Episode 175: Headache and Migraine News, February 2024

Lindsay Weitzel, PhD:
Hello, everyone, and welcome to HeadWise, the weekly videocast and podcast of the National Headache Foundation. I'm Dr. Lindsay Weitzel. I'm the founder of Migraine Nation, and I have a history of chronic and daily migraine that began at the age of four. I'm here today with Dr. Tim Smith. Hi, Dr. Smith, how are you?

Tim Smith, MD:
Doing well, thanks for the opportunity to be on with you again.

Lindsay Weitzel, PhD:
Thank you for being here. Dr. Smith is here because this is our monthly news episode where we like to update everyone on the latest data and research and devices, et cetera, that's out. And so this is an exciting episode. Dr. Smith is a regular because of his extensive experience in migraine clinical trials as the CEO of Study Metrix Research. He is also a board member of the National Headache Foundation.

Let's begin our news. We're going to start with a fun topic that's one of my favorite topics. We're going to start with a study. It's actually a review article on screen-time in kids and migraine. Now, the reason this is one of my favorites is I was a kid with migraine. And I used to watch empowering movies, like superhero movies to make me feel strong and keep me upbeat when I had a migraine. And a lot of people would say, doesn't that make her migraine worse? And it didn't in my case. It was not a trigger. I always say, if it doesn't trigger the kid, gosh, please don't make them stare at the wall. And I am always wondering if the research backs me up or not. So today we have a review article. I think it's like 48 studies or so that they reviewed on screen time and headache in kids. And what did they find, Dr. Smith?

Tim Smith, MD:
They did this PubMed search and some other search engines looking at all the studies they could find, looking at this topic. And then they compiled the results from everything. And basically, what they came up with was that there doesn't appear to be any true association with screen time and headache severity and frequency. There are some methodological problems with doing a study like this. Your results are only as good as the studies that you included into the analysis. And they had some problems with standardizing how they rated screen-time and duration and those kinds of things.

And I think a couple of the studies didn't actually define the type of headache that they were talking about either. So those issues could water down the results somewhat, but there certainly is not a striking signal from the compilation of all these study projects. They wind up concluding that better studies are needed, which obviously is true. But you would think if there was something striking about this, then we would see it. But it's not apparent based on the data that we have before us today.

Lindsay Weitzel, PhD:
This doesn't mean that if you're someone that you feel like it causes you head pain to watch a screen, that you should run out and do it, because we are all different, right?

Tim Smith, MD:
Well, I think that's true. So, we all know that for many, many years, we always talked about chocolate being a dietary trigger, and then well-done studies, that placebo-controlled studies that looked at chocolate consumption, even in people who thought they had that as a trigger, did not prove that that was the case. But if I eat chocolate and every time I eat chocolate I get a migraine, I'm going to avoid chocolate.

So I think we just have to pay attention to screen-time, and just because they don't see an association here, doesn't mean it doesn't exist. And then, counter-distinction of that is, if you are able to have hours of screen time and not trigger migraines, then it obviously doesn't apply to you. So it's kind of like a common-sense thing.

Lindsay Weitzel, PhD:
Another study that we're going to move on to that was just published, is also on something that is a little bit controversial in the migraine and headache field. It's on caffeine. We have a study that's out in *Headache* this month that I think might be a little bit surprising to our audience. What does it say about caffeine intake?

Tim Smith, MD:
This was a study where they identified people with episodic migraine from practices and had them complete questionnaires and other assessments. And basically, they did analysis to look for associations between degree of caffeine intake and frequency, severity, and duration of migraine attack. And they broke them into three categories, those with no intake, those with one to two beverages per day, and the last group was three to four beverages per day.

And their scores look pretty close to identical across all three groups with regard to their migraine frequency, number of migraine days per month, the intensity of the migraine attacks, and the average duration of the attacks. The higher caffeine use was not correlated with an increase or a worsening of any of those observations.

Lindsay Weitzel, PhD:
That's good news for those of us with migraine who like caffeine and don't feel like it triggers us. I think that a lot of us were worried that it could chronify us if there had been some data. If you feel like it does, then stay away from it. But now we have some data that maybe doesn't hurt.

Tim Smith, MD:
I was kind of surprised. I wondered why there wasn't a more than four beverages category in the study. So do those people do not exist or they just didn't count them or what. And I wonder what their associations would look like. We may have just missed the population on this report. I don't know.

Lindsay Weitzel, PhD:
We exist on some days. I have to admit I have my days. Moving on to our next study, we are all so interested in the anti-CGRP monoclonal antibodies and how can we predict if we're going to respond to them. Do you know some of us are non-responders, some people respond, and why is that? And there's a group this month that published a study trying to find out some of that information. And so what information did they come up with?

Tim Smith, MD:
These researchers did a retrospective study looking at a cohort of patients that they have claims data on and look at their medication use, and they also have patient reported outcomes, and some genetic data. In other words they've done genotyping or gene sequencing on these folks to go into a big, basically a registry, and they can do some data mining research on those patients. And they were looking for things that were associated with better response or poorer response to the CGRP monoclonals.

They studied the three subcutaneous injectables. For all migraine treatments, we've always tried to be able to find some kind of biomarker or phenotype or some suggestive information that would predict who was going to be a good responder and who was not. And so this is just another way of looking at some of these factors to see if there's something predictive.

And they did come across a few things that they reported out. Just a quick hitter summary of it, is that patients that had the reduction was proportional to the number of monthly migraine days. Meaning the more migraine days you had, the more reduction you're going to get. Well, that may not be a medication effect. That could be anything. You have more days to potentially reduce the migraine load.

But the other things were female gender was associated with a better response and a previous hospitalization for migraine, recent hospital presentation for migraine, and then the more previous failed medications they had, those were predictors of a poorer response or less robust response to the CGRP blockers.

Gives us some things to go on. I think some of this may be common sense. If you think about, patients that are more refractory would be more likely to be presenting to the hospital and would be more likely to have had refractory previous attempts at medications. But it does sort of fly in the face of the current trend of part of insurance plans to deny payment unless you failed two or more previous. You're actually selecting for a population that's less likely to respond. If you're trying to narrow it down, they may be doing the opposite thing. It's a money thing, and I get it, but it's just sort of an interesting way of looking at it.

The other thing they did find, though, in this study, there were a couple of genetic markers. It's not stuff that people would know about themselves, and I don't think we're ready to go out and do mass gene defect screening for this before you would administer the drug. But there were a couple of them. One of them was a gene that's associated with the RAMP1 protein, which is part of the CGRP receptor.

Lindsay Weitzel, PhD:
We all know this about ourselves. We all know our RAMP1 status.

Tim Smith, MD:
Yeah, that's right. So anyway, but it would make sense if your CGRP receptors, I don't know, maybe the drugs don't bind to them. You can make up your causality statement on that, but it's just an association for right now. But at least it does suggest there may be some things we can look at or get closer to finding these out. But the quest goes on. This is helpful information to have. We'll continue looking at it, more studies on the way.

Lindsay Weitzel, PhD:
All right, so at least we know that there's people out there looking for the characteristics that are going to help us determine who's going to respond to the MAPs and who's not. This is a good thing to know. Our last study that we're going to report on is actually published in a journal we've never reported from before. It is not a headache journal. It's a journal called *Menopause*, but it is such an interesting study, and it really does apply to people with migraine. So I wanted to talk about it. The researchers in this study set out to determine if people with both vasomotor symptoms, which are really just hot flashes, and migraine were at greater risk of cardiovascular disease, including stroke. What did they find?

Tim Smith, MD:
They looked at, they have a large database looking at risk factors and outcomes and those kinds of things. It's called the Coronary Artery Risk Development in Young Adults Study. And they call it CARDIA, C-A-R-D-I-A, if anybody wants to look at where the database comes from. But it's looking at multiple risk factors. And this group looked at the occurrence of what they call vasomotor symptoms, commonly refer to that as hot flashes, flushing of the skin, night sweats and those kinds of things commonly experienced in perimenopausal and or postmenopausal women.

Basically, they were looking at the predictive value of understanding the degree to which women had these vasomotor symptoms and migraine. And as it turns out, patients had persistent. They looked at women with no symptoms, with women with increasing symptoms, and then women that have persistent hot flashes. So, this would be just not going through perimenopausal and they go away. These are persistent hot flash symptoms.

Those women who have persistent vasomotor symptoms and the history of migraine, their hazard ratio or their likelihood of having a coronary event, a heart attack or a stroke, was, they call it the hazard ratio, which is the result, was 2.25. Which means you're like 125% more likely to have an event than someone who did not have those characteristics of the combination of migraine history and these persistent hot flashes. And when they adjusted for other cardiac risk factors, cholesterol, blood pressure, all that kind of stuff, smoking history, it did attenuate that ratio a little bit. It decreased it to 1.51, which basically still means you're associated with a 50% higher likelihood of having a stroke or a heart attack.

And when they looked just at the occurrence of stroke alone, that ratio was even higher. It was 3.15. And when they adjusted, it was down to 1.7. That means a 70% higher risk. I mean, those are increased risk factors there.

Lindsay Weitzel, PhD:
That's really nice to know that not only did you get migraine and persistent hot flashes, but now you're at increased risk for a stroke. That's not actually, now that I think about it, the best way, that's not the

way I really wanted to end this episode. I would have liked to tell everyone some good news. Like, please remember that we now know some of the characteristics that will help us know if we're going to respond to monoclonal antibodies. I should have ended it on something positive.

But anyways, those are some awesome studies, some awesome research. They just came out in the last month that we're all updated on now. And I can't wait to see what comes out again so that we can invite you back on in about four weeks. So, thank you for joining us, Dr. Smith, and thank you everyone for listening in to our monthly news episode of HeadWise. Thank you so much.