthalmol*. 1963;70:482.
5. Armaly MF. Effect of corticosteroids on intraocular pressure and fluid dynamics. II. The effect of dexamethasone in the glaucomatous eye. *Arch Ophthalmol*. 1963;70:492.
6. Nguyen N, Mora JS, Gaffney MM, et al. A high prevalence of occludable angles in a Vietnamese population. *Ophthalmology*. Sep 1996;103(9):1426-31. [Medline].
7. Ohji M, Kinoshita S, Ohmi E, et al. Marked intraocular pressure response to instillation of corticosteroids in children. *Am J Ophthalmol*. Oct 15 1991;112(4):450-4. [Medline].
8. Panday VA, Rhee DJ. Review of sulfonamide-induced acute myopia and acute bilateral angle-closure glaucoma. *Compr Ophthalmol Update*. Sep-Oct 2007;8(5):271-6. [Medline].
9. Polansky JR. Side effects of ophthalmic therapy with anti-inflammatory steroids. *Curr Opin Ophthalmol*. 1992;3:259-272.
10. Rhee DJ, Peck RE, Belmont J, et al. Intraocular pressure alterations following intravitreal triamcinolone acetonide. *Br J*

Ophthalmol. Aug 2006;90(8):999-1003. [Medline].

11. Rhee DJ, Ramos-Esteban JC, Nipper KS. Rapid resolution of topiramate-induced angle-closure glaucoma with methylprednisolone and mannitol. *Am J Ophthalmol*. Jun 2006;141(6):1133-4. [Medline].

12. Wolfs RC, Grobbee DE, Hofman A, et al. Risk of acute angle-closure glaucoma after diagnostic mydriasis in nonselected subjects: the Rotterdam Study. *Invest Ophthalmol Vis Sci*. Nov 1997;38(12):2683-7. [Medline].