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Exploring Current Trends in the Treatment of Retinal Diseases

Announcer:
You're listening to ReachMD, and this is *Eye on Ocular Health*. This episode is sponsored by Regeneron. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Retinal diseases like diabetic retinopathy, diabetic macular edema, and WET age-related macular degeneration affect tens of millions of patients every single year. But what's even more troubling is that the prevalence of those diseases is only expected to increase. So, what direction can we take based on the current treatment paradigms to combat this growing threat, and more importantly preserve our patients' vision? Coming to you from the ReachMD studios, this is *Eye on Ocular Health*. I'm your host, Dr. Jennifer Caudle and joining me to review current trends in the management of retinal diseases is Dr. Christina Weng, an Associate Professor of Ophthalmology at the Baylor College of Medicine. Dr. Weng, thanks so much for being here today.

Dr. Weng:
Of course. Thank you for having me, Dr. Caudle.

Dr. Caudle:
Well, we're excited that you're here. And to start us off, Dr. Weng, can you give us an overview of the current types or classes of treatments that are available to address the range of retinal diseases you're encountering in practice?

Dr. Weng:
Yeah, absolutely. Well, just like you said, we have a lot of different retinal diseases that are actually growing in prevalence and those include things like diabetic retinopathy, diabetic macular edema, wet macular degeneration, and something called a retinal vein occlusion. So, I just want to touch on each of these briefly because I think it'll nicely summarize what types of treatments we have these days because we really are in a much different terrain than where we were even as recent as 20 years ago; it's super exciting.

I'll start off with diabetic retinopathy, a disease that's really near and dear to my heart. So, as you and I both know because of the patients that we treat, diabetes mellitus is truly a global epidemic at this point. It affects nearly 10 percent of the population and globally that's nearly half a billion, actually some estimates have surpassed that already, over half a billion people around the world. And this is increasing because of a lot of different factors, but partly because of the obesity epidemic that's also, sort of, running in parallel. And diabetic retinopathy we know from our epidemiologic studies is going to affect the vast majority of patients with diabetes mellitus. And the sad truth of diabetic retinopathy is that it's one of the most common causes of blindness around the world, but it's also something that doesn't necessarily have to happen. In my opinion, it's really a cause of needless blindness. Nobody should go blind from diabetic retinopathy these days because we have fabulous treatments that are available. And some of those include laser treatments. But really, far and away, the most common type of treatment these days in proliferative diabetic retinopathy as well as diabetic macular edema and wet macular degeneration and retinal vein occlusion are these injections that we give into the vitreous cavity called intravitreal injections of an agent called anti-VEGF, or vascular endothelial growth factor.

And then, you know, of course, diabetic macular edema, like you mentioned also affects a good proportion of patients who do have diabetes mellitus. About a third of people with diabetes eventually will have diabetic macular edema, also known as DME at some point in their lifetime. This is a common cause of vision loss in this group of patients. And diabetic macular edema, there's a lot of different ways to treat it, as well. We sometimes turn to laser that was, an older type of treatment. Sometimes we'll inject steroids into the vitreous cavity. Very rarely we'll turn to surgery. But far and away the most common treatment once again are these anti-VEGF injections that we give, very similar to what I mentioned early for proliferative diabetic retinopathy, which we also use to treat that

disease. But diabetic macular edema is something that responds well to these anti-VEGF injections. The only drawback is that these patients who are affected with this disease oftentimes are a lot younger than patients with some of the other diseases that we treat, for example, wet macular degeneration, and as a result, they have a lot of other responsibilities and demands on their time. For example, it's people who are employed who have family, who have young children that they're taking care of, and it makes it difficult for them to come in for these recurrent injections that are needed to stabilize their visual acuity. And that's really one of the directions I think where treatment is headed.

I wanna move on to wet macular degeneration, which is another disease that you mentioned. This is also increasing in prevalence but it's because of our aging population. So, this is really affecting millions and millions of people around the world at this point, for wet macular degeneration about 200,000 new cases of wet AMD are diagnosed each year in North America. And like I said, we're only expecting this to grow. In the past, we treated wet macular degeneration with a cold type of laser called photodynamic therapy. There was even a short period of time where we were looking at surgical approaches. But truly it's the anti-VEGF intravitreal injections that have revolutionized the treatment of wet macular degeneration. And we actually have four agents to choose from these days, three of them of which are FDA approved. And like I said, this was once a blinding disease and now patients can actually do very, very well as long as they receive sufficient and enough of these injections on a frequent basis. Again, one of the drawbacks is that these patients often times have to be treated recurrently and for oftentimes the rest of their life in order to control their disease. And so again, just like with diabetic macular edema, we're looking at other avenues that we can potentially take to reduce that treatment burden.

And then the last one I'll touch on is just retinal vein occlusion. Retinal vein occlusion is one that we don't talk about as much, necessarily, as some of these other diseases, but it's actually the second most common retinal vascular disease, only secondary to diabetic retinopathy. And retinal vein occlusion can cause something called cystoid macular edema or swelling of the back of the eye, macular edema, in the retina. And again, we used to use laser at periods of time, some people actually still will use intravitreal steroids, which are very effective, but I would say the first line agent these day is again anti-VEGF injections. And so, there's a lot of research going on in those areas, too, and a lot of these longer durability agents that are being studied may also eventually be able to be applied to this condition, as well.

Dr. Caudle:
And where would you say the current guidelines land on treatment recommendations across retinal disease types? Are there any notable strengths or weaknesses in the available data behind our current standards of care?

Dr. Weng:
Well, I think one of the primary guidelines for all of these diseases is early detection. And we know that the earlier you detect any of these diseases and the sooner you can start treatment the better off these patients will be and the better their visual acuity outcomes tend to be. So, it's difficult to, sort of, speak on a whole for all of these diseases because the guidelines are quite different. But for example, for diabetic retinopathy, I'll start there because this is one of the leading causes of vision loss and the number one cause of vision loss amongst working age Americans, actually. The guidelines there are that every diabetic patient should have at least an annual dilated funduscopic examination. I strongly recommend this because I think one of the myths out there is that if they're seeing OK then they don't need to worry, and that's just not true with diabetic retinopathy.

Dr. Caudle:
Excellent. And based on this data, do any safety concerns stand out to you among these treatment categories applied to specific diseases, such as anything that makes the risk-to-benefit ratio more difficult to navigate?

Dr. Weng:
Well, sure. I think again, just narrowing in on a couple of comments that are, sort of, relevant to the current point here. You know, one of the things we've done traditionally for non-proliferative diabetic retinopathy, for example, is to watch those patients. We actually haven't typically intervened from an ophthalmologic standpoint. What we would usually recommend for patients with proliferative diabetic retinopathy is that they control their blood glucose levels, optimize their cardiovascular risk factors, and keep their A1C below 7. You know, it was really more of a medically managed type of condition. But lately in the past couple of years we've had two major trials that have come out looking at whether anti-VEGF injections should be started in these patients even earlier on in the disease spectrum. And those two were called PANORAMA and Protocol W and both of them showed that we might be able to significantly reduce the risk of progression to vision-threatening complications if we give injections of aflibercept, which is one of the anti-VEGFs and that was the drug that was studied in both of these trials. And, you know, just to be specific, I think the numbers are pretty impressive. For example, in the PANORAMA trial, for example, at the 52-week endpoint between 65 and 80 percent of aflibercept groups had a 2 or greater step improvement in the DRSS score, meaning their retinopathy looked significantly better with these injections given and fewer had vision-threatening complications, as well.

There's actually the newest anti-VEGF that was most recently approved for wet macular degeneration, was called brolucizumab. And what we've learned just speaking more broadly about all of these is that, you know, while a lot of them do offer a potentially longer duration of effectiveness, and that would potentially lower the treatment burden, there seems to be some safety trade-off, at least to some extent, for example with brolucizumab. We noticed after it was actually approved and in the market and being used, we noticed that patients, a small proportion were having significant intraocular inflammation and that a small proportion of that small group were actually having vision-threatening vasculitis, in the back of their eye and so we've become a little bit more wary I think as a community about some of the she newer agents that are coming down the line. We just have to learn more. I think what we've learned in general is that the phase 3 trials that we study for these agents may not be enough. You know, thousands of patients is great, but I think sometimes for these rare events, you needs tens of thousands, hundreds of thousands, or even millions of patients to really feel confident about their safety profiles. And I mentioned also the port delivery system that was recently FDA approved for wet macular degeneration. That's really exciting, but it's also our first surgical options for wet macular degeneration. And while I'm very excited I think about the benefits that it can bring for our patients with wet macular degeneration, I think we also need to be cautious in the way we introduce this to the community because it is a surgical procedure. In the phase 3 studies, there were some adverse events that we don't typically see with our medical treatments of intravitreal injections simply because it is a surgery. You know, some patients had bleeding in the back of their eye, some people have conjunctival retraction and there was a very low rate of endophthalmitis. And so, we need to really refine and exchange best practices for how we're gonna perform these surgeries in the safest way possible so that we can really maximize the benefit to our patients and maximize that benefit/risk ratio.

Dr. Caudle:
And before we close, are there any other take-aways you'd like to leave with our audience with regarding the management of retinal diseases?

Dr. Weng:
Sure, well, again thank you Dr. Caudle for having me today. I think that the most important take-away is that you can't treat what you don't diagnose and what you don't know about. And so again, we all need to work together, collaboratively in our medical community.

And just remember that, you know, and I always, this is always near and dear to my heart because my grandmother actually went blind in her 50s from wet macular degeneration and it was a time before we had agents like anti-VEGF unfortunately and that you know, is something I always share with my patients because I remind them that we are in a totally different era. You don't need to go blind from wet macular degeneration anymore. You don't need to go blind from proliferative diabetic retinopathy anymore. If we can detect these diseases early enough and get these patients treated on a regular and sufficient basis, we have a very good chance, a very, very good chance of keeping their vision healthy and keeping these patients productive citizens and happy people for the rest of their lives.

Dr. Caudle:
I couldn't agree more and I do appreciate you sharing your experiences with us. And then I'm sorry to hear about your grandmother, I do appreciate you sharing that with us and, and highlighting the need for, for everything that you've talked about. And, you know, given everything we've talked about today, set against this rising prevalence of retinal diseases is clearly more important than ever to keep our management approaches up to date. With that, I'd like to thank again my guest Dr. Christina Weng for sharing her key insights on the therapeutic landscape. Dr. Weng, it was great having you on the program.

Dr. Weng:
Thank you so much for having me.

Announcer:
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