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Breaking Through Compliance Barriers

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Identification of Medical Compliance Barriers

You can improve the success of pharmacologic glaucoma therapy by offering practical solutions to enhance compliance.

Has this ever happened to you? After carefully examining and diagnosing a patient's glaucoma status, you send him home with a new medication, confident his IOP will be much lower at the next office visit. But when the patient returns, his IOP is not as low as expected. What should you do next?

You could add a drug to the existing regimen. You could switch to another drug. But before you change your treatment plan, you may want to ask a few questions.

Keeping Secrets

Glaucoma patients are reluctant to admit they don't always use their medications as directed.¹ Two studies, completed before the availability of once- and twice-daily prostaglandin analogues, found that 24% to 59% of glaucoma patients missed scheduled doses of IOP-lowering eye drops.^{1,2} Noncompliance can have serious consequences for disease progression, not only because it reduces the benefits of IOP-lowering agents, but also because it obscures the true reason patients don't respond to medication.³

As Bieszka and colleagues⁴ discovered, physicians are more likely to blame disappointing results on poor drug performance than on nonadherence. When the researchers compared physicians' estimates of patient compliance with actual drug refill patterns, they found doctors tended to overestimate patient compliance substantially.

Patients may not want to talk about how they're using their eye drops, especially if they're embarrassed or they feel guilty

about not following the proper directions. The best way to elicit information from patients about lack of compliance is by adopting a nonconfrontational approach.

When we counsel glaucoma patients about medication non-compliance, we must consider whether their problems are situational or environmental, patient-related, practitioner-related or regimen-related. We're more likely to offer a practical and effective solution if we take time to examine all possible barriers to compliance.⁵

Situational/Environmental Barriers

Situation-related barriers to glaucoma drug compliance include travel disruptions, poor manual dexterity and changes in daily routines.

In fact, elderly patients who live in nursing homes may be more likely to use their eye drops than those who live at home. Nurses and technicians in nursing homes always are available to

Barrier Category	Category Subgroup	Responses (%)
Situational/ Environmental	Accountability/lack of support	49
	Major life events	
	Travel/away from home	
	Competing activities	
	Change in routine	
Patient	Knowledge/skill	32
	Memory	
	Motivation/health benefits	
	Comorbidity	
Provider	Dissatisfaction	3
	Communication	
Regimen	Refill	16
	Cost of medication	
	Complexity	
	Change	

Data adapted from Tsai CT, McClure CA, Ramos SE, et al. Compliance barriers in glaucoma: A systematic classification. J Glaucoma. 2003;12:393-398.

Almost half of the 71 unique compliance barriers identified by Tsai and colleagues⁵ were attributed to situational or environmental factors.

dispense drops at scheduled intervals,⁶ and because they work so closely with patients every day, they're often better equipped to observe and resolve common compliance barriers.

Many patients miss doses when they travel, either because they forget to pack their eye drops or the drops get lost with their luggage. Remind patients of the importance of packing their eye drops close to them in their carry-on bags, especially in the summer when extreme temperatures can affect medications in stored luggage.

For working patients who use medications that require mid-day doses, consider prescribing a 60- to 90-day supply so these patients can keep a bottle at work. Although opening more than one bottle at a time may introduce sterility and expiration issues, this option may ensure compliance in patients with work-related obstacles.

Patient-specific Barriers

Patient-related factors that compromise compliance include inaccurate application, dispensing more than one drop at a time or not waiting long enough between drops to prevent washout. For example, patients with poor corneal sensation can dispense eye drops more accurately by keeping the bottle in the refrigerator.

A commonly cited patient-specific compliance factor is forgetfulness.⁷ Getting patients to admit they forget to use their eye drops isn't enough. We must work with patients to incorporate glaucoma therapy into everyday life, no matter how complex the regimen.

Never assume patients know how to use their eye drops properly, even if they say they do.⁷ Remind them to:

- ▶ Dispense eye drops by tapping or squeezing the bottle, depending on the type of container.
- ▶ Keep their eyes closed for several minutes after applying eye drops to minimize washout.
- ▶ Use punctal occlusion to maximize corneal penetration.

Reinforce your verbal instructions by watching every patient instill eye drops while they're in your office. Patients who continue to have problems may benefit from devices that can help them dispense drops properly.

Encourage patients to associate medication use with activities of daily living, such as meals, grooming or routine tasks. For example, to remember a morning dose, patients can keep their eye drops on their nightstand and use them before turning off the alarm. They can link nighttime doses with brushing their teeth. Some patients prefer to keep a tracking chart on which they record the time they instilled each dose.⁷

Prostaglandin analogues are most effective when used at night,⁸ but patients who can't follow this schedule can instill the drops in the morning. Improving daily compliance may compensate for any slight reduction in drug efficacy.

Provider-specific Barriers

Patients who are dissatisfied with the level of care provided by their physicians are less likely to comply with their medication regimen. A recent Glaucoma Research Foundation survey⁹ found 60% of glaucoma patients who left their doctors did so because of poor doctor-patient communication.

We constantly must remind patients glaucoma is a chronic disease that requires life-long treatment. Many patients underestimate the consequences of noncompliance, especially if the doctor tells them their glaucoma is mild when it's actually more advanced.^{5,10} Every time we see a patient, we must reinforce the importance of continuing treatment to prevent disease progression and blindness.

Regimen-specific Barriers

We can maximize glaucoma compliance most readily by offering patients safe, simple treatment regimens. Of all available IOP-lowering medications, the prostaglandin analogues — bimatoprost (Lumigan),¹¹⁻¹³ latanoprost (Xalatan)^{14,15} and travoprost (Travatan)^{16,17} — best fit these requirements.

Studies^{18,19} have shown diurnal IOP fluctuations are independent and critical predictors of glaucomatous visual field loss. These findings suggest follow-up examinations should be scheduled at different times of the day to detect any diurnal IOP fluctuations. If a patient's IOP varies widely during the day, consider switching him to a prostaglandin analogue, such as travoprost, if he's not using one currently.

Who Should Not Use Prostaglandin Analogues?

Prostaglandin analogues quickly are becoming the glaucoma drug of choice. However, not all patients may benefit from these agents. Avoid prescribing prostaglandin analogues to:

- ▶ Patients who cannot tolerate the ocular side effects of these agents
- ▶ Aphakic patients
- ▶ Patients with ocular inflammation
- ▶ Patients with a high risk of macular edema
- ▶ Patients with quiescent herpetic keratitis.

Instead, consider prescribing these patients once-a-day timolol gel,¹ but only after confirming they don't have cardiovascular conditions that can be exacerbated by this agent.

1. Schenker HI, Silver LH. Long-term intraocular pressure-lowering efficacy and safety of timolol maleate gel-forming solution 0.5% compared with Timoptic XE 0.5% in a 12-month study. *Am J Ophthalmol.* 2000;130:145-150.

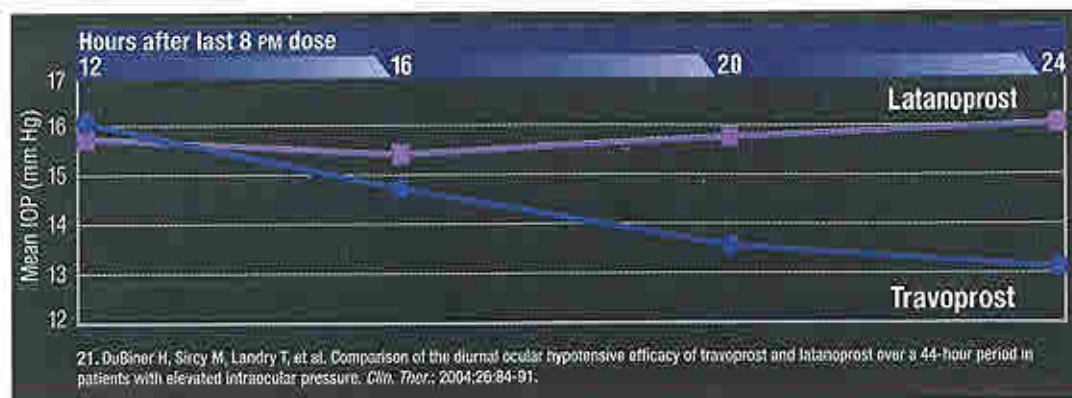
All three prostaglandin analogues appear to control IOP for 24 hours or longer. Bimatoprost provides excellent 24-hour control,²⁰ and preliminary evidence indicates travoprost's hypotensive effect lasts for up to 84 hours after instillation of the last dose.²¹

Finally, data from a recent 3-month trial²²

suggested once-weekly dosing with latanoprost lowered IOP as effectively as once-daily dosing with the same agent.

If patients can't achieve target IOPs with prostaglandin monotherapy, they may benefit from a fixed-combination product. The only fixed-combination ocular hypotensive treatment currently available in the United States contains dorzolamide hydrochloride (Trusopt) and timolol maleate (Timoptic) ophthalmic solution (Cosopt). Other combination agents, such as latanoprost and timolol (Xalacom) are available only in Canada and Europe, whereas fixed combinations of bimatoprost and timolol, brimonidine (Alphagan) and timolol and travoprost and timolol, are still in development and awaiting FDA approval.

Anecdotal evidence suggests patients who use once-daily prostaglandin analogues may be more compliant with their glaucoma medications than those who use drugs requiring two or



Travoprost (Travatan) maintains a lower mean IOP than latanoprost (Xalatan) 24 hours after the last dose.

more doses per day.

Another factor that may affect medication adherence negatively is comorbidity. As ophthalmologists, we tend to focus on preserving sight and sometimes fail to consider obstacles posed by nonophthalmic conditions that also require medications. One study⁶ showed the average glaucoma patient has filled at least 10 other prescriptions before filling his first glaucoma prescription.

Any measures we can take to reduce the number of medications a patient uses in a day, such as prescribing combination glaucoma drugs, may improve compliance. Patients may achieve even better results with combination drugs.

For example, dorzolamide and timolol solutions administered concomitantly during clinical trials lowered IOP as effectively as a fixed combination containing both agents (Cosopt).²³ However, in real clinical practice, patients achieved better IOP results with the fixed combination drug.²⁴

Most studies that link glaucoma drug noncompliance with adverse effects^{1,5} were published before prostaglandin analogues came into widespread use. These agents cause very few side effects, the most common of which is ocular hyperemia. However, Abelson and colleagues²⁵ reported ocular hyperemia usually is mild and typically dissipates within 30 days of starting bimatoprost. We can prevent patients from discontinuing prostaglandin medications prematurely by telling them they may experience hyperemia, eyelash growth, iridal pigmentation and lid darkening before they start using the drug.¹

Addressing Multiple Factors

Of all the strategies discussed in this article for improving patient compliance with glaucoma medication, the most important is ensuring patients return for scheduled follow-up visits. One study¹⁰ reported patients usually missed appointments because they didn't understand the severity of their disease (a patient factor) and didn't like the prohibitive cost of medications (a regimen factor). Surprisingly, many patients claimed their doctor never told them they needed to return for additional visits.

This study illustrates the importance of educating glaucoma suspects about the seriousness of their condition. We must strive

Affordable Pharmacologic Therapy

How can we prevent patients from discontinuing glaucoma therapy because they can't afford to buy the drugs? Managed-care formularies may cover the full cost of generic timolol, but patients usually are responsible for prostaglandin analogue copayments. To complicate matters, some insurance companies charge different copays for different prostaglandin analogues. In the long run, patients may spend less for prostaglandin analogues by using a single agent that's as effective as two or three different drugs combined.

Many pharmaceutical companies supply free or reduced-cost medicine to eligible low-income patients who don't have drug coverage. However, we must initiate the application for these programs on the patient's behalf. In addition, 23 states now offer drug assistance programs. Finally, encourage patients to check www.RxHope.com, which includes a searchable database of patient assistance programs for 1,000 medications.

Playing Favorites

A recent study¹ analyzing glaucoma drug refill patterns found patients who used latanoprost (Xalatan) were more likely to refill their prescriptions and stay on their regimen longer than patients who used beta-blockers, alpha-agonists or topical carbonic anhydrase inhibitors. Latanoprost users were more likely to refill prescriptions than those who used bimatoprost (Lumigan) and travoprost (Travatan).

1. Reardon G, Schwartz GF, Mozaffari E. Patient persistency with topical ocular hypotensive therapy in a managed care population. *Am J Ophthalmol.* 2004;137(suppl 1):S3-S12.

to prevent patients from exiting the health care system abruptly, lest they return 5 years later with severe vision loss that could have been prevented with regular care.

References

- Patel SC, Spaeth GL. Compliance in patients prescribed eyedrops for glaucoma. *Ophthalmic Surg.* 1995;26:233-236.
- Rotchford AP, Murphy KM. Compliance with timolol treatment in glaucoma. *Eye.* 1998;12:234-236.
- Lee MD, Fechtner FR, Fiscella RG, et al. Emerging perspectives on glaucoma: Highlights of a roundtable discussion. *Am J Ophthalmol.* 2000;130(suppl 4):S1-S11.
- Bieszk N, Patel R, Heaberlin A, et al. Detection of medication nonadherence through review of pharmacy claims data. *Am J Health Syst Pharm.* 2003;60:360-366.
- Tsai JC, McClure CA, Ramos SE, et al. Compliance barriers in glaucoma: A systematic classification. *J Glaucoma.* 2003;12:393-398.
- Gurwitz JH, Glynn RJ, Monane M, et al. Treatment for glaucoma: Adherence by the elderly. *Am J Public Health.* 1993;83:711-716.
- Taylor SA, Galbraith SM, Mills RP. Causes of non-compliance with drug regimens in glaucoma patients: A qualitative study. *J Ocul Pharmacol Ther.* 2002;18:401-409.
- Alm A, Stjernschantz J. Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. A comparison with timolol. Scandinavian Latanoprost Study Group. *Ophthalmology.* 1995;102:1743-1752.
- 2003 Glaucoma Research Foundation Patient Survey. San Francisco, Calif.
- Kosoko O, Quigley HA, Vitale S, et al. Risk factors for noncompliance with glaucoma follow-up visits in a residents' eye clinic. *Ophthalmology.* 1998;105:2105-2111.
- Sherwood M, Brandt J. Bimatoprost Study Groups 1 and 2. Six-month comparison of bimatoprost once-daily and twice-daily with timolol twice-daily in patients with elevated intraocular pressure. *Surv Ophthalmol.* 2001;45(suppl 4):S361-S368.
- Higginbotham EJ, Schuman JS, Goldberg I, et al. One-year, randomized study comparing bimatoprost and timolol in glaucoma and ocular hypertension. *Arch Ophthalmol.* 2002;120:1286-1293.
- Cohen JS, Gross RL, Cheetham JK, et al. Two-year double-masked comparison of bimatoprost with timolol in patients with glaucoma or ocular hypertension. *Surv Ophthalmol.* 2004;49(suppl 1):S45-S52.
- Camras CB, Alm A, Watson P, Stjernschantz J. Latanoprost, a prostaglandin analog, for glaucoma therapy. Efficacy and safety after 1 year of treatment in 198 patients. Latanoprost Study Groups. *Ophthalmology.* 1996;103:1916-1924.
- Watson P, Stjernschantz J. A six-month, randomized, double-masked study comparing latanoprost with timolol in open-angle glaucoma and ocular hypertension. The Latanoprost Study Group. *Ophthalmology.* 1996;103:126-137.
- Goldberg I. Comparison of topical travoprost eye drops given once daily and timolol 0.5% given twice daily in patients with open-angle glaucoma or ocular hypertension. *J Glaucoma.* 2001;10:414-422.
- Netland PA, Landry T, Sullivan EK, et al. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol.* 2001;132:472-484.
- Nouri-Mahdavi K, Hoffman D, Coleman AL, et al. Predictive factors for glaucomatous visual field progression in the Advanced Glaucoma Intervention Study. *Ophthalmology.* 2004;111:1627-1635.
- Asrani S, Zeimer R, Wilensky J, et al. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. *J Glaucoma.* 2000;9:134-142.
- Walters TR, DuBiner HB, Carpenter SP, et al. 24-Hour IOP control with once-daily bimatoprost, timolol gel-forming solution, or latanoprost: A 1-month, randomized, comparative clinical trial. *Surv Ophthalmol.* 2004;49(suppl 1):S26-S35.
- Dubiner HB, Sircy MD, Landry T, et al. Comparison of the diurnal ocular hypotensive efficacy of travoprost and latanoprost over a 44-hour period in patients with elevated intraocular pressure. *Clin Ther.* 2004;26:84-91.
- Kurtz S, Shemesh G. The efficacy and safety of once-daily versus once-weekly latanoprost treatment for increased intraocular pressure. *J Ocul Pharmacol Ther.* 2004;20:321-327.
- Hutzelmann J, Owens S, Shedden A, et al. Comparison of the safety and efficacy of the fixed combination of dorzolamide/timolol and the concomitant administration of dorzolamide and timolol: A clinical equivalence study. International Clinical Equivalence Study Group. *Br J Ophthalmol.* 1998;82:1249-1253.
- Choudhri S, Wand M, Shields MB. A comparison of dorzolamide-timolol combination versus the concomitant drugs. *Am J Ophthalmol.* 2000;130:832-833.
- Abelson MB, Mroz M, Rosner SA, et al. Multicenter, open-label evaluation of hyperemia associated with use of bimatoprost in adults with open-angle glaucoma or ocular hypertension. *Adv Ther.* 2003;20:1-13.

Clinical Implications

Noncompliant patients are not unique to glaucoma specialists. Physicians who treat patients with diabetes, HIV, hypertension or elevated cholesterol deal with the same issues.

Most glaucoma compliance studies are at least 10 to 20 years old. If we want to understand and improve patient compliance, we need to initiate new research to measure the extent to which ocular side effects, dosing schedules and medication cost contribute to glaucoma therapy noncompliance. Most important, we must show our patients we're sympathetic to individual barriers that prevent full drug compliance. Finally, we must continually strive to help them incorporate effective treatment techniques into their daily glaucoma regimen. **OM**

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