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Innovations in Glaucoma Therapy

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Here's Dr. Pradeep Ramulu.

Dr. Ramulu:
This is CME on ReachMD, and I'm Dr. Pradeep Ramulu.

Dr. Craven:
And I'm Dr. Randy Craven.

Dr. Dunbar:
Hi, and I'm Dr. Mark Dunbar.

Dr. Ramulu:
So, to get us started, Dr. Dunbar, can you discuss some of the differences between the pharmacologic and surgical approaches for the treatment of glaucoma? When do you decide to pursue pharmacologic therapy, and when do you decide to pursue surgical therapy? And what patient factors play into this patient selection?

Dr. Dunbar:
Medical therapy in the form of topical pharmacological eye drops have really been the mainstay in glaucoma treatment for many, many years – I think for many good reasons. These are noninvasive, highly effective ways to lower the intraocular pressure. So I think the idea of medical therapy is these are safe with minimal side effects, and in the day and age that we're practicing today, we've really got a full armament of eye drops or medications to choose from, but I think we recognize there's drawbacks. And so one of the questions was when do you choose to go from medical therapy to surgical therapy? Whenever I make a diagnosis – whether of glaucoma or if a patient is new to me – that's really one of the – kind of the discussions I have with a patient. You know, instead of brushing compliance under the rug, I kind of bring it out in the beginning to just let them know that not everybody is good at taking a drop; not everybody can remember to take a drop, and that's okay. So, I talk about the fact that there's other ways to lower the IOP besides using an eye drop, including surgical therapies such as trabeculectomy or shunt therapy. And so we know that those advances will also work. They're very effective in the treatment of glaucoma. Typically, surgical therapy has really been reserved for really more of the severe glaucoma patients. You know, patients where they may come in with advanced glaucoma and its damage, and you need to get the pressure down to that 10 to 12. And there may be no other way to do that other than surgery in patients where you can't take the chance of being compliant or not compliant because they've already got advanced visual field loss. So, I think those are some of the considerations that we think about when we're making a decision. Do we keep this patient just on medical therapy, do we add a drop, or is it time to pull the

trigger and perhaps recommend a surgical therapy?

Dr. Ramulu:
I think that's a great summary, and I think that all these new treatment options are both a blessing and a curse – a blessing because we have so many options, and a curse because we have to figure out which one to use and when. So a great summary.

Dr. Dunbar, in the last three years or so, we've seen the approval of a number of new pharmacologic agents. Can you tell us about some of these new medicines? What are their mechanisms of action, dosing schedules, and the results from the seminal clinical trials which described these agents? What else do we as practitioners need to know about them?

Dr. Dunbar:
I think one of the – kind of the new and exciting class of drugs are the Rho-kinase inhibitors particularly. The first one out of the gate was netarsudil, or Rhopressa. These drugs have really a unique mechanism of action by inhibiting Rho-kinase. They lower the intraocular pressure really three ways. They increase aqueous outflow, they decrease episcleral venous pressure, and of course, they also reduce aqueous production. And so these drugs, as I said, are really very effective. I think the unique mechanism of action, particularly decreasing episcleral venous pressure, is pretty exciting. So you're looking at patients, for example, with normal-tension glaucoma where, you know, in a sense there's only so low you can get the intraocular pressure. You can't get it below episcleral venous pressure, and so by being able to kind of lower episcleral venous pressure, we're able to maybe get the pressure down even a little bit lower, particularly in that group of patients. So, again, I think one of the advantages of Rhopressa, it's really good as a single agent first-line, but it's also additive to other agents. This is a medication that you can expect in clinical trials of about 4 to 5 mm Hg, so maybe not quite latanoprost level, but it's a drug that can be added to latanoprost. And, again, I think the unique mechanism of action makes it really very exciting.

I think the one that came out of the gate that we really liked was the Rocklatan, so that's the combination of netarsudil and latanoprost in combination. So Rocklatan is one of those that really, when you combine it, did a particularly good job. So you're talking an addition of about 1.5 to 3 mm of IOP lowering than you did each drug individually. So, again, the idea of a combination therapy, if we can lower the burden of treatment, improve quality of life, I think from a patient perspective it's really a winner. And, again, the fact that it really has a unique mechanism of action really makes this a very exciting drug.

There's two other latanoprost molecules that have been FDA-approved. Of course, Vyzulta, which is latanoprost bunod; it has that nitrous oxide attachment to it. And we know that nitrous oxide has an effect by relaxing smooth muscle. So, again, this is a unique formulation of latanoprost that may get us an additional 1 to 3 mm Hg beyond what we were able to get with latanoprost. And, of course, the downside is we talk about sometimes now you're competing with generic latanoprost, but again, within terms of a unique mechanism of action, this really may be a good first-line therapy in terms of glaucoma medications. In the clinical trials when it was being compared to timolol, again, about 8 to 9 mm Hg compared to about 6 to 7 with timolol. So again, very powerful, very effective medications. And again, the third one in that list, or the fourth one, being Xelpros. So this is latanoprost that doesn't have benzalkonium chloride. So, again, when you think about your patients who've got ocular surface disease and dry eye and many elderly patients, this really may be a good go-to medication because it removes that BAK element to the medication.

Dr. Ramulu:
Well, thank you, Dr. Dunbar. Those are great comments, and it's very exciting that we have some new pharmacologic options after so many years. I think one of the things that we've struggled with are maybe some side effects from these medications and also getting prior authorizations.

For those of you just tuning in, you're listening to CME on ReachMD. I'm Dr. Pradeep Ramulu, and I'm joined by Dr. Mark Dunbar and Dr. Randy Craven. We're examining surgical and pharmacological innovations in glaucoma therapy and how to apply them to clinical practice.

Now that we've had a very good discussion about the latest innovations and pharmacologic therapy, Dr. Craven, can you tell us about some of the exciting new advances that are happening in surgical therapies for glaucoma?

Dr. Craven:
Yes, I'd be happy to. You know, Dr. Ramulu, there's been so many things that have changed over the years. The most prominent thing that people hear about when they go into their ophthalmologist's or optometrist's – in many cases because they're working in conjunction with co-managing cataract surgery – is about some sort of a microinvasive or microincisional glaucoma surgery; the MIGS they call that. And two of the most common ones you've heard about are the eye stent, and then the other one is the Hydrus, which was released recently. And then for a while we had one called the CyPass that's been withdrawn. But the MIGS devices have gone through different generations and revisions.

So the most recent release was one called the iStent inject wide, which is a little bit of a larger injectable implant that's put in with a guidewire that we go across the anterior chamber, go up to the trabecular meshwork, gently deploy it so it goes through the meshwork. And the wide is a little bit bigger, so it doesn't go too deep, and it stays just right at the – flush with the surface of the trabecular meshwork. And it allows, basically, a snorkel for the aqueous to go into the canal of Schlemm and bypass the trabecular meshwork, and as we all know, that's where the source of resistance is for aqueous outflow.

The other area that we really tried to improve upon is that of completely doing a scleral bypass, which is a trabecular bypass as well as going through the sclera itself, so a fistula or a filtering surgery or some kind of a stent surgery. And there's one on the horizon and one that was released a few years ago, an implant that that we've been using. One is called the XEN implant, and that's basically a refined porcine collagen tube.

Dr. Ramulu:
Great, super. Do you want to talk about some of the new sustained delivery implants, also?

Dr. Craven:
Yes. You know the world of sustained release has always personally intrigued me, all the way back to when I used to use the Ocusert, which was a little ring that we had that we'd put on the surface of the eye, almost like a small contact, that delivered pilocarpine. And it was two polymers sandwiched that let pilocarpine slowly leak out, and it worked great.

So the bimatoprost sustained-release implant – the marketed name for it is Durysta – was approved by the FDA for a single use, and the patients, as you talk to them about this as being something that we could try for them and see how they do with it, are much less resistant to the idea of an injectable or an implantable medication than I thought they would be because I just didn't know how responsive patients would be to that. But many people know how much they hate using drops, so they're interested in it.

So, I've already been using it in the clinic. We have a little procedure room set up to do this. It's done either at the slit lamp or in a procedure room. Patient comes in, they receive some topical anesthetic, some antiseptic – we usually use 5% povidone-iodine – and then have the patient look or fix on something straight ahead. You come up to the temporal cornea and just gently go through the cornea with a very sharp needle that's on this inserter and put the pellet inside the anterior chamber. That slowly releases the drug in the anterior chamber. And the studies that we evaluated this in show that up through three months, the vast majority of patients, like over 90%, have pressure control that was the equivalent of one or two medications that they had been on topically going into receiving the implant, and in a subset of patients, get sustained pressure control.

I was an author on one of the papers where we looked at what happened up to two years out after patients had received this, and 28% of the patients after a single injection of the Durysta had pressure control up to two years, which is really quite remarkable. The things that we obviously have concern about is what does something inside of the eye do to the cornea? This was one of the reasons that the FDA has approved it just initially for a single use until that gets worked out better to understand the effects of the implant and the medications on the cornea over a sustained period of time.

Dr. Ramulu:
Great, thank you for that. Dr. Dunbar, did you have any additional commentary to Dr. Craven's description of these new surgical innovations?

Dr. Dunbar:
Yeah. I think, obviously again, an exciting time for glaucoma management. I think the bimatoprost insert, from an OD perspective, I think is perhaps the most exciting. You know, this is a procedure that can be done – as you point out, it can be done in the office. You know, it's almost taking what the retina world is doing in terms of intravitreal injections, and again, not that it's that simple, but, you know, I think in an efficient and effective way to deliver a drug over a long period of time. You talked about, Dr. Craven, the issue of compliance, and we've talked about it earlier. I think this is really an exciting mode of lowering intraocular pressure in a – kind of a noninvasive format, if you will.

Dr. Ramulu:
Well, thank you for what's been a very valuable conversation, and as we wrap up, I'd like both Dr. Dunbar and Dr. Craven to maybe share with the audience one take-home message you want them to remember from our discussion. Dr. Dunbar, do you want to go first?

Dr. Dunbar:
I think from an optometric perspective, obviously we know that glaucoma is a huge burden. There's a number of patients who have it. We see a number of patients who maybe aren't able to get in, are not able to be effectively treated, and I think the fact that we've got some new medications that are now available is an exciting time.

Dr. Ramulu:
Terrific. Dr. Craven?

Dr. Craven:
I personally think that we're just on the tip of a huge iceberg. We're going to see a lot of changes occur as a result of intraocular drug deliveries. And I do think as the microinvasive surgeries keep getting evaluated and tweaked, we're going to see better ones come out.

Dr. Ramulu:
All right. Well, I think for me the real take-home is that we need to understand what our patients want on an individual level better because I think right now, with so many different options available, there's no single solution for each individual patient, so we need to really customize our therapy. Are we looking to lower the pressure more with medicines? Are we looking to get people off medicines? Are we looking for people who are more comfortable and need to be on preservative-free therapy? So, I think there's more customization than ever that needs to happen, and so there's a lot of learning that needs to happen about the different ways that we have available to do this.

Well, thank you all. Unfortunately, that's all the time we have for today, so I want to thank our audience for your participation, and thank you, Drs. Dunbar and Dr. Craven, for joining me and sharing all your valuable insights. It was great speaking with you both today.

Dr. Dunbar:
Thank you, guys. It was a great discussion. Appreciate being involved in this.

Dr. Craven:
Thank you, Dr. Ramulu, Dr. Dunbar. It was great.

Announcer:
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