CME Monograph

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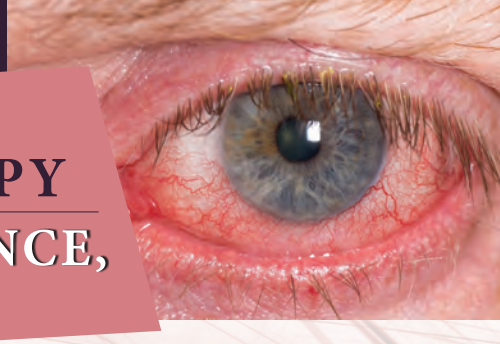

GLAUCOMA MEDICAL THERAPY

OCULAR TOLERABILITY, ADHERENCE, AND PATIENT OUTCOMES

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from an expert roundtable discussion held on August 25, 2016.

This continuing medical education activity is jointly provided by **New York Eye and Ear Infirmary of Mount Sinai** and MedEdicus LLC.

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ACTIVITY DESCRIPTION

Therapy to lower intraocular pressure effectively reduces the risk of glaucoma progression. The rate of nonadherence with therapy, however, remains high. Therapeutic nonadherence is a complex and multifactorial issue that is influenced by factors attributable to the physician, patient, and medication. All medications have side effects, and tolerability issues can contribute to nonadherence if patients perceive that the disadvantages of therapy outweigh the benefits of controlling a disease that is often asymptomatic. Therefore, the selection of initial and adjunctive therapy should consider the potential for tolerability issues that may adversely affect adherence. Novel therapies in late-stage clinical development will offer innovative mechanisms of action and unique risk/benefit profiles. The purpose of this educational activity is to update ophthalmologists on the prevalence of and contributors to therapeutic nonadherence to glaucoma treatment, potential methods of addressing nonadherence, and emerging medications with novel mechanisms of action for managing glaucoma.

TARGET AUDIENCE

This educational activity is intended for ophthalmologists.

LEARNING OBJECTIVES

Upon completion of this activity, participants will be better able to:

- Counsel patients on optimal administration and adherence strategies
- Describe the effect of tolerability of glaucoma medications on patient adherence
- Describe the mechanism of action of current and emerging topical glaucoma therapies

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OCULAR TOLERABILITY, ADHERENCE, AND PATIENT OUTCOMES

GOALS OF GLAUCOMA THERAPY

The goal of glaucoma therapy is to prevent progression of the disease. The approach to this goal is to lower intraocular pressure (IOP) because it is considered a risk factor for glaucoma and its progression, and is the only established therapy for glaucoma. Numerous clinical trials have demonstrated that IOP reduction lowers the risk of disease progression.[1,2] Other independent risk factors for glaucoma progression include older age, thinner central corneas, bilateral disease, and disc hemorrhages.[3]

The optimal IOP reduction necessary to halt progression differs among patients and is not easily determined prospectively. Risk assessment allows identification of the patients most at risk. These patients may benefit from greater IOP reductions than those whose risk of progression is lower.

Many major clinical trials have demonstrated that lowering IOP can prevent or delay the development of glaucoma in eyes with ocular hypertension,[4] as well as prevent progression in both low-pressure[5] and high-pressure open-angle glaucoma.[1] The benefit of IOP reduction is consistent, whether it is accomplished by medications, laser therapy, or surgery.[2,6]

> "I determine each patient's target IOP range on the basis of his/her individual risk factors and prior clinical course."
> – Dr Parrish

Dr Parrish: How do we best assess whether therapy is effective in accomplishing this goal? I use the target IOP approach, in which I determine a narrow range of IOP within or below which I feel progression is unlikely to occur. I determine each patient's target IOP range on the basis of his/her individual risk factors and prior clinical course.

Dr Realini: This is a common approach and represents the best standard, according to our current knowledge. However, setting a target IOP necessitates some guesswork on our part, and we do not know which of our patients are well controlled, except in retrospect. The well-controlled patients are the ones who do not progress under therapy. We cannot know with certainty whether a patient is well controlled, in part, because we do not fully understand the optimal IOP profile that halts the disease. We lack clarity on the specific IOP behaviors that lead to optic nerve damage progression, so we cannot design interventions to achieve those proactively. Future research may help clarify the specific goals of therapy. In the meantime, we lower peak IOP using the target IOP approach, and that in turn lowers mean IOP and variability.

> "Selection of therapy dictates the quality of IOP reduction achieved."
> – Dr Realini

Dr Tsai: Our approach is also limited by the nature of circadian IOP variability. Most of our patients experience their highest circadian IOP at night when asleep **(Figure 1).**[7] We cannot assess this easily, so this information is not available to us. Therefore, we cannot be certain that we know our patients' peak untreated IOP, or whether the therapies we apply effectively reduce this nocturnal peak.

Dr Fechtner: Physicians who manage diabetes and systemic hypertension have the benefit of tools with which patients can self-measure the biologic parameter of interest, whether it is blood glucose levels or systemic blood pressure. We lack such tools in glaucoma. Patients cannot easily and safely measure their IOP at home, so we are limited to the measurements we obtain in the office during limited hours of the day. Our sampling rate is low; because of this, we likely do not have a complete picture of our patients' true IOP behavior. We often have to make decisions in the face of uncertainty.

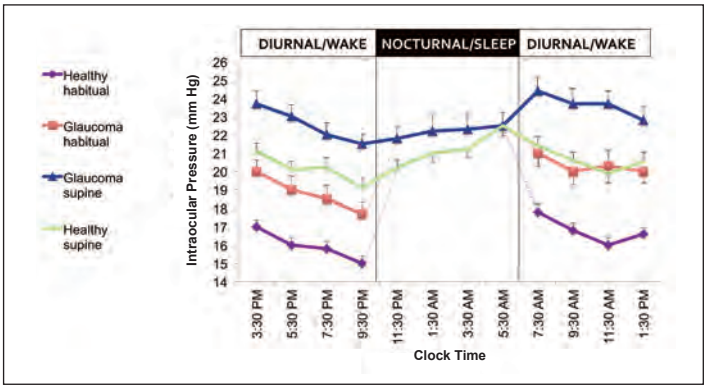

Figure 1. Intraocular pressure is highest at night in the supine position among patients with glaucoma[7]

Republished with permission of Association for Research in Vision and Ophthalmology, from Twenty-four-hour intraocular pressure pattern associated with early glaucomatous changes, John H. K. Liu, Xiaoyan Zhang, Daniel F. Kripke, Robert N. Weinreb, 44, 2003; permission conveyed through Copyright Clearance Center, Inc.

Dr Tsai: In the face of these uncertainties, the target pressure approach remains important. I agree that a range is better than a single number. We should also avoid rigid enforcement of our target. If the patient's IOP is 1 to 2 mm Hg above target, we have to ask whether the incremental risks associated with the next intervention outweigh the benefits of additional therapy.

Dr Parrish: Having acknowledged that we lack the tools to fully characterize IOP and its response to therapy, we can all agree that IOP lowering is the only option to slow or halt progression. Once we have initiated medical therapy in a patient with newly diagnosed primary open-angle glaucoma (POAG), what are the factors that affect the quality of IOP control achieved by our intervention?

Dr Realini: Selection of therapy dictates the quality of IOP reduction achieved. Ideally, a glaucoma drug would lower mean IOP, collapse variability, and provide 24-hour IOP reduction, while posing no serious safety or tolerability issues, and all this at a reasonable cost. Not every available drug offers all of these qualities, and no drug can provide these qualities if it is not taken by the patient.

NONADHERENCE: AN EVERYDAY CHALLENGE

Numerous studies have demonstrated that patients with glaucoma tend to adhere suboptimally to glaucoma therapy.[8,9] Nonadherence takes several forms. Some patients do not take their medication, either intentionally or because of chronic forgetfulness. Others are motivated and take their medication, but technique issues limit effectiveness (eg, missing the eye or instilling multiple drops too closely together). Such patients can often be identified by poor response to therapy. Others, more problematically, only take their medication before scheduled office visits. Such nonadherence is more difficult to detect and may only manifest with progression. Others habitually miss appointments, depriving providers of the opportunity to detect both nonadherence and the resulting progression.

Barriers to adherence in glaucoma have been evaluated in many studies and include factors related to the patient, to the physician, and to the drug itself.[10-12] Risk factors for nonadherence have been identified, and include younger age, African American race, and poor overall health.[13,14]

Dr Parrish: What do you think are the most common reasons that your patients are nonadherent to medical therapy?

Dr Realini: For most of our patients, the disease is diagnosed incidentally and is asymptomatic. We ask patients to take it on faith that they have a blinding disease, and our ability to convince them to take responsibility for dosing every day is directly tied to the strength of the relationship we form with them. In reality, the only symptoms most of our patients will ever experience from glaucoma are the side effects of the therapies we prescribe. Patients only get negative reinforcement. There is no positive reinforcement. There are no symptoms of glaucoma that therapy improves. The patients are left with no perceptible benefit of therapy and significant detriments: tolerability, safety issues, cost, and the inconvenience of daily dosing. These are significant hurdles to overcome.

Both patient and physician behaviors and beliefs can contribute to nonadherence. Characteristics attributable to treatment itself can also adversely affect adherence. Qualities such as tolerability, safety, convenience of dosing, and cost can all contribute to nonadherence. To effectively assist our patients in optimizing adherence to glaucoma therapy, we must understand the reasons why adherence is suboptimal. The Glaucoma Adherence and Persistency Study (GAPS) evaluated both patient-centered and physician-centered barriers to adherence to glaucoma therapy.[15]

> "50% of the patients on topical IOP-lowering therapy reported some degree of ocular surface discomfort."
> – Dr Fechtner

Patient Behavior

Health-related beliefs of patients are a key determinant of adherence. In the GAPS study, several patient beliefs that were associated independently with low adherence were identified. These included not believing that reduced vision is a risk of having a problem paying for medications and not taking medication as recommended or having difficulty, especially while traveling or being away from home.[15] Knowledge of these barriers can inform the design of better interventions to reduce nonadherence and preserve visual function among patients with POAG.

Interventions designed to address the barriers to adherence can improve patient behavior. A study of 196 patients with glaucoma who were treated with a prostaglandin analogue evaluated adherence using the Travatan Dosing Aid (TDA) (Alcon, Fort Worth, TX).[16] In this cohort, the mean adherence rate over 3 months was 71%. Overall, only 56% of subjects took > 75% of expected doses. Of note, physicians were found to be unable to identify the patients who were nonadherent. The subjects from this study who took 75% or less of their expected doses were entered into a randomized trial, in which half underwent a structured intervention designed to educate on the need for adherence, barriers to adherence, and solutions to poor adherence, and which provided regular dosing reminders by telephone; the remaining half was told to continue the drops as prescribed, with no intervention.[17] These subjects' adherence was again monitored for 3 months using the TDA. Those in the intervention group showed a significant improvement in adherence, from a mean of 54% to 73%, whereas the control group's adherence remained statistically unchanged (46% to 51%). This study demonstrated that appropriate interventions can positively affect adherence.

Tolerability/Side Effects

Tolerability encompasses specific complaints, such as allergy, stinging, burning, blurred vision, hyperemia, and ocular surface effects. These issues provide negative feedback that diminishes the dosing incentive, which is already quite low, given that many patients with glaucoma are asymptomatic and perceive no appreciable benefit from therapy.

The topical adverse events associated with eye drop glaucoma medications can be attributable to excipient ingredients in the drug formulations, such as preservatives. The chronic use of benzalkonium chloride–preserved topical IOP-lowering therapy can contribute to ocular surface disease signs and symptoms and chronic subconjunctival inflammation.[18]

Issues with tolerability have an effect beyond adherence. Hyperemia is a common adverse event associated with the use of prostaglandin analogues. In a prospective, 12-week, investigator-masked trial, hyperemia rates with the 3 prostaglandin analogues ranged from 47.1% (latanoprost) to 58.0% (travoprost) and 68.6% (bimatoprost).[19] It has been shown that the extra office visits and medication switches necessitated by the occurrence of hyperemia when initiating prostaglandin therapy effectively doubles the cost of care compared with that of patients who experience no hyperemia.[20]

Dr Parrish: To what extent do the topical and local side effects of IOP-lowering treatments affect adherence to therapy?

Dr Tsai: This varies from patient to patient. Some can tolerate significant side effects to protect their visual function, whereas others are intolerant to even the mildest conjunctival hyperemia. To some extent, the expectations and/or perceptions of patients govern the degree of this tolerability. Mild hyperemia may not be a significant issue for an older, retired patient, but can be significantly bothersome in a young executive who must function daily in professional settings.

Dr Fechtner: One factor that may explain intolerance to the ocular side effects of therapy is the unrecognized prevalence of ocular surface disease in our glaucoma practices. We evaluated the prevalence of ocular surface complaints in patients with glaucoma and found that 50% of the patients on topical IOP-lowering therapy reported some degree of ocular surface discomfort, of whom more than half fell into the moderate or severe range **(Figure 2).**[21]

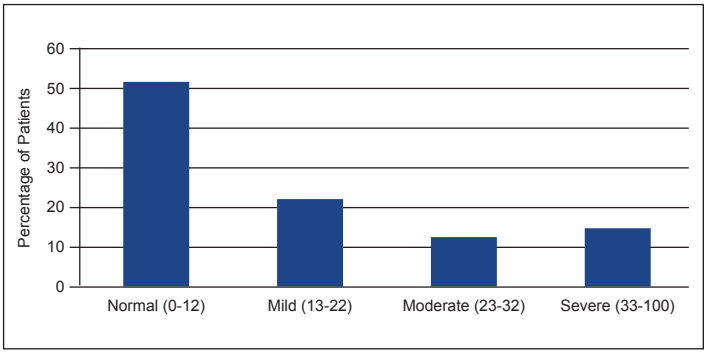

Figure 2. Prevalence of mild, moderate, and severe symptoms of ocular surface disease in treated patients with glaucoma.[21] Numbers in parentheses represent Ocular Surface Disease Index scores.

Republished with permission from Wolters Kluwer. Fechtner RD, Godfrey DG, Budenz D, et al. Prevalence of ocular surface complaints in patients with glaucoma using topical intraocular pressure-lowering medications. *Cornea.* 2010;29(6):618-621.

Dr Parrish: Your excellent study and others have contributed to a general recognition that ocular surface disease is far more common among our patients than we realized.[22] Patients with inflamed meibomian glands and loss of glandular structure are those who are more likely to tell me that their eyes are irritated and uncomfortable.

Dr Fechtner: The addition of a second drug increases symptoms of ocular surface disease.[21] Both the active ingredient and the excipients (including the preservative) can be implicated. Patients without ocular surface disease may have the ability to tolerate a nominal preservative load. In 1 study, patients on no medications or 1 preserved medication had a similar ocular surface status, but when a second preserved medication was added, there was a substantial increase in ocular surface symptoms.[23] For our patients with preexisting ocular surface disease, this ability to tolerate preservatives may be reduced or lost, and they can become symptomatic with a single medication.

Physical Limitations

Dr Parrish: In addition to tolerability and side effects, what are some other reasons for therapeutic nonadherence to glaucoma treatment?

Dr Fechtner: A number of physical limitations can contribute to nonadherence. These include issues such as tremor or arthritis, which prevent self-dosing of topical eye drop medications. There are also cognitive issues, such as memory loss or dementia, which preclude reliable self-care.

Dr Realini: In these patients, I often try to enlist a spouse or caregiver to assist with dosing. In some cases, medical therapy becomes impractical, and I find that laser trabeculoplasty is a useful alternative in this clinical setting. There is 1 other form of nonadherence worth mentioning. We all have patients who run out of their medication before the end of the month and cannot get refills until the calendar runs out. A few days of nonadherence at the end of every month can add up to significant progression over time, and this is in patients who are making every effort to be adherent.

Physician Behaviors

Physician behaviors also play an important role in patient adherence. The GAPS research team evaluated physician beliefs and behaviors related to adherence.[11] The investigators found that physicians generally fell into 3 categories. The first were "reactives," who tended to avoid considering the extent or causes of nonadherence unless compelled to react if patients raised the issues. The second were "skeptics," who acknowledged the problem of nonadherence, but had little faith that they could change patient behaviors, so they did not generally discuss nonadherence with patients. The third were "idealists," who recognized the problem, believed they could help make it better, and actively addressed adherence with their patients. Interestingly, the idealists were also more likely to engage in active patient education, reinforcing key messages about the risk of blindness, the need for adherence, and techniques for medication dosing.

NONADHERENCE AND RISK OF GLAUCOMA PROGRESSION

The frequency with which a medication is dosed—once, twice, or 3 times daily—is determined by its duration of action. Dosing medications less frequently than indicated creates gaps in therapy, during which IOP can rise and cause optic nerve damage. It therefore stands to reason that frequently missing doses can lead to inadequate treatment of glaucoma, which can contribute to disease progression over time.

Several studies have evaluated the effect of nonadherence on glaucoma progression, with mixed results. One study from the era of pilocarpine evaluated a medicine dispenser—designed by the investigators—that recorded the date and hour that the bottle was opened.[24] In this study, the extent of adherence to therapy was not found to be a predictor of glaucoma progression, but the type of glaucoma, severity of visual field defects, and mean IOP were significant predictors of progression.

A study in 1993 evaluated 72 patients followed for 5 years to identify factors associated with progressive glaucomatous optic neuropathy.[25] Patients in this study who lost visual function were significantly more noncompliant with medical or surgical recommendations for treatment than those whose vision remained stable ($P < .001$). Glaucoma progressed in 50% of all patients noted to have poor compliance, whereas glaucoma remained stable in 90% of compliant patients.

In the modern drug era, a study in 2011 evaluated the relationship between adherence and progression in 35 patients with glaucoma administering travoprost or travoprost/timolol using the TDA for 36 months.[26] The mean adherence rates were 72% after 1 month of follow-up and 77% at 12 months. Overall, 71.4% of the patients maintained stable visual fields and had a median adherence rate of 85%. The remaining 28.6% of patients experienced visual field progression during the study and had a median adherence rate of 21% ($P < .001$). Patients with an adherence rate of at least 90% remained stable, whereas 43.5% of the patients with an adherence rate below 90% progressed ($P = .01$) **(Table 1).**

Table 1. Relationship Between Adherence and Progression in Glaucoma*[26]

	Worsened Visual Field (n = 10)	Stable Visual Field (n = 25)	*P* Value†
Age, years	71 (67-73)	69 (61-74)	.14
No. of concomitant systemic therapies	2 (0.75-4)	2 (1-5)	.72
Adherence rate	45% (20%-45%)	88% (75%-97%)	.0001
No. of patients with very good adherence (> 90%)	0 (0%)	12 (100%)	
No. of patients with intermediate adherence (50%-90%)	2 (14.3%)	12 (85.7%)	
No. of patients with poor adherence (< 50%)	8 (88.9%)	1 (11.1%)	< .001‡

* Data are median (interquartile range)
† Mann-Whitney
‡ Test for trend

Dr Parrish: What is the strength of evidence linking poor adherence with medical therapy and the risk of glaucoma progression?

Dr Realini: We lack the tools and methods for measuring adherence. The patients who consent to participate in an adherence study may represent a biased sample of those most likely to be adherent. Also, knowing that they are being monitored likely motivates better adherence. Therefore, estimates of adherence may be inflated. We cannot easily obtain objective assessments of adherence.

Dr Tsai: Very few studies have directly addressed this important question. Logically, we all believe poor adherence contributes to inadequate IOP control and ultimately results in disease progression.

STRATEGIES FOR BETTER ADHERENCE

Dr Parrish: What can we do to help our patients become more adherent to medical therapy?

Dr Tsai: There are a few obvious things. It seems that we are not very good at identifying the nonadherent patients in our practice, so we should maintain a high level of awareness that some of our patients may have adherence issues. We also have to understand that nonadherence is multifactorial in nature, with different factors at play in different patients. Education is important, but most patients understand that they should follow the recommendations of their doctors, so motivation is at least as important.

Dr Parrish: How do we ask our patients about adherence?

Dr Tsai: Using open-ended questions is better than simply asking, "Are you taking your medications regularly?" Also, as a rule of thumb, if a patient admits to some degree of nonadherence, the severity of the issue is likely worse than what is admitted.[27]

> "Using open-ended questions is better than simply asking, 'Are you taking your medications regularly?'"
> – Dr Tsai

Dr Realini: I go 1 step further when I talk to my patients about adherence. I say, "We all miss a dose of our medicine every now and then. Roughly how many times a week or every 2 weeks do you think you miss a drop?" This grants them permission right up front to be honest with you. I get what I think is a more honest answer. I agree with Dr Tsai that if patients admit to missing 1 or 2 doses, it is probably twice that or more.

Dr Fechtner: Because adherence and tolerability are linked, it is important to discuss potential side effects at the time we are prescribing a new therapy. This gives patients a chance to decline a drug with unacceptable side effects. It also prepares patients for what they may experience once they start the medication. I believe patients can best tolerate adverse effects if you discuss them in advance.

> "I believe patients can best tolerate adverse effects if you discuss them in advance."
> – Dr Fechtner

Dr Tsai: Using an electronic medical record has made me aware that focusing on adherence to 1, 2, or even 3 glaucoma medications is only a small part of the bigger picture. Our patients are on many systemic medications for other medical conditions. For these patients, therapeutic adherence is a bigger issue than can be addressed in our office.

Dr Parrish: This is an excellent observation. As we face an aging population, the burden of eye drops cannot be considered just as an ocular burden, but one on their general medical health because the patients are taking so many medications already.

Dr Tsai: Also, every additional drop we prescribe will negatively affect adherence to the currently prescribed medication.[28]

Dr Realini: When we advance therapy, our patients may retreat from it.

Counseling for Better Administration and Adherence

Discuss potential adverse effects of medications at the time you prescribe them.

Engage the patient by saying, "Tell me how you are taking your medications," rather than asking questions that can be answered "Yes" or "No."

Acknowledge that we all periodically miss a dose. Ask the patient, "Roughly how many times a week or every 2 weeks do you think you miss a drop?"

EMERGING THERAPIES FOR BETTER TOLERABILITY

After a 20-year gap in glaucoma drug innovation, several novel IOP-lowering compounds are in development, potentially offering new ways to lower IOP.

Latanoprostene Bunod

Latanoprostene bunod (LBN) is a modification of the latanoprost molecule that adds a nitric oxide–donating moiety to the compound. Latanoprostene bunod offers a dual mechanism of action: the latanoprost component increases aqueous outflow through the uveoscleral pathway, and the nitric oxide component activates the cyclic guanosine monophosphate pathway, leading to trabecular relaxation and increased conventional outflow.[29] A phase 2 study showed LBN provided superior IOP reduction compared with latanoprost (by 1-1.5 mm Hg; $P \leq .009$).[30] In this study, the conjunctival/ocular hyperemia rate was comparable in the combined LBN-treated groups (7%) and in the latanoprost group (8.5%). In a pair of phase 3 studies, compared with timolol, 0.5%, dosed twice daily, once-daily dosing of LBN, 0.024%, produced a lower mean IOP at each of the 9 time points (8 AM, 12 PM, and 4 PM at weeks 2, 6, and 12) in 1 study,[31] and at 8 of 9 time points in a second study.[32] Common side effects (> 2% incidence) included eye irritation (3.9% vs 2.2% for timolol) and conjunctival hyperemia (2.8% vs 1.5% for timolol).[31]

Rho-Kinase Inhibitors

The Rho-kinase inhibitor netarsudil mesylate also lowers IOP through several distinct mechanisms. The molecule inhibits the enzyme Rho kinase, which results in trabecular relaxation and produces IOP reduction via increased trabecular outflow and reduced episcleral venous pressure.[33,34] This drug also inhibits the norepinephrine transporter, which increases adrenergic activity, reducing aqueous production. Two phase 3 trials have been completed, but have not yet been published. Development of this drug includes both a single agent and a fixed combination with latanoprost. In a phase 2b, 28-day study evaluating the fixed combination compared with either agent dosed separately, mean IOP reduction of the fixed combination was 7.8 to 8.6 mm Hg, compared with 6.3 mm Hg for netarsudil mesylate monotherapy and 7.6 mm Hg for latanoprost monotherapy.[35] The most common side effect was conjunctival hyperemia, which occurred in 40% to 41%, 40%, and 14% of patients receiving the fixed combination, netarsudil mesylate monotherapy, and latanoprost monotherapy, respectively. Fixed combinations offer a simplified regimen and a reduction in exposure to excipients.[36]

Adenosine Agonists

Trabodenoson is an adenosine receptor agonist with high affinity and specificity for the adenosine A1 receptor. When activated, the A1 receptor lowers IOP in nonhuman primates, in part by regulating the composition of the extracellular matrix of the trabecular meshwork, resulting in increased aqueous outflow.[37,38] A topical ophthalmic formulation of trabodenoson is in clinical development for the reduction of elevated IOP in patients with ocular hypertension or POAG. In a phase 1 evaluation, the drug was well tolerated, with eye pain being the most common ocular side effect (< 10%), and demonstrated no systemic accumulation or toxicity.[39] Only 1 subject experienced hyperemia. In a dose-ranging phase 1/2 study, IOP reductions with the highest tested dose ranged from -4 to -7 mm Hg.[40] In this study, the prevalence of conjunctival hyperemia did not increase from pretreatment baseline in any dose group. Phase 3 clinical development is under way.[41]

Advances in Drug Delivery

The need for daily self-administration by patients is an important contributor to nonadherence in glaucoma therapy. Several novel drug delivery strategies are currently under investigation. A sustained-release formulation of bimatoprost, packaged in a bioerodable implant, is designed to be injected into the anterior chamber and may provide IOP reduction for up to 4 months.[42] A phase 3 trial vs timolol is under way.[42] A similar approach aims to deliver travoprost in this fashion.[43] Less invasive options include a punctal plug that elutes travoprost[44] as well as a silicone ring that rests on the peripheral ocular surface and elutes bimatoprost.[45]

Dr Parrish: What is the unmet need in glaucoma medical therapy?

Dr Realini: We tend to focus on efficacy, but the prostaglandin analogues set the bar very high for efficacy. A new drug does not need to have better efficacy than a prostaglandin to be of value. A drug with equal efficacy to a prostaglandin, but which is better tolerated, would satisfy the unmet need of patients who cannot tolerate prostaglandin side effects.

Dr Fechtner: Likewise, a drug with similar efficacy and safety that is dosed less often than a prostaglandin would have value for many patients. One or more of the novel drug delivery systems described above may satisfy this unmet need.

Dr Tsai: These are all promising new drugs. Their place in our treatment strategy will only become apparent once they are approved and we gain experience with them.

SUMMARY

The goal in managing patients with glaucoma is to optimize their quality of life as they live with the disease. Both the disease and its treatment can adversely affect quality of life. Reduction of IOP is the only established therapy for glaucoma, and therapeutic adherence remains a significant clinical challenge in maintaining target IOP. Nonadherence to therapy can lead to progression of glaucoma. The side effects of therapy—particularly ocular tolerability issues—is a common reason why patients do not take their medications regularly. Selection of therapy should consider its direct effect on quality of life in relation to its side-effect profile, as well as the indirect effects that may occur if tolerability issues lead to nonadherence and disease progression. Physicians and patients can work together to optimize therapeutic adherence. Novel drugs in development may provide new options for well-tolerated therapy.

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1. **Which of the following would not raise your estimate of a patient's risk for glaucoma progression?**
   a. Disc hemorrhage
   b. Thin central cornea
   c. Hyperopia
   d. Older age

2. **Regarding adherence with glaucoma therapy, it is true that:**
   a. Nearly 80% of patients take their glaucoma medications regularly
   b. Physicians can easily identify nonadherent patients
   c. It is not possible to improve patients' adherence to glaucoma therapy
   d. Nonadherence can involve both not taking medications and not keeping appointments

3. **Risk factors for nonadherence include:**
   a. Younger age and Hispanic ethnicity
   b. African American race and older age
   c. Younger age and poor overall health
   d. Myopia and diabetes

4. **Conjunctival hyperemia occurs in _____ patients using topical prostaglandin analogues.**
   a. 8% to 17%
   b. 14% to 22%
   c. 33% to 45%
   d. 47% to 69%

5. **What percentage of treated patients with glaucoma have symptoms of ocular surface disease?**
   a. 10%
   b. 25%
   c. 50%
   d. 75%

6. **Which of the following is a potential consequence of adding a second medication to a patient whose glaucoma is inadequately controlled on a single medication?**
   a. The risk of ocular surface symptoms increases
   b. Adherence to the first medication improves
   c. Patient experiences improved quality of life
   d. The visual field test improves

7. **Physicians can address adherence by:**
   a. Asking patients, "Do you take your drops every day as prescribed?"
   b. Recognizing that many patients are nonadherent to therapy
   c. Assuming they can identify the nonadherent patients in their practice
   d. Minimizing the risk of side effects when initiating new therapy

8. **Which of the following is the correct pairing of an IOP-lowering drug and its mechanism of action?**
   a. Latanoprostene bunod increases both trabecular and aqueous production
   b. Trabodenoson increases trabecular outflow
   c. Netarsudil mesylate increases trabecular outflow and episcleral venous pressure
   d. Latanoprost increases aqueous production

ACTIVITY EVALUATION/CREDIT REQUEST

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☐ Yes ☐ No **Did you perceive any commercial bias in any part of this activity? IMPORTANT! If you answered "Yes," we urge you to be specific about where the bias occurred so we can address the perceived bias with the contributor and/or in the subject matter in future activities.**

_____

Circle the number that best reflects your opinion on the degree to which the following learning objectives were met:
5 = Strongly Agree 4 = Agree 3 = Neutral 2 = Disagree 1 = Strongly Disagree

Upon completion of this activity, I am better able to:

- Counsel patients on optimal administration and adherence strategies 5 4 3 2 1
- Describe the effect of tolerability of glaucoma medications on patient adherence 5 4 3 2 1
- Describe the mechanism of action of current and emerging topical glaucoma therapies 5 4 3 2 1

1. Please list one or more things, if any, you learned from participating in this educational activity that you did not already know.

_____

2. As a result of the knowledge gained in this educational activity, how likely are you to implement changes in your practice?
4 = definitely will implement changes 3 = likely will implement changes 2 = likely will not implement any changes
1 = definitely will not make any changes

4 3 2 1

Please describe the change(s) you plan to make: _____

_____

3. Related to what you learned in this activity, what barriers to implementing these changes or achieving better patient outcomes do you face?_____

4. Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced for you through participation in this activity.
☐ Patient Care ☐ Practice-Based Learning and Improvement ☐ Professionalism
☐ Medical Knowledge ☐ Interpersonal and Communication Skills ☐ Systems-Based Practice

5. What other topics would you like to see covered in future CME programs? _____

ADDITIONAL COMMENTS _____

_____

POST TEST ANSWER BOX

1	2	3	4	5	6	7	8