**Episode 242: News - January 2026**

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

**Tim Smith, MD:**
Doing well. Thanks for having me on again.

**Lindsay Weitzel, PhD:**
Thanks for being here. We have Dr. Smith on because he's so knowledgeable and he does our news episodes, among other things. We love having him. Dr. Smith is the CEO of StudyMetrix Research. He is also a member of the board of the National Headache Foundation. And he knows so much about all the things that we talk about, whether it's medications, etc. on these news episodes, so let's dive in. We have a lot to talk about today.

We're going to start with a new announcement that was made. The American Headache Society just published an update to their guidelines for the acute treatment of migraine for adults in the emergency department[1]. This is their first update since 2016 and it's so important. Although we may not want to, there are times when people with migraine just cannot avoid having to go to the ED. Dr. Smith, can you tell us the highlights of these recommendations? What's changed since 2016?

**Tim Smith, MD:**
Sure. And what the authors did on this was basically a literature review of clinical trials, randomized clinical trials. And so, and then it's sort of kind of tantamount to a meta-analysis where they look at the quality of the data and break it out into basically, they call it level A evidence, and so it's what they say you must offer. And then they have level B, which you should offer this drug or that drug. Level C, which is you may offer. So, it's like must, should, and may offer. And then they have some that they don't make a recommendation on and then some that they recommend strongly against that you must not offer.

The last time this was done is in 2016. And a new group of reviewers now, it's been almost ten years since this was looked at. And basically, the big change in 2016, the must recommends were basically metoclopramide and prochlorperazine (Reglan and Compazine) and sumatriptan, which we have been familiar with decades from now, and then dexamethasone steroids. So that was basically the must recommends in the 2016 guidelines.

This year they reiterated the prochlorperazine, but they added this greater occipital nerve block. So, they broaden their review to look at nerve block injections and the GON (greater occipital nerve) block. It's the one in the occiput, back here in the back of the head. The evidence was strong. They had multiple level I studies that showed benefit. And so, they've added that to the must recommends. I think a lot of us would look at that as a significant change from the previous guidelines because they never even considered nerve blocks before.

**Lindsay Weitzel, PhD:**
I think a lot of us who have had nerve blocks of various types, occipital or in our head or neck, are wondering, we probably haven't had them given by an ER physician before. Is this something they normally do?

**Tim Smith, MD:**
Largely, no. The emergency room docs are not specifically trained in this as a usual intervention. They will usually give analgesics, they'll give opioids, they'll give other anti-migraine, bona fide anti-migraine drugs and anti-inflammatories. But typically doing a nerve block injection is not in their armamentarium. So, I would assume that this would be something that would need to be added to their training to update them to be compliant with the guidelines.

**Lindsay Weitzel, PhD:**
This sounds like a great addition. Hopefully this is something that we can all get from now on. Let's move on to, since migraine is an invisible illness, it's always awesome if we can find a way to measure it or a biomarker by which we can tell what it is, or if someone has it, or if it's different from something else. A paper just came out looking at biomarkers of migraine in blood[2]. What did they find? And more importantly, how will this matter to patients?

**Tim Smith, MD:**
So, the biomarker or some phenotype. Well, we have phenotypes, but they're not always consistent. And there's such variation in the presentation. That's the point you're making, is if we had some kind of biological marker that could be diagnostic of migraine, that would help us, in selecting treatment. It would help me and my world a lot.

In the research world and clinical trials, we try to get as pure a population as we can, but without a reliable biomarker we just have to do what we can with the diagnostic criteria, which are good, but they have their limitations.

These researchers looked at four different biomarkers. This is their blood test results, that are substances that we know are part of the migraine cascade. And they looked at CGRP, they looked at something called PACAP-38. So, most of our listenership will be familiar with that, because it's been something that's been on the radar screen of researchers for the last several years. No drugs in the market to treat in that arena yet. And they also looked at something called vasoactive intestinal peptide (VIP), which has also been shown to be involved in migraine development. And substance P, another

long acting, sort of pro-inflammatory, molecule that's released into the bloodstream and into the nerves and brains of patients with migraine during attacks.

The question is, can you draw blood samples and look at those, and do any of those match up with a bona fide migraine diagnosis? And the answer that they came up with was that this VIP molecule turns out to be the one that is elevated during a migraine attack and then goes back to normal in between attacks. There was no consistency on PACAP or substance P, and the CGRP marker was elevated, even interictally in migraine patients.

We don't have any clinical trials to really put these to the test and show how they're through the validation work. We have to take these small studies like this and then develop a hypothesis and then do the real validation work, which will get us with the sensitivity and specificity of the testing. But this is suggested that we may be able to do blood markers to help zero in on the migraine diagnosis from a blood test standpoint, something we've never been to do.

**Lindsay Weitzel, PhD:**
I think that's probably helpful from a clinical trial standpoint, etc. I mean, I know if my head hurts, you know if your head hurts, I'm curious to know if the design of this study allowed for differentiation between types of headache. For example, if you have a migraine versus NDPH or something like that.

**Tim Smith, MD:**
Basically, this study looked at just migraine without aura and compared against patients without any kind of chronic pain headache syndromes. So, I think it speaks to the suggestion, if you're going to have a pure population of migraine without aura, that kind of makes sense to me for a small study like this.

But to your point, I think to generalize that out to some of the other more problematic migraine subtypes or post-traumatic headache or new persistent daily headache, those kinds of things, we can't really make that jump or to cluster or any other primary headache disorder. Just a lot of work to be done, but it is encouraging. I'm just happy somebody is looking to try to find some answers on this, but, and to suggest that there may be some clues here. I think we need to refine the work and continue it.

**Lindsay Weitzel, PhD:**
Let's move on to a study on cognitive issues. I mean, most of us with migraine can relate to having cognitive issues during our migraine attacks referred to as ictally, often even between migraine attacks, or they often refer to that is interictally. One group just published a study to compare cognition during these two time points in people with migraine[3]. What did this study tell us?

**Tim Smith, MD:**
In a nutshell, it shows that something we kind of already know, and some studies have suggested in the past that cognition does take a hit during migraine attacks. Not a big surprise I don't think. And much more, so it's just something like a threefold worsening compared to the interictal phase (the phase when the patient feels normal). So that's not exactly earth-shattering science to show that, but they use different tools, different models to look at this, is something called ecological momentary assessment. And I think the big advantage that this may give is that basically they ask this population of

very dedicated patients to complete this assessment, something like five times a day on their phone. It's an app on their phone.

Basically, they're capturing prospective, contemporaneously captured data in the moment. So, it's not waiting until after it's over and then asking a bunch of questions about how you felt after the fact or get a sampling of how you normally do and then have you complete a questionnaire during a migraine attack and to look at that. They did a number of cognitive assessments and basically matched it up with their pain scores and with how they're feeling.

They raised the question about potentially doing more testing looking at episodes in increments of time that have to do with prodrome and like, because some older studies have suggested that the cognitive decline actually begins during the prodromal phase even before the pain begins. And I've had lots of patients tell me over the years, I can tell even before my head starts bumping, I know it's going to be, because I started getting a little muddled, sort of lose my ability to concentrate and focus. And it's almost a prodromal symptom in and of itself for some folks. It would be interesting if they can duplicate these assessments and particularly zero in on the different phases of migraine, not just the attack itself versus non attack periods of time. But good work, they did some very strong work on this.

**Lindsay Weitzel, PhD:**
For some of us, there's certain migraines where that's the worst symptom every once in a while, I think. Not many of them, but every once in a while. So, I love it when people look at that at that endpoint.

The next study[4] was on sleep patterns in adolescents with what they referred to as continuous headache. The authors point out that this population is expected to be more complex than the population of kids with what they would like to call remitting headache, meaning headache that does go away at times. I found their report of this information quite interesting, and I'll mention why after you tell everyone what they found. What did they find and what were your thoughts?

**Tim Smith, MD:**
Well, this was a complex study. And they looked at adolescent migraine patients. Basically, they compared what they call refractory. So, these are patients who are presenting to the clinic with more than a month of continuous daily headache. And they were in need of infusion therapy, basically.

And they compared that to a population in the same clinic of patients who had chronic migraine but non refractory. So, to your point they could remit. They could become headache free at times. And then they compared that against the episodic migraine patients with 14 or fewer migraine days per month. And basically, they showed in this refractory population there was a 60% increase in insomnia symptoms and more than a third increase in poor sleep hygiene, which means basically poor control over their sleep environment and bedtimes and wind downs and how you try to address your sleep needs and that sort of thing.

And when they looked at the three subcategories, they measured symptoms of falling asleep and reinitiating sleep, which is kind of one category. And then return to wakefulness, they called it. And on their return to wakefulness and falling asleep and staying asleep kinds of issues, the refractory chronic migraine kids scored about the same as the remitting category.

And both were worse than the episodic migraine. There were worse mood issues and things like that that were associated with the higher scores. And basically, the authors concluded that this sort of supports the notion of transformation of migraine with comorbid psychological issues and sleep disturbances. And they get progressively worse along the continuum of that transformation.

**Lindsay Weitzel, PhD:**
The thing I wanted to bring up, did you noticed if they had any indication in this study of whether they thought the sleep problems could have been due to the head pain, or did they believe it was the cause? Because that really gets to me.

**Tim Smith, MD:**
Yeah, yeah, they were they were curiously quiet on that question. It basically shows an association and as we say many, many times on this show, association does not equal causation. It would make a lot of sense that someone with a thumping headache is probably not going to sleep very well. And that would stand to reason. I think we can all see the logic in that. That's a little more difficult to tease out, but you make a really good point on that.

**Lindsay Weitzel, PhD:**
You can tell I have a personal bias. I'm not going to bring it up. So, moving on, previous studies have shown that ACEs (adverse childhood experiences), we hear about this a lot in the migraine world, are associated with chronic migraine. One group just published a study[5] looking at whether the group of people with refractory chronic migraine who were recommended for inpatient infusion therapy, meaning they were really having a rough time with it so they had to go stay in the hospital for infusions, had more adverse childhood experiences than people with non-refractory chronic migraine. What did they find?

**Tim Smith, MD:**
They did a battery of assessments on these kids and looked at the adverse childhood experiences. And if you compared to the refractory chronic migraine to the non-refractory chronic migraine, again, no difference on the adverse childhood experiences, but a stark difference between those in the episodic migraine or in the non-pain controls.

It's interesting. I notice that they looked at median headache days for the refractory patients, these were the 30, obviously is refractory so they're non relenting. But in the non-refractory ones so-called they had their median headache days were 25 per months. So there were not much difference between the two populations days, 5 days, but it's essentially the entire month is totally occupied by headache days. And the episodic migraine group was 8. When they looked at MIDAS, the peak MIDAS scores, the big difference here was when you looked at the refractory population, the median score was 108. Anything over 20 is severe. So, you can say these kids are really severely impacted by their migraine attacks. And then the non-refractory group was 36, so still clearly over 20, but not nearly as impactful as the as the refractory patients. But there was a no statistically significant difference in the median ACE scores (the adverse childhood experience scores) between the refractory and the non-refractory chronic migraine population.

**Lindsay Weitzel, PhD:**
I found that very interesting. I do like to hear about the ACE data. I don't like the assumption that everyone with chronic migraine has had a rough life or whatever. And so, I always like to read about it, and I find the data interesting. And I found it interesting that in this particular case it wasn't related.

This is our last study, but it is something that everyone loves to hear about. There's been a lot of talk about GLP-1 inhibitors in weight loss, but also how they affect people with migraine. This study[6] that was just published looked at the effects of liraglutide (Victoza) when given to people with obesity and high frequency chronic migraine. I think everyone will be interested in what they found.

**Tim Smith, MD:**
Well, they showed a decrease in the monthly migraine headache days of 9, so you reduce 9 migraine days per month in this population. That's quite a nice reduction. We have a lot of bona fide migraine preventives that don't reach that kind of result. I think the average was 19 days. And usually for these chronic migraine studies, it's usually on the order of 18 to 20. So, this is the same population. And I will point out this was not a controlled study. It was a prospective pilot where they got baseline numbers of headache days and then did their intervention and looked at their outcomes.

Interestingly, in this study, there was no significant change in body weight. And so, these patients used liraglutide, which is also marketed as Victoza. Victoza is the diabetes brand and the weight loss brand, same drug, is called Saxenda. And this is a once-a-day injection, but it is a GLP-1 agonist, and it is FDA approved as a weight-loss agent.

I will say in the study, they only went up to 1.2mg. So, for the weight-loss arm of most of the studies they would go up to 3mg. I think it's interesting that this did was associated with a decrease in migraine days. Which brings up the other discussion around these drugs, because it's starting to become largely recognized that these drugs, the GLP-1s, may have a significant anti-inflammatory effect in the body.

We know that they're associated with decreases in CGRP, for example. And they've also been shown in large population studies to be associated with decrease in c-reactive protein (CRP), which is a marker for inflammation in the body. We use that to monitor inflammation in lots of disorders, autoimmune disorders, and also for infections and those kinds of things.

We know that CRPs run higher in overweight patient populations. And it's been suggested that this runs high by and large in migraine patients. And so, you start to wonder if you can put all that together. And these patients have an improvement in their migraine attacks because of that. And we can't say for sure based on these data, but it's certainly suggestive. And anecdotal evidence tells us all that we see these kinds of improvements with patients that are on these medications. So, it's good to see some prospective data to confirm that our eyes are not just fooling us.

There is something to this. So, I think the interesting thing that the authors suggested is they were talking about this concept of elevated ICP (intracranial pressure). So, there's this ICP, increased cranial pressure without papilledema. So these patients don't have eye pressure. Their optic nerves are not swollen, and they don't have any symptoms of that. But they may have increased intracranial pressure. So, they made that kind of connection here, but there's nothing about this study that even addresses that point. So, I think it may be just some deductive reasoning on that, but I think, in my opinion,

there's a lot of evidence that's starting to suggest that this may be due to inflammation markers being reduced by the GLP-1 drugs.

**Lindsay Weitzel, PhD:**
I love that study. I love talking to about drug studies because you're so knowledgeable in this area, and I just love learning about the drugs and the mechanisms and how they can help us, even when we didn't think they were a drug made for migraine or head pain. Thank you so much. That was so fun to learn about. And thank you for talking to us today. And thank you everyone for joining us on this episode of HeadWise. Please join us again for our next one. Have a great day. Bye bye.



[1] https://pubmed.ncbi.nlm.nih.gov/41321235/
[2] https://pubmed.ncbi.nlm.nih.gov/40454710/
[3] https://pubmed.ncbi.nlm.nih.gov/40391826/
[4] https://pubmed.ncbi.nlm.nih.gov/40525592/
[5] https://pubmed.ncbi.nlm.nih.gov/40542535/
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