Reducing the Release of Pigment

Methods for decreasing pigment particles in the anterior chamber in exfoliation syndrome and pigment dispersion syndrome.

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The release of pigment into the anterior chamber is a well-known phenomenon in both exfoliation syndrome and pigment dispersion syndrome. The deposition of pigment in the trabecular meshwork is an underlying cause of elevated IOP and glaucoma. This article describes what triggers the release of pigment and suggests methods for reducing the problem.

EXFOLIATION SYNDROME

Overview

Exfoliation syndrome is the most widespread, classifiable cause of open-angle glaucoma worldwide.1 In this age-related disorder, fibrillar extracellular materials are produced by and accumulate in various ocular tissues (Figure 1). Friction between the anterior lens capsule and the iris disrupts the iris pigment epithelium, dispersing pigment throughout the anterior chamber. The result is corneal pigmentation, iris sphincter transillumination defects (Figure 2), and a characteristic increase in the trabecular meshwork's pigment (Figure 3). Pigment dispersion may occur before the physician even detects exfoliation syndrome with a slit-lamp examination.2

The release of pigment into the anterior chamber is common and profuse after pupilary dilation in patients with exfoliation syndrome.3-8 Subsequent increases in IOP can be as high as 30 mm Hg above baseline and may peak as many as 2 or 3 hours after dilation.9 It is particularly important for physicians to measure IOP and assess the degree of pigment release in the anterior chamber after pupilary dilation. If the spread of pigment is extensive, the clinician should continue follow-up until the patient’s IOP is safely under control. Unrecognized pressure spikes may exacerbate glaucomatous damage, particularly in patients whose disease is moderate to severe. We have seen a patient with exfoliative glaucoma who suffered a central retinal vein occlusion and an IOP spike to 55 mm Hg after pupilary dilation.

Drug Therapy

In patients with exfoliation syndrome, inhibiting the release of pigment should slow glaucomatous progression by blocking the mechanism most responsible for elevated IOP in these eyes. Theoretically, miotics should be the first line of treatment. Decreasing pupilary movement may reduce indolentlicular friction and thus avert the liberation of iris pigment, slow the progression of trabecular blockage, and perhaps allow the meshwork to clear.

Although physicians’ use of pilocarpine decreased upon the introduction of newer classes of IOP-lowering medications, this agent may still have a role in exfoliation syndrome. One drop of pilocarpine 2% daily may be sufficient to reduce pupillary reactivity for 24 hours without severely constricting the pupil.10 Other IOP-lowering agents may be

Figure 1. Three zones are present on the anterior lens capsule in exfoliation syndrome. Note the clear area between the central disc and the peripheral zone.

Figure 2. Iris sphincter transillumination defects in exfoliation syndrome result from the dispersion of pigment into the anterior chamber.
used concomitantly as needed. After undergoing treatment for sufficiently long periods with miotic therapy, we observed an early pigment reversal sign, which indicates that pigment has cleared from the trabecular meshwork.

**PIGMENT DISPERSION SYNDROME**

**Overview**

The onset of pigment dispersion syndrome, which is an autosomal dominant disorder, typically occurs when patients are in their early 20s, but the condition begins to regress with increasing age, enlargement of the lens, and the loss of accommodation due to the onset of presbyopia. The mechanism underlying IOP elevation in patients with pigment dispersion syndrome and pigmentary glaucoma is analogous to that in exfoliation syndrome. In pigment dispersion syndrome and pigmentary glaucoma, the iris insertion is typically posterior, and the peripheral iris configuration tends to be concave. Iridozonular contact during accommodation as well as during normal pupillary constriction and dilation disrupts the iris pigment epithelium and results in the deposition of pigmentary granules throughout the anterior segment. The classic diagnostic triad consists of corneal pigmentation (Krukenberg’s spindle); slit-like, radial, midperipheral iris transillumination defects; and dense trabecular pigmentation (Figures 4 to 6).

Patients with pigment dispersion syndrome or pigmentary glaucoma can also experience sudden IOP spikes after pupillary dilation. The examination and treatment of these patients is similar to that described earlier for exfoliation syndrome. Although exercise may cause the shedding of pigment and a subsequent pressure spike in some patients with pigment dispersion syndrome, the majority of patients do not appear to be affected. Pigmentary shedding is most commonly associated with jogging or bouncing. Ultrasound biomicroscopy indicates that cycling increases the iris’ concavity in both healthy eyes and those with pigment dispersion syndrome. The effect was eliminated in the latter by laser iridotomy. Vibration-induced increases in trabecular pigmentation have also been reported in rock drillers.

**Drug Therapy**

Because miotics both constrict the pupil and increase aqueous outflow, they are, in principle, first-line therapy. In practice, pilocarpine completely stops the exercise-induced release of pigment and elevation of IOP whereas dapiprazole has a lesser effect and indotomy provides incomplete inhibition. Miotics convert the concave iris configuration (Figure 7A) to a convex one and eliminate iridozonular friction (Figure 7B). Pilocarpine drops are poorly tolerated, however, because of accommodative spasm and induced myopia in younger patients. Pilocarpine Ocuserts were ideal for patients with pigment dispersion syndrome or pigmentary glaucoma, because these drugs were well tolerated and effective at both lowering IOP and inhibiting pigmentary release. Unfortunately, they are no longer manufactured, which has created a serious problem for our younger patients.
Laser Intervention

Laser iridotomy can eliminate reverse pupillary block, flatten the iris’ contour (Figure 8), and reduce the extent of iridolenticular contact. The technique also appears to prevent the accentuation of the iris’ concavity that accompanies accommodation. Moreover, it decreases the number of melanin granules present in the anterior chamber. Although iridotomy may relieve IOP spikes, it does not lower baseline IOP, because it takes years for pigment to clear from the trabecular meshwork. Wang et al conducted a review of 23 patients with pigment dispersion syndrome and elevated IOP who had no or only mild glaucomatous damage and who had undergone laser iridotomy. The investigators found no significant difference in the long-term reduction of IOP in the lasered eyes compared with the medically treated fellow eyes. The latter had mostly received treatment with pilocarpine Ocuserts and latanoprost. Now that Ocuserts are no longer available, the use of laser iridotomy will probably increase.

By preventing the liberation of pigment from the iris, laser iridotomy should allow the trabecular meshwork to clear itself and avoid further pigmentary deposition. Candidates for the procedure, therefore, are in the pigment-liberation stage. In such individuals, pupillary dilation likely will lead to the release of pigment into the anterior chamber. Patients with uncontrolled glaucoma are poor candidates for laser iridotomy, since clearing of the meshwork and the subsequent IOP reduction requires a long time after the laser iridotomy.

As a rule of thumb, we restrict iridotomy to patients under 45 years of age who have elevated IOP, demonstrate no early glaucomatous damage, and experience a release of pigment upon pharmacologic dilation or spontaneously after exercise. Because not all patients with pigment dispersion syndrome develop elevated IOP, and because the iridotomy procedure itself results in a significant release of pigment, we do not currently advocate treating normotensive eyes.

CONCLUSION

The release of pigment into the anterior chamber and the subsequent deposition on the trabecular meshwork constitutes a major mechanism in IOP elevation and glaucoma in patients with exfoliation syndrome and pigment dispersion syndrome. Reducing the release of pigment may slow the progression of these diseases and may even lead to a clearing of the trabecular meshwork. ❑
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