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Managing Migraine: Inadequate Responses and Treatment Transitions

Announcer:
You're listening to *Neurofrontiers* on ReachMD. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss suboptimal treatment response in patients with migraine and strategies for addressing it is Dr. Vincent Martin. He's the Director of the Headache and Facial Pain Center at the Gardner Neuroscience Institute of the University of Cincinnati, where he's also a Professor of Clinical Medicine in the Division of Internal Medicine. Dr. Martin, thanks for being here today.

Dr. Martin:
Oh, thank you for having me. This is a pleasure.

Dr. Turck:
Well, to start us off, Dr. Martin, would you walk us through the toll inadequate treatment response takes on patients with migraine and why it's so important to address?

Dr. Martin:
Well, the first thing I'd say is that migraine is the second leading cause of worldwide disability in terms of days lived with disability. And it's the leading cause of days lived with disability in women. So inadequate treatment of migraine can lead to a lot of disability, missed work and social events, and even can cause problems with relationships if the headaches become quite frequent. So there's an enormous impact on a given patient if the migraines are not adequately treated.

Dr. Turck:
And when you're working with patients who aren't responding as well as you'd hoped to treatment, how do you characterize their response profile?

Dr. Martin:
Well, I assess both their response to acute and response to preventive therapy. And I think you really need to maximize both of those to actually have an adequate treatment response for a given patient. But in terms of the acute therapies, I'll usually ask a couple of questions. One is, are they getting pain free or near pain free at two hours post dose? And we also tell them often that you want to take the medication as early as possible in the course of the migraine to make sure that they respond optimally. Because if they wait too long, then you reach a point of no return.

And then the other question we ask to assess acute therapy is, are they able to function normally or near normally at two hours post dose. So if either of those two questions are not answered appropriately, then they may not be responding as well as they might be to their current acute therapy. And that acute therapy could either be a prescription or an over-the-counter medication. Frankly, if they're responding to over-the-counter meds, and they meet those two criteria, then you may not even need to advance on to prescription medications at that point.

And then in terms of preventive therapies, we try to assess what the burden of migraine is in a given patient. So for example, probably the easiest thing for, say, a primary care physician, or maybe even a physician that's maybe not as savvy in headache, would be to assess how many moderate-to-severe headache days a person has if they have migraine. And if it's more than four days per month, then that's a person that might be a candidate for preventive therapies. If they're savvy and they know what a migraine day is—I usually

tell people a migraine day is a day with moderate-to-severe headache with any associated symptoms, so nausea, sensitivity to light, or sensitivity to noise—if you want to take it to that and use that definition as opposed to moderate to severe, we usually use four days or more per month as a cut-point for starting a preventive med. And you say, well, why do we use four? Well, we use four days per month because that's when disability starts to go up in a migraine patient.

So those are the ways I assess whether someone needs either a prescription acute therapy or maybe even a change from an existing acute therapy to a new one, or whether someone needs a new preventive therapy, an addition of a second one, or dose titration on the existing med. So those are the two ways I assess whether someone needs an additional therapies.

Dr. Turck:
And what else can you tell us about switching therapy and how to do it, whether that means switching acute therapies or considering preventives?

Dr. Martin:
Well, a switch usually means that you're stopping one and going to another therapy, but it could also be just an addition of a therapy too, simply because maybe they've had a partial response with drug A, so then you add drug B on top of it. And sometimes, when you're trying to treat patients, particularly ones that have more frequent headaches, you need drugs that work by different mechanisms. So that would be an addition. A switch would be that drug A is just not working very well, and/or maybe they're having side effects, and then you need to switch to drug B to maximize therapy. And it does happen.

When patients are choosing a preventive therapy in particular, they're often—and sometimes in acute therapy—basing it on med side effects and how well the drug is going to work. So you as a clinician need to talk to them about what the side effects of drug A and drug B are.

And then also the comorbidities come into play. For example, if you're trying to choose an acute therapy and they've got a lot of risk factors for heart disease, or if they've got known coronary artery disease, cerebral vascular disease, or even peripheral vascular disease, then you're not going to want to use the class of meds called the triptans because they're contraindicated.

So comorbidities, med side effects, and how well the drugs work are all discussion points when we're trying to decide whether to switch someone to a new acute, to a new preventive, or to add it on.

Dr. Turck:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Vincent Martin about managing inadequate responses and treatment transitions in migraine care.

Now, Dr. Martin, if we zero in on the calcitonin gene-related peptide, or CGRP, pathway for just a moment, what do you consider when choosing a CGRP-targeted therapy for your patients in both the acute and preventive settings?

Dr. Martin:
Well, in the acute setting, it really is, in part, forced by the insurance to be honest with you, because right now, within the acute setting, most insurance plans are requiring a patient to fail either one or two acute triptans before you can even get to the new CGRP therapies, which in this case are gepants.

But I think the main consideration is, how are they responding to the triptan? Or is there a contraindication to use of the triptans because of known cardiovascular disease, like history of stroke, heart attack, or a lot of other cardiovascular risk factors? Maybe they don't have known disease, but you might want to stay away from triptans in that setting and go immediately to the next category, which would be the gepants.

And then the other issue is side effects. For example, the triptans have what we call the triptan side effects, which is where you can get pins and needles in your fingertips, a warm flush sensation, neck tightness, and then one to five percent of people can get some chest tightness, which in the vast majority of cases is not coming from the heart. However, with that said, there have been some extremely rare cardiovascular events that have been associated with the triptans like heart attacks and stroke. So consequently, you don't want to use triptans in people that have cardiovascular disease, and then you've got this burden of side effects that they can have.

There's some people that delay their triptan use just solely because of side effects. They just don't like the way they feel. And the problem with that is that we're trying to get people to use the drug as early in the course of the migraine attack as possible, before you get sensitization of the second- and third-order neurons, which can occur even as early as within an hour after the onset. So you really want to treat as early as possible. So these triptan side effects can be a real problem.

The advantage of the CGRP and acute therapy is that they have very few side effects: nausea in maybe three percent, sleepiness in

like three percent, and that is about it. So they're very, very well-tolerated medications. And then some people, even if they have responded to the triptans, occasionally, only eight out of 10 times, even with the best therapies, are going to actually have a response, so that sometimes they need another therapy, and a gepant in that situation as an add on can be a very effective therapy as well. So I would say that gepants are great on side effects as an acute therapy. And they're very efficacious, and they don't have the cardiovascular warning like the triptans do.

So in terms of preventive therapies—to kind of switch gears a bit—the CGRP monoclonal therapies and monoclonal antibodies are once a month. They're taken by subcutaneous injection. There's autoinjectors that they can use, or actually there's a syringe that they can use. It's given either once a month or once every three months. They too have a very low side effect profile. Only one of them, in all honesty, causes constipation. They all have a warning for Raynaud's phenomenon in rare cases of elevating blood pressure, but that is extremely rare. And you also have to fail more than, usually, two preventive therapies before you can even get to these. So those are the CGRP monoclonals.

And then you've got the gepants that we use as prevention as well. And those have side effects of constipation, sleepiness, and, rarely, nausea. But those are very effective therapies, particularly if patients are needle phobic, or they just tend to favor the gepants over a monoclonal antibody.

But I will tell you that the CGRP monoclonal and gepants—the CGRP therapies—have revolutionized the way that we treat migraine patients, both in the acute and preventive arena.

Dr. Turck:
Now, when it comes to transitioning patients from one therapy to another, would you share some best practices for making sure they're feeling their best physically and emotionally during that whole process?

Dr. Martin:
Well, I think if you're going to transition them off of one and then onto another, I usually don't do that at the same time. I usually will taper off one and then wait a couple days and start the other. There sometimes can be withdraw side effects from some of the meds. So if you have some people on, for example, antidepressants like an SNRI as a preventive, sometimes pulling them off that medication abruptly can be problematic, so you have to gradually taper them off.

For things like topiramate, I wouldn't just take somebody off 100 milligrams of topiramate, just zap them and take them off right away, because migraine patients don't like abrupt transitions. Taking someone from 100 down to zero on topiramate, it's like dropping a migraine patient off of a cliff. So it needs to be a tapering process when you're going to transition them.

And then, like I said, I usually don't overlap drugs. I usually wait a couple days and then start the new one, so we can differentiate between withdrawal side effects and any potential side effects they may have with the new therapy that I put. Because you could start and you could overlap them, and they could be having withdrawal side effects from drug A, and they may assume it's from drug B that you just started. So I tend to kind of gradually tape them off one and then put them on another.

But I think the gradual tapering is super important now with these meds. And when you start a med—I have a slightly different way I start meds, I don't ramp them up maybe as quick as some other people, because migraine patients tend to be really sensitive to medication side effects. So for example, with topiramate, this typical regimen is to ramp them up to 100 milligrams over four weeks. I'll usually ramp them up to 50 over two months, and then I'll ramp them up from 50 to 100 between months two and four.

Now with the newer meds, the CGRP therapies, another one of the strengths of these meds is that they don't require, for the most part, dose titration. A lot of the CGRP monoclonals—there's actually only one in which you can dose titrate, and that's erenumab, but the other ones are just fixed dose. And with some of the gepants used as preventive therapies, there is one drug, atogepant, with three different dosages, but for the most part, you can kind of stick with one dose, and there's not a lot of dose titration. So that's another advantage of some of the newer CGRP therapies.

Dr. Turck:
And before we wrap up, Dr. Martin, what final thoughts would you like to share with our audience about managing treatment inertia and recognizing when to switch therapies?

Dr. Martin:
Well, I would say that you just need to assess the adequacy of your acute and preventive therapies. And then you have to decide whether you need to add a therapy to the existing one or withdraw the first medication if it was ineffective. But I will tell you for acute therapies, I might have somebody on a triptan, and I might have somebody on a gepant, so I might have two different therapies and the patients love that, and they can decide whether they take one first or the other one second. They can kind of play with it and so forth. So

I would say that when you're transitioning people to other therapies, sometimes you combine them, sometimes you get rid of the first one, and you just have to kind of assess what the patient wants to provide optimal therapy for a given patient.

Dr. Turck:
Well, with those final thoughts in mind, I want to thank my guest, Dr. Vincent Martin, for joining me to discuss how we can effectively identify and navigate suboptimal treatment responses in patients with migraine. Dr. Martin, it was great speaking with you today.

Dr. Martin:
Thank you. It was a pleasure.

Announcer:
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