Clinicians: prostaglandins are the clear choice for first-line glaucoma therapy

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NEW YORK — Boasting once-a-day dosing, minimal side effects, persistence and efficacy, some practitioners feel prostaglandins are a clear choice as first-line treatment for glaucoma. Although only one prostaglandin — Xalatan (latanoprost ophthalmic solution, Pfizer Inc., New York) — is currently FDA approved as first-line therapy, many clinicians strongly recommend this indication for all available prostaglandins.

“These are all great medications, and they all work very well,” said Bruce E. Onofrey, OD, RPh, a Primary Care Optometry News Editorial Board member based in Albuquerque, N.M. “They are a godsend to the treatment of glaucoma. There has been a huge drop in the number of patients who have needed to go forward and have surgery, and there has been a drop in the use of other glaucoma medications since these drugs came along.”

Dr. Onofrey lectured on prostaglandins at last year’s Primary Care Optometry News New York Symposium.

Efficacy debate

While Xalatan is the only one of the three that has a first-line indication in the United States, the European Commission approved Lumigan (bimatoprost ophthalmic solution, Allergan, Irvine, Calif.) and Travatan (travoprost ophthalmic solution, Alcon, Fort Worth, Texas) as first-line therapy for the reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension patients.

According to Dr. Onofrey, clinical comparisons between Xalatan, Lumigan and Travatan have escalated into an all-out efficacy “war.”

Take-home pearls

- The effects of prostaglandins are consistent over time.
- Minimal absorption of the drug occurs outside the eye
- In patients who experience hyperemia, the goal is to get them past the first 2 weeks, when the redness will decrease.
- Beta-blockers are still a viable option for some patients.

Exhibit 1058

“Although these are all excellent drugs, there is a lot of pressure on the companies right now to differentiate their products in some way,” he told the audience.

Dr. Onofrey cited one of the most recent studies conducted on this topic, by Robert J. Noecker, MD, and sponsored by Allergan.

This 6-month, multicenter, randomized, masked, prospective, parallel-group clinical comparison found that mean changes from baseline IOP were 0.9 mm Hg to 2.2 mm Hg greater with Lumigan than with Xalatan. The greater IOP-lowering efficacy of Lumigan relative to Xalatan was also confirmed by the mean IOP, which was “statistically significantly lower in the Lumigan group at all timepoints on all follow-up visits,” Dr. Onofrey said.

Dr. Onofrey also discussed a Pfizer-sponsored study by Richard K. Parrish, II, MD, of Bascom Palmer Eye Institute, University of Miami. This study determined that all three prostaglandin analogs have similar effectiveness.

This 12-week, randomized, parallel-group, masked-evaluator study was conducted at 45 U.S. sites. The study compared the IOP-lowering efficacy of the three drugs, as well as ocular tolerability and systemic adverse events.

The determination was that the three medications had comparable IOP-lowering effectiveness in patients with open-angle glaucoma or ocular hypertension. Study participants reported a greater tolerability for latanoprost.

Shortcomings of the studies

Dr. Onofrey said that although both of these studies were well done, the International Glaucoma Review was concerned with some of the flaws of each study.

“Anne Coleman, MD, PhD, editor of the International Glaucoma Review, stated that ‘the fact that manuscripts or clinical studies come to different conclusions despite similar study designs has caused a lot of consternation and confusion among clinicians,’” Dr. Onofrey said.

Some of the study differences cited were the fact that Dr. Parrish’s subjects were older, fewer of them were Caucasian, more were brown-eyed and more were open-angle glaucoma patients vs. Dr. Noecker’s slightly higher percentage of ocular hypertensives.

In addition, Dr. Onofrey stated that there was a higher baseline IOP in Dr. Parrish’s patients, although not clinically significant.

Dr. Onofrey said that another major shortcoming of both studies is that they do not include central corneal thickness data. “You can see the variability and adjusted pressures that can occur by including that particular data,” he said.

Dr. Onofrey said that, at this point, there is no clear evidence of superiority among the prostaglandins. “If this is true, then the deciding factor should be side effects,” he said.

Side effects of prostaglandins

According to J. James Thimons, OD, a lecturer and Primary Care Optometry News Editorial Board member based in Fairfield, Conn., the topic of side effects and contraindications of prostaglandins is thankfully not a very broad one. “We all know the side effects are fairly superficial,” he said. “No evidence exists of any serious side effects of these drugs.”

Dr. Thimons also addressed the PCON New York Symposium crowd.

Hyperemia is one noted side effect of prostaglandins, especially in the first 2 weeks of treatment, Dr. Thimons told the audience. Lumigan tends to have the highest incidence of hyperemia, he added.

“So your goal as a clinician is to get the patient past that 2-week zone where hyperemia decreases and be able to maintain the use of the drug, even though you are going to get a little bit of red eye,” he said. “One way around this is to instruct patients that the drug will make their eye a little red for the first few days, and we expect that to happen. I ask them to please call me if they *don’t* get a red eye.”

According to Allergan, data presented at the recent American Glaucoma Society meeting by June Chen showed that vasodilation — not inflammation — appears to be the cause of hyperemia following Lumigan instillation.

Iris pigmentation tends to be quite variable in terms of its prominence in a particular practice. “My patients are probably 35% to 40% Irish, English, Scottish or Northern-European Caucasians with glaucoma,” he said. “The vast majority do not have brown eyes, and there is a large population of high-risk irises in our practice that we feel compelled to identify and follow.”

Dr. Thimons said iris pigmentation is the major irreversible complication and needs to be explained to patients. “The actual complication is not a problem medically for patients. It is simply cosmetic,” he said. “There is no indication that the change of the size of the melanocytes will affect outcome. However, I do refrain from first-line use of this therapy in pigmentary dispersion patients.”

Not all prostaglandins are “created equal” in this area, Dr. Thimons said. “There is a difference in the drugs in this category. Both Travatan and Lumigan have significantly lower rates of iris pigmentation, somewhere between 1.5% and 3%, whereas Xalatan has a significantly higher rate at 16% at 12 months,” he said.

Dr. Thimons said in patients with high-risk irises, he would adjust his prescribing habits based on this information. “I also think it is important to discuss this issue with patients at risk before starting them on therapy,” he added.

Hypertrichosis is another side effect that is rather benign and, in some cases, desirable, Dr. Thimons said. “The increased number, density and pigmentation of eyelashes is interesting,” he said. “It is not necessarily a negative effect. It is also an interesting indirect monitor of compliance.”

Periorbital pigmentation is a much less cosmetically appealing side effect of prostaglandins, Dr. Thimons said. This side effect, which occurs in fewer than one out of every 500 patients, appears as a deepening of the coloration in the immediate periorbital area. However, this side effect is reversible, he said. “It takes about 2 to 3 months to come on, and once the medication is stopped, the reversal takes about the same amount of time,” he said.

The incidence of cystoid macular edema is an infrequent side effect of prostaglandin use, Dr. Thimons said. “It does occur,” he said. “But if you have an uncomplicated cataract surgery, you can use this drug afterwards, and, in all probability, it will be a safe drug for you.”

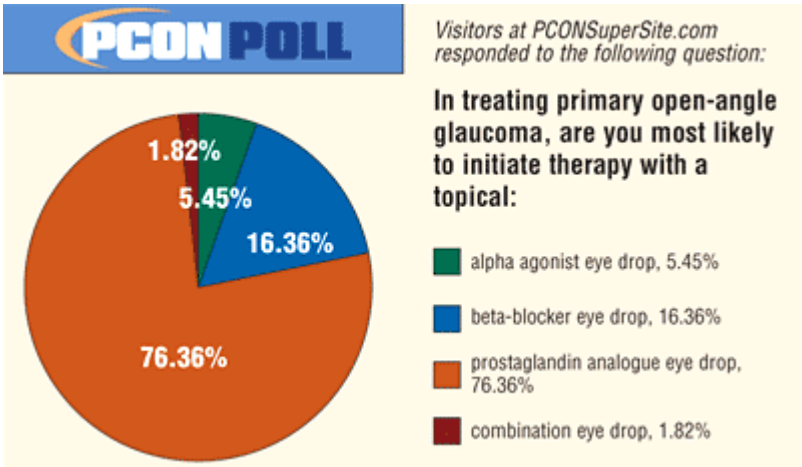
Dr. Thimons did advise against the first-line use of prostaglandins for patients with a history of herpes simplex keratitis or herpes zoster keratitis. “I would also put into this category patients with chronic uveitis, because the drug does activate an inflammatory cycle as part of its mechanism of action,” he said.

Chemical structure of prostaglandins

Dr. Onofrey discussed the chemical structure of prostaglandins. He said that all three of the main prostaglandin drugs start with the same basic nucleus, to which side chains have been attached.

“They all have an important factor, and that is their ability to bind to receptors. These are receptor-based medications,” he said.

"When we combine these drugs, we try to produce synergism. Prostaglandins are one of the few medications that work by increasing outflow, so we try to combine a drug that increases aqueous production, he continued."



A word about beta-blockers

Dr. Thimons emphasized that the emergence of prostaglandins as first-line therapy has not eliminated other options, such as beta-blockers, the previous first-line choice. "Prostaglandins have just supplanted a broad portion of the selection process and made themselves the first-line choice," he said. "The selection has not been reduced."

Dr. Thimons added that beta-blockers are still a viable option for glaucoma treatment and, in some cases, are the best therapy for some patients. "There has been a lot of beta-blocker bashing going on, but they are very good drugs," he said. "They have been around a long time, and there have been only 38 recorded deaths out of millions of patients."

He added that many glaucoma patients will still end up using a beta-blocker at some point in their treatment. "If you have a patient on two drugs, one of the drugs will be a beta-blocker in 90% of patients," he said. "So don't give up on beta-blockers. They are really good drugs. They are just not the drug we are using as first-line therapy anymore."

Prostaglandins: the drugs of the future?

According to Dr. Thimons, there is little question that prostaglandins have arrived at the forefront of glaucoma treatment.

He said prostaglandins feature a once-a-day dosing, which is quite effective. In addition, he said, prostaglandins show persisitence and endurance over time.

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