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How Real-World Adherence Is Shaping Preventive Migraine Treatment

Dr. May:
This is *NeuroFrontiers* on ReachMD. I'm Dr. Alexandria May, and joining me to examine how real-world adherence is shaping treatment decisions in migraine prevention is Dr. Jessica Ailani. She's a Clinical Professor of Neurology at MedStar's Georgetown University Hospital and Director of the MedStar Georgetown Headache Center. Dr. Ailani, welcome to the program.

Dr. Ailani:
Thank you so much. It's my pleasure to be here.

Dr. May:
Well, let's start by looking at some data. Studies have found that many conventional, oral, preventive treatments for migraine are non-specific, and about half of patients discontinue them within the first six months. With that being said, how do you interpret the gap between efficacy in trials and adherence in real-world practice?

Dr. Ailani:
I think this is a great place to start for any of our audience members that see patients with migraine or have started treatment before. They'll recognize that the most common types of treatments used for prevention of migraine are very old drugs. They're beta blockers, some anti-epilepsy drugs, and certain types of antidepressants like tricyclic antidepressants. These medications have been around a long time and they're very inexpensive—that's a huge benefit—but they're not specific to migraines, so they come with a host of side effects. The other downside to these treatments is most of them have not actually been studied in chronic migraine—only episodic migraine.

And many times when we're starting people on prevention, while we should start prevention at the point where they're having four to five attacks per month, many patients really don't start prevention till much later when they're having almost daily headaches. So these traditional medications don't really have great evidence in those particular areas, and they come with a lot of side effects. So it's not surprising that you'll see people start the treatment and discontinue very quickly, with evidence showing that over the course of a year, only about 12 percent of people remain on traditional oral therapies. And so I think this teaches us a lot about while something might show some efficacy and might be inexpensive, benefit in the actual disease process and side effects are really important things to patients.

Dr. May:
So in your own practice, what would you say are the most common reasons patients discontinue or switch conventional therapies?

Dr. Ailani:
I think the number one reason people stop some of our oral traditional medications have to be because of side effects. So like I said, these can be very difficult to tolerate, and even though we spend quite a lot of time talking about how to manage side effects and what to expect, sometimes they're still so intolerable that even if they're feeling better, they need to stop the treatment.

Second most common reason these treatments are stopped is because they don't feel the benefit they're gaining in the disease process is enough to warrant the side effects they're going through. So again, coming right back to that side effect profile. So these are often reasons people stop treatment.

Something else that we might see that if we don't educate patients on might become a big problem is it does take time for these traditional therapies to start to become effective—time being weeks to sometimes months. And if you don't talk to the patient about that

in advance, they would stop the treatment if they're not feeling better within a week. And so oftentimes we have to have a very prolonged and lengthy dialogue like, 'you might only see side effects and not see benefit, but please keep going because side effects can sometimes get better, and that's when the benefit starts to kick in.'

Dr. May:
And when we compare those conventional therapies with migraine-specific therapies like calcitonin gene-related peptide, or CGRP, targeted options, what differences stand out in persistence and switching patterns?

Dr. Ailani:
Well, in clinical practice, I think when these treatments first came out, we immediately saw a difference in patients not contacting us after starting treatment because they didn't have side effects. And the other thing we saw were patients remaining on treatment for a very long period of time and not requesting to come off therapy when they were doing better, which we often will see with traditional treatments. When we look to the evidence, we have some evidence for the CGRP-monoclonal antibodies, like erenumab, galcanezumab, and fremanezumab, and the IV treatment eptinezumab. And what we see with those treatments are adherence and persistence rates are about 50 percent at six months. So that's actually pretty high for any kind of treatment for a disease process. The patients are tolerating it, they're staying on it, and they're consistent on it.

The other thing we notice in clinical practice is if the patient's doing well on the treatment, they really don't ask not only about stopping, but about changing to something different. So there's not the cycling of treatment that tends to happen. In fact, the only time treatment is changed is really when insurance forces the issue and has a new formulary and requires us to make a change with the patients.

The one thing I do want to mention is we don't have any evidence about adherence and persistence with our gepants, like rimegepant and atogepant, which are FDA approved for preventive treatment of migraine. But in clinical practice, we are seeing these adherence rates to be pretty high as well because patients tolerate the treatment and they're finding it to be pretty effective.

Dr. May:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Alexandria May, and I'm speaking with Dr. Jessica Ailani to evaluate patient adherence to conventional versus migraine-specific preventive therapies.

So, Dr. Ailani, we know that access cost and comorbidities can complicate our treatment decisions. How do you weigh these factors when choosing and sequencing preventive therapies?

Dr. Ailani:
I think this is a really great question because I think it explains why there's not a great algorithm in the treatment of migraine. A lot of times, we might have a sense of where to start treatment for a patient based on things that they're telling us in the clinical visit—they want to find a medication that's limited in side effect and that's specific to their disease process, but also something that's inexpensive and easy for them to get at their local pharmacy. But we really don't have one treatment that fulfills all of those roles. So sometimes we're looking at other factors as well. What kind of insurance plan do they have? Does that insurance plan allow us to start with an anti-CGRP treatment first versus step through a different therapy, like a generic oral medication first?

We also are looking at comorbidities because we see many comorbidities with migraine. We might have a patient who's mentioned that they're struggling with their weight and they're thinking about going on a weight loss program, and so you might actually think about a medication that causes weight loss in those patients and that might be a first option for you. We might see a patient who has borderline blood pressure—I think of as high in the late 130s to 140s, whereas the primary might still tell the patient they're just fine and they don't need treatment—and in a patient like that, we might opt for an anti-hypertensive, like a beta-blocker or candesartan, which has good evidence for migraine prevention. And in that case, we're trying to really optimize putting them on a preventive for migraine that might have a side effect that's beneficial to the patient as well.

It's important to realize though that we really can't dual manage with one drug, meaning the best medicine for migraine is not going to be the best antidepressant for the patient. Same thing about blood pressure. Same thing about weight loss. So it's important we don't get fixated on that idea that we can do a two-for-one for all our patients. It's an idea that we can start that way, but we really have to monitor and if they're not responding for the secondary disease, like high blood pressure, or their mood isn't getting better on a tricyclic antidepressant, we really need to push that the patient's starting to get better management for their other disease process.

Dr. May:
And as a follow-up to that, how do you approach decisions around switching therapies versus continuing or optimizing a current preventative?

Dr. Ailani:

So oftentimes when we start a preventive treatment, we'll start with one preventive treatment and have the patient come back to see us in three months. It's really important we guide them through the process of what to expect, and the expectations are a little bit different if they have episodic migraine or chronic migraine and if they're going on an oral generic treatment, which might carry a lot of side effects versus going on an anti-CGRP treatment. Anti-CGRP treatments do start to work faster, and especially in patients with episodic migraine, you might see responses within days. Our oral traditional therapies do take a little bit more time to work, and we might have to go up slower on the dose because of potential side effects. So I always talk through the fact that this isn't a race; the whole thing is to try to get patients feeling better with minimal side effects, so we're going to have to go slow, and it really can take time to see the change.

When they come back in three months, we are looking at guideposts like 50 to 75 percent reduction in headache and migraine days and also improvement in disability and function. If a patient comes back in three months and tells me, "I am so much more functional, but my frequencies only come down a little bit," then we're really looking at, do we want to stay on that particular treatment? Do we want to layer on additional therapeutic options, like a supplement treatment or a neuromodulation device, and give them a little bit more time and then reassess how they're doing? Or do we want to make a change because the benefit hasn't been great enough for them to feel that they're really able to function? And that's a very individual conversation, and the response can change from patient to patient.

I do want to note though that it's really important we recognize that migraine's a very episodic and fluctuating disorder, and sometimes patients will just have more frequent attacks certain times of the year, and some things happen in their life that cause their attacks to become more frequent. And if we change medications every time this happens, you can run out of options pretty quickly, and the patients will often tell you that they feel like they're just on a rollercoaster of treatments and they're having a hard time feeling balanced and getting a sense of control. So again, having that dialogue is probably a very important factor in the treatment visit.

Dr. May:
Before we wrap up, Dr. Ailani, what are some practical strategies clinicians can use early on in a patient's care journey to improve adherence and long-term success?

Dr. Ailani:
I think the most important factors involved in adherence and a patient persistently taking their treatment is recognizing what their concerns might be. So before starting prevention, I like to ask my patients what their concerns might be about being on a treatment option. What's their absolute most, like, 'you cannot do this to me, Dr. Ailani; I will not tolerate gaining weight,' or 'I cannot tolerate being sleepy because I have young children.' Understanding their most disliked adverse event or side effect is really important in help making that shared decision and making conversation happen.

And then expectation setting. Depending on the treatment we're starting, let them understand how long it might take before they see benefit, what the side effect profiles can be, what to expect, and then how to contact you if they are struggling. I feel like having an understood way to contact you might help them feel more comfortable about starting a treatment option, especially in someone who's never been on medication before.

Dr. May:
Those are great insights for us to take away as we come to the end of our program. I want to thank my guest, Dr. Jessica Ailani, for joining me to discuss how real-world adherence is reshaping the way we think about preventative therapy in migraine. Dr. Ailani, thanks for being here today.

Dr. Ailani:
Thank you again for having me.

Dr. May:
For ReachMD, I'm Dr. Alexandria May. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.