Episode 235: Understanding Acute Migraine Treatments: What's Available and How They Work

Lindsay Weitzel, PhD:
Hello everyone, and welcome to HeadWise, the videocast and podcast of the National Headache Foundation. I'm Dr. Lindsay Weitzel. I'm the founder of MigraineNation, and I have a history of chronic and daily migraine that began at the age of four. Today our guest is headache specialist and board-certified neurologist Dr. Robert Kaniecki. Hello, Dr. Kaniecki, how are you doing this morning?

Robert Kaniecki, MD:
I'm doing great. Lindsay, thanks for the invitation. Pleasure to be here today.

Lindsay Weitzel, PhD:
Well, thank you for being here. We have a really important episode today. I think everyone's going to get something out of it. Dr. Kaniecki is an associate professor of neurology at the University of Pittsburgh and the director of the UPMC Headache Center. He's very knowledgeable and he's the perfect person to talk to us about our topic today, which is acute migraine treatment.

Many people in our audience know that these treatments have changed and improved in recent years. We have more options. It's even improved in the last few months. It's time we did an updated episode that includes the latest options. So, we're going to run through these in case there's some things that anyone out there wants to go to their doctor and ask questions about and possibly look into.

We're going to start with the over-the-counter options. Interestingly, I've had migraine my entire life, and I've tried pretty much every medicine out there. And believe it or not, I still have an over-the-counter medication in my acute medicine toolbox. So, Dr. Kaniecki, can you list for us, talk to us about some of the over-the-counter options that people might take for migraine acute treatment?

Robert Kaniecki, MD:
Certainly Lindsay. And in my intro, I should have added one thing: a former migraine sufferer. I had them between the ages of 34 and 51. My mother had migraine with aura most of her entire life until she was 90. Fortunately, mine were not as long lasting. I've had a period of time when I had them and also tried just about everything at the time that was on the market. So now that I'm in my 60s, I've been a decade or so free of these things, so I can tell you about all the ones that I've tried in the past, plus what we have available.

Over-the-counters have always been the place where patients start, exactly where they'll go to first. They will go to their pharmacy and pick something out and they'll listen to their relatives. The products that have been investigated over time include acetaminophen (Tylenol), which at a hefty dose can be

helpful for migraine. But it was studied in a subset of migraine where it was only mild to moderate intensity, not the bad attacks, so there's a little caveat to the acetaminophen (Tylenol). However, the other products, the non-steroidal agents and the aspirin products, aspirin as standalone or aspirin as part of the aspirin, acetaminophen, caffeine combinations which Excedrin being the most popular, are also extremely effective and have excellent data in not only mild to moderate migraine but severe migraine. So, they're a great place to start. The guideline recommendations are to start with a high dose non-steroidal agent, one of those products, if you have moderate to severe migraine and try them out first. And make sure you take a good dose, a full dose of the medication, not a half dose, a full dose of one of those agents. And the ones that have the data in the non-steroidal group that are over the counter are primarily naproxen and ibuprofen.

Lindsay Weitzel, PhD:
That is a perfect rundown of everything pretty much that I can think of that we would get over the counter, so let's move on. There is this fact that there are some of those NSAIDs are available in different forms and different strengths with a prescription that you can get from your healthcare provider. So, let's cover and describe a few things that might be helpful in the setting of migraine that are NSAIDs that you need a prescription for.

Robert Kaniecki, MD:
We use those a lot. A lot of times patients that have maybe partial results with their non-prescription medications, they like non-steroidal agents. They may need them for another reason. We do you want to start with that. So, we'll go with again the higher doses, so the prescription doses of ibuprofen at 600, 800, for example an 800mg dose by prescription single pill or naproxen at 500 or 550 when the dose is 220 and even two will get you 440mg. So, you get higher dose non-steroidal agents. There is an agent called diclofenac in solution that can be helpful as well.

Going back to these higher doses, interestingly, before we had the newer agents, the migraine specific agents, which we're going to talk about shortly, the dose of aspirin that was often suggested by the European and American physicians, 900 to 975mg, three of them, three full strength. Now that was expected to be a single dose. High doses of these non-steroidal agents, including high-dose aspirin, can be helpful for a number of patients.

Lindsay Weitzel, PhD:
Let's move on to what most people think of when they get their migraine and they think they need to take something. Let's move on to the triptans. These first came onto the scene when I was a teenager, and it was quite an exciting time for those of us with migraine back then. And now we have many that are available for oral use, a couple that are available as a nasal spray. Let's run through these and their route of administration in case anyone needs a new route to take or just hasn't heard of the various ones that are out there.

Robert Kaniecki, MD:
There are a number of triptans. In fact, there are seven that were developed over time. Additional ones were developed but never released and marketed. So, we have a total of seven that remain with us

today. They all have generic names now that patients may be familiar with and they end with triptan. These are the triptan medications.

So, the first of the group was sumatriptan (Imitrex), interestingly, the first one out of the gate back in 1992, 1993. So, I grew up with these, by the way. Not literally, but my career grew with these because I started headache in 1992. The first triptan Imitrex injection (sumatriptan injection) was approved in 92 and released in 93. So, throughout the 90s and into the early 2000s, seven of them were released. And so sumatriptan (Imitrex) first with injection and then tablet and then a nasal spray. So, there are three different options that were made available over time. And interestingly, from the very start, the very first one, the Imitrex injection, nothing since has ever been proven superior.

So, it continues to be a very important piece of migraine treatment. It often gets neglected. So, it's injectable, so you don't have to worry about nausea or vomiting. And it also is something that we find it's very helpful for those people who have wake-up migraines where it's already going full throttle. They wake up with it. It's already severe, and sometimes those are very challenging to get under control, particularly if you're trying to get to work or the airport or school. So, the injection was the first, but then the tablets obviously much more convenient and also more cost effective. And then the nasal spray, which is probably is the least used of all the three.

The second to come out was rizatriptan (Maxalt), and Maxalt came as both a regular tablet and a dissolvable tablet which some people preferred, one over the other. Very effective as well. The third was zolmitriptan (Zomig), which came out as a regular tablet, a dissolvable tablet, and a nasal spray.

Again, the nasal sprays of both the Imitrex and the Zomig (sumatriptan and the zolmitriptan) [is] helpful in settings where there is a rapid onset headache or nausea or vomiting or wake-up migraine that maybe patients don't want to do an injection. I find these particularly helpful in teenagers and younger people. They say, I don't want to do a shot. Let's try the nasal. So those are the first three released.

The other four that came out subsequently were basically only tablet versions. So naratriptan which is Amerge is a tablet. Relpax which is eletriptan, Axert which is almotriptan, and Frova which is frovatriptan all came out with oral tablets, so no nasal sprays, no injectables, but different options.

I think you can kind of consider these in more or less two bigger buckets. They do differ, mind you, but the similarities significantly outweigh the differences. One bucket is the hard hitters. They're faster, they're stronger, they’re more likely to be effective within a 1-to-2-hour period of time. But with power come side effect profile. If it's stronger, you're more likely to get benefit, but there may be some side effects. And that’s sumatriptan, rizatriptan, and zolmitriptan and eletriptan. So Imitrex, Maxalt, Zomig, and Relpax.

Lindsay Weitzel, PhD:
So, these are the ones if you want quick effect.

Robert Kaniecki, MD:
You got it. Those are the quick hitters. They are the big hitters. But what if you say I have a couple problems with those, and typically we start with one of those. And most formularies prefer the sumatriptan and rizatriptan generic at this point in time. So, you kind of end up being with one of

those. But if you say, okay, the problem is I get side effects that's too much. Right? I tried these things. They give me problems. I want to try something different. Now, the most common triptans side effects are washing sensation, a warm, kind of hot flash in a sense, and then pressure, jaw pressure, chest pressure, shoulder pressure, head pressure. And some people say it actually makes their headache worse before it makes it better.

Nausea, dizziness, these are all if they're particular problems and you say, okay, these are not for you, maybe you want to do one of the kinder, gentler triptans. So those are a little slower. They don't have the punch, but they have the benefit of a lower side effect profile. And often they also seem to have a lower chance of the headache returning, what we call recurrence, so you get a benefit, but it comes right back. It goes away but comes right back.

That can be a challenge with the triptans. And so that recurrence sometimes or the side effects are often addressed by going to, in my mind, the kinder gentler ones. So that's naratriptan (Amerge), frovatriptan (Frova). Almotriptan (Axert) is kind of a little bit in between, a little bit faster than those, but it's not less likely to cause recurrence. So, it's kind of an in between-er. But those could all be considered a little bit of a step down in terms of potency, which means maybe a little less chance of rapid onset, but also a decreased chance of side effects.

Lindsay Weitzel, PhD:
So, triptans are a first-line for many people and we really wanted to name them all in case you're someone that's wondering if there's one out there that might suit you better, and that you want to go talk to your physician or your healthcare provider and try.

So, let's move on to our next group of acute medicines. Some companies have taken two different medicines and combine them to make a combined medication. This is the case in one of our newest medicines that just came out in January 2025, where they took a triptan and another medicine and combined it. So, let's knock out these medicines really quick, these combined medicines. Which ones are those?

Robert Kaniecki, MD:
Before we probably hit on those directly, one thing to keep in mind, a combination therapy often is very beneficial. And one combination over the years, let's say just when we had the non-steroidals, was adding a nausea medicine to them. And so, in the emergency department the migraine cocktail, for example, has an anti-inflammatory and an anti-nausea medicine that goes together, IV.

So, we commonly thought of combination therapies in the past. Now these newer products you just mentioned, there are two of them, Symbravo and Treximet. Treximet has been available since 2008 and Symbravo just more recently. Treximet is sumatriptan (Imitrex) plus naproxen. Symbravo is rizatriptan (Maxalt) plus meloxicam (Mobic).

So, they are two medication categories and combining them in a single dose. So that's what we have available, a single pill that has both compounds in it. So, think of that in a way like the Excedrin was aspirin and acetaminophen and caffeine and it seems the combo is better than any of the individual items. Well same thing here.

The concept is hey, if we put these together, do we get better results? And I've always been a fan of combining triptans and non-steroidals because I believe you get better results. Not only better results, but a lower recurrence rate, what I mentioned earlier, the chances of the headache coming back within 24 hours seems to be reduced if we add a non-steroidal in. This is very welcome, the approach of combining these and obviously the convenience of having a single tablet, combining both of them. And both in their brand forms have had perhaps some chemical properties. That's probably the simplest way to put it. Chemical properties and the way the two medicines are released or interact, that may make it more effective than just taking the two separate products together.

Why not just take Imitrex and naproxen or take meloxicam (Mobic) and Maxalt? Well, yeah, you could, which we've done for years, but it seems like there's a somewhat of a synergy and it's very interesting at least and certainly a matter of convenience. So exciting developments for us. We really like to see that kind of thing.

Lindsay Weitzel, PhD:
That's an interesting class that I think a lot of people don't think of is the combined class, so I'm glad we hit on that. Now we're going to move on to one of our newer classes which is the gepants. Gepants are small molecule CGRP receptor antagonists. We have three options for gepants that are used for acute treatment in migraine. That is for acute. So, let's discuss those in case there's one that people haven't tried, etc. This is an exciting class and a newer class.

Robert Kaniecki, MD:
Right. And then simply I'd like to have people understand why they take medicine, what it does. There are probably three important chemicals in the migraine pain process. There are the inflammatory chemicals which the anti-inflammatories, the non-steroidals, take care of, is inflammation in the membranes that surround the brain. There is chemical serotonin we've known for years is a big factor in migraine. So, this is a neurotransmitter, a neurochemical that the triptans hit.

And then part of that story, an increasingly recognized important part of the story has been calcitonin gene-related peptides (CPRP). And that's these newer agents that have been directed. There are some preventive drugs which we're not going to discuss today, but acutely you have three different products that are targeted towards that chemical. So, these are migraine specific. So as the serotonin triptans were migraine specific, the CGRP antagonist are migraine specific.

They include rimegepant (Nurtec) which we can use as needed and also as preventive. You have the ubrogepant (Ubrelvy) and zavegepant(Zavzpret) nasal spray. So two of them are tablets. The Nurtec is a dissolvable tablet, the Ubrelvy is a swallowing tablet, and the Zavzpret is a nasal spray. So, no injectables of this type that are commercially available.

Interestingly, more than 20 years ago, the *New England Journal* published an article on the intravenous version of one of these three, and it was extraordinarily beneficial. But the IV or injectables never really materialized in terms of commercial marketing. But we have three now that can be extremely useful. And they're different. Now we have not only an effective group of medications that is migraine directed, but they solve some problems that we maybe need to address when we have non-steroidal people, or triptan people who need to move on.

So, these have been, for example, if you have intolerance to those medicines, side effects or problems, if you have certain medical conditions, if you have kidney disease you can't use a non-steroidal agent, if you have heart disease, you can't use a triptan. So, there are clinical settings where we say you know what, those other medicines are not really part of our consideration right now. Let's look towards these. So, the presence of certain medical conditions, the absence of response, or appearance of side effects with the other drugs that we've discussed, are all important considerations when deciding on when to use one of these gepants.

So, the gepant, like the triptan, is the version of the broad family of medications. This is a gepant family of medications. So Ubrelvy, Nurtec, and Zavzpret all [are] extremely beneficial. They have also a very favorable side effect profile. So again, when people have a bunch of triptans side effects, chest pressure, dizziness, for example, then sometimes these agents can really prove to be part of somebody's effective treatment strategy without giving them too many problems with side effects.

Lindsay Weitzel, PhD:
So, we've done the gepants, which are newer. We did the three of those. So, there are some new and exciting products for the delivery of dihydroergotamine (DHE). Now, DHE has been around for treating migraine since long before my time. I don't know the year. I think someone told me the year once, I don't know what it is.

Robert Kaniecki, MD:
I'll tell you the year. It's 1945.

Lindsay Weitzel, PhD:
Long before my time. Yes. But we now have some new, amazing ways to deliver it at home that I wanted to make sure people were aware of. And one of them is really new. It came out, I think, in May of 2025, and some of the others came out or was approved, let's see one of them in April 2025 and another in 2021. So, they are very new, so let's discuss what those are.

Robert Kaniecki, MD:
Sure. So DHE, this will be easy to remember now. DHE, the original product was DHE-45. The reason it had 45 is because it was released in 1945.

Lindsay Weitzel, PhD:
Oh okay. There we go. Thank you.

Robert Kaniecki, MD:
So think of that. These two that were released this year, 80 years later, 80. That's how long these drugs, this DHE, has been around. It's hanging around because it's extremely effective. The challenge with it has always been administration. So DHE-45 still today remains the most important strategy in managing migraine in patients who are hospitalized.

So somebody needs to break a cycle, they're in for 2 or 3 days in the hospital, this is extraordinarily effective. And it was effective, given intravenously. That's the way we use it in the hospital. But also, people could do it intramuscularly or subcutaneously. But it's an injection, and it was never in a pen. You had to get a vial, a glass vial, break a glass vial and draw it up into your syringe and give yourself a shot. So, deal breaker for lots of people.
Also some vascular concerns, so like the triptans you can't take it with vascular disease. And it was a cousin to the old ergots. I don't know if you remember those, Ergotamine or Cafergot, these older medications which were oral, never really all that great.

This was really good. So, the DHE stuck around for that reason. And then Trudhesa came out in 2021. So, it was a different kind of nasal formulation, a different delivery system, and seemed to deliver more drug to the circulation, so higher concentrations. There was another nasal spray prior to that, Migranal, which was the first DHE nasal spray. But this seemed to be a step forward. And that step forward had a lot to do with the formulation, the way it's delivered through the sinuses.

The 2025 iteration, so the 80 year later iterations of medications, have taken us to a pre-loaded pen, basically an auto injector, which is Brekiya, and then also the Atzumi, which is the different form of nasal powder formulation. So that's not the nasal spray in a different device, but a nasal powder that is delivered. And then the injectable, instead of drawing it up out of this glass vial, which again, pretty complicated. Breaking glass vials can be tricky. It's not just removing it from a vial, where you stick it into a rubber top. You actually break the glass, turn it over, pull it out, and in the middle of a bad migraine.

Lindsay Weitzel, PhD:
I was going to say, when you're that sick, it's not fun or simple.

Robert Kaniecki, MD:
So that's where we are. So if you can get a nasal spray that works and is effective and tolerated or an injection that's easy. Again, these wake-up migraines are ones where you're already throwing up with, as I mentioned for Imitrex injection earlier and Imitrex and Zomig nasals and the Zavzpret for example, this would all be reasonable considerations for people who have migraines that wake them up, migraines where they're throwing up. The availability of DHE now in other formulations and other formats is actually very, very exciting.

Lindsay Weitzel, PhD:
So, we have those three options, nasal spray, nasal powder and the Brekiya is the one that's the auto injector. And so, we've really made it through, I believe, tell me if I'm wrong most of the acute treatments other than we do have obviously neuromodulation devices, which are beyond the scope of this episode. We're going to have to come back and do that another day. But I do want to mention that we have some awesome neuromodulation devices out there that can be used for acute treatment. Do we have any other medications that you think we've missed for acute treatment?

Robert Kaniecki, MD:
No, but I think we would be remiss if we did not mention what people should do in addition to their medicines. You know the strategies, if you have a migraine, what do you do? And you should make sure whatever you're doing here, you hydrate extra. Whatever medication you're taking, as long as you're not throwing it out, make sure you get extra hydration. And if you need to control the nausea in other ways, as I mentioned, adding anti-nausea medicines have value.

The approach of removing yourself from the environment that is overstimulating, so a quiet, dark room. And that takes away the light noise sensitive pieces. And then also cold. The cold application people have used whatever corn or peas from their freezer or their commercial ice caps that you basically put in your freezer and just stick it on your head. And when you pull it out and put on there, people really like that, and they can be of significant value. So, the kind of non-drug steps that are adjunctive to the things that you and I have discussed can also provide additional benefit.

Lindsay Weitzel, PhD:
All right. Well, thank you so much. Thank you for being here. And thank you, everyone for listening. And I hope there was something for everyone. Please join us again on the next episode of HeadWise. Bye bye.