Announcer Introduction:
This is CME on ReachMD!

Welcome to this CME activity, titled, “Headache Disorders: How Can We Better Manage the Pain?”. This activity is brought to you by Forefront Collaborative and supported by an educational grant from the Lilly grant office.

Prior to beginning this activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Here is your host, Dr. Andrew Wilner.

Dr. Wilner:
For patients and caregivers, the burden of a primary headache disorder, such as migraine or cluster, is felt personally and professionally. I am your host, Dr. Andrew Wilner, and I would like to welcome my
guest, Dr. Merle Diamond to the program. Dr. Diamond is the president and managing director of the Diamond Headache Clinic. Dr. Diamond is joining me to speak about what we can do now for our patients as well as promising therapies on the horizon.

Dr. Diamond, welcome to ReachMD.

Dr. Diamond:
Thank you so much. I appreciate having the opportunity to talk to you today.

Dr. Wilner:
Dr. Diamond, your clinic specializes in patients with intractable headaches, it has so for many years. As a practitioner, I know that whenever I send a patient to the Diamond Headache Clinic it is a very challenging problem. Can you tell me what state are most patients in by the time they come to see you?

Dr. Diamond:
They have headaches that are disabling them and they are really having trouble participating in their own lives. They are not only missing work, but they are missing family events and they just can't be counted on and that creates tremendous disability within their families. The average patient we see has seen 6 or 7 providers before they get to us. Sometimes they don't even know what their diagnosis is even though they have been suffering with headaches for a long time. It is not only the headache pain which is often disabling, but also the associated symptoms and these symptoms are somewhat unpredictable and the headache times are unpredictable, and the other piece that brings them to our office is that a lot of people have tried a variety of different therapies and really come up against a wall in terms of getting things that work effectively for them.

Dr. Wilner:
How can a clinician know when a headache signals a primary headache disorder, such as migraine or cluster, that requires only symptomatic treatment or when the headache signifies another disorder that must be diagnosed and treated? This is a daily challenge for primary care physicians.

Dr. Diamond:
Absolutely, and that's a great point. So, we divide headache types into primary headaches, which are the tension type, cluster and migraine headaches, and then secondary headaches, which I always say come with bells and whistles, because there is usually something in the history that lets us know that we need to be aware that there could be some other process going on than a primary headache disorder. And there are a lot of good tools for doing that. So, there was a study that done by David Dodick some years ago that was published, that has a mnemonic in it SNOOP4, which helps us to
screen for secondary headaches,

Dr. Wilner:
I have worked with Dr. Dodick. Can you tell us a little bit more about SNOOP4?

Dr. Diamond:
SNOOP4 is just a really easy mnemonic to make sure you are asking those screening questions for organic or secondary headaches. So, S stands for systemic symptoms or secondary risk factors. So, for example, a pregnant woman might be at risk for listeria meningitis, just as an example, or somebody with immunocompromise might be at risk for some type of abscess. N stands for neurologic symptoms or abnormal signs. O stands for onset, because we never want to forget first worst headache, and subarachnoid hemorrhage is a potential possibility. The second O is for older, so greater than 50 years old is rare to get a primary headache disorder. And then P allows you to think about what previous headache history the patient has, because we need to remember that people with primary headache disorders can sometimes develop secondary headache disorders, so is this different; is it sort of similar to what you have had in the past?

Dr. Wilner:
Primary headache disorders, such as migraine and cluster, can be really disabling for patients. They are painful; they can cause missed work and missed opportunities, why does it take so long for patients to get effective treatment?

Dr. Diamond:
Well, treatment is difficult for a number of different reasons, but I am going to divide it sort of into acute, preventative, and then the rest of the migraine toolbox that patients may have. And so, what we know first and foremost is that up until a few decades ago we didn’t have acute treatments that were developed that were very specific for migraine, and then when the triptans came out on the market that really helped patients in terms of acute treatment. But in terms of prevention, today we are still prescribing medications which we found out worked for migraines. They worked for migraine too, I always say, because they were all developed for some other disease state. So, for example, beta blockers were for blood pressure and heart rate, antiseizure drugs, obviously, for seizures, antidepressants for moods, and we have found over time that those drugs can be efficacious in treating migraines, but they have significant issues with the time it takes for them to work and also the side effect profile that goes along with that.

So, there is a huge amount of frustration around patients who have migraine that really need prevention, and finding a medication that they can tolerate and that’s actually efficacious. Over 30% of migraineurs probably need a preventative treatment based on the frequency and severity of their
headaches, and clearly anyone with chronic migraine, which is more than 15 days of headache per month and at least 8 of those look like migraines. They clearly need prevention, but only a small percentage of that 30-something percent are actually using prevention; some because they have never tried it and some because they have tried it and really have trouble finding something that could work and that they tolerate. And last, but not least, it is important to always talk about what else is in your toolbox when you treat migraines. So, what’s your sleep pattern, are you eating regularly, do you get exposed to a lot of triggers and can you identify your triggers?

Dr. Wilner:
For those who are just joining us, this is ReachMD. I am your host, Dr. Andrew Wilner, and I have the pleasure of speaking with today’s guest, Dr. Merle Diamond, on the topic of primary headache disorders.

Dr. Diamond, we consider migraine to be a primary headache disorder, but something must be causing it. What’s the etiology?

Dr. Diamond:
Well, we do know that migraine is a genetic neurologic disorder that has varying phenotypic expression, and so what that means to me, is that most people with migraine carry the genetic sport, if you have one parent with it you have about a 50% chance of getting migraine and two parents over 75%. So, within each individual patient there is a varying phenotypic expression, and so some patients will have 2 migraines a year; more likely, most patients have a few per month. We also know that migraine is a fairly complex process. We used to think of it being the blood vessels dilate and there is inflammation, and we now know that it’s a much more complex process that involves the trigeminal nucleus caudalis. It is initiated with sort of a spreading cortical depression across the cerebral cortex, and then activation of the trigeminal nucleus caudalis and then sensory afferents release neurochemicals which lead to dilatation and inflammation, and if that process isn’t stopped early on, the migraine proceeds up into the cerebral cortex and there is central sensitization. We also know that there is this autonomic piece with migraine as well, with nausea, light and noise sensitivity, sometimes some vestibular symptoms or lightheadedness.

Dr. Wilner:
So, it is not just a headache.

Dr. Diamond:
No, migraine is way more than the headache, although the pain of the headache is usually moderate to severe, some patients can have symptoms up to a day, day and a half before they get their migraine. We call that prodrome. They have the migraine attack itself, which is associated with what we are all
sort of comfortable with, the nausea, the light sensitivity, the noise sensitivity and the severe throbbing pain which might or might not be one-sided. But then there is this postdrome that can also last for a day or two where the patient is slow cognitively, doesn't feel good, their head is sore. And so, it is really a complex process that is very important to treat because it leads to a lot of disability.

Dr. Wilner:
Given that migraine is often a genetic disorder, does the family history help? Is genetic testing available?

Dr. Diamond:
So, family history is helpful and we occasionally find a patient who has migraine that doesn’t have it, but typically, you do find somebody somewhere. And really the genetic testing that is available today is not really useful for the very common form of migraine, which is migraine without aura. Some of the more rare hemiplegic migraine, migraines with more extensive neurologic symptoms, some of those have genetic markers, but we are not able to use those tools yet in terms of treatment.

Dr. Wilner:
There are many treatments for migraine of different classes of medications, and yet, many patients are still suffering. What are some of the new therapies that are coming down the pike that may help our patients?

Dr. Diamond:
Well, this is the step that is really fun because finally we are going to have some real world migraine-specific preventative medicines coming out on the market, and so it is important for people who are really struggling with their migraines. There are new medications that actually target what is the most inflammatory peptide that we have identified, CGRP, and it not only is inflammatory but it causes vasodilatation. There are some new acute medicines coming out including 5-HT$_{1F}$ agonist called lasmiditan, and then not only that, but we have some blocks that we found can be helpful for patients like sphenopalatine ganglia blocks, and last, but not least, we have some devices.

Dr. Wilner:
How are the emerging therapies different from current treatment options?

Dr. Diamond:
Well, specifically, for prevention, as I said earlier, we are always using medications that we found work after the fact. They were developed for other disease states. So, the newer preventative medicines are very targeted for CGRP or calcitonin gene-related peptides, and they bind up CGRP, and the cool thing about them is they can work really quickly, so we don’t have to wait for a month to see impact or longer
and tolerability is really amazing. So, we are very excited.

Dr. Wilner: How does CGRP blockers work and why is it exciting?

Dr. Diamond: GGRP is a vasodilator, very potent vasodilator, and also causes inflammation and has been implicated in afferent pain signaling as well. So, what the receptor blockers did was they could turn off an acute migraine attack, but what we noticed when we looked at those drugs, was that they also increased the time between attacks. So, we were all excited that these receptor blockers would be great preventative drugs for migraine, but unfortunately, the early drugs that we called them the gepants had liver toxicity associated with them. So, people went back, scientists went back to the lab, and created monoclonal antibodies which either bind up CGRP or bind to the receptors, and so preventatively, these drugs have been shown to have really good safety and efficacy both in Phase II and Phase III trials.

Dr. Wilner: I can think of a number of my patients that would like to try a drug like that. Can I write a script today? Is it FDA approved?

Dr. Diamond: Not yet, so the first two of these products are at the FDA right now. They have been submitted for approval. That process takes some time. But we are very excited, and in the end, we will probably have four of these products that get approved for our patients, and so, it is going to be good for people.

Dr. Wilner: Would you like to briefly comment on neuromodulation therapy, such as magnetic or other non-medication therapies for primary headache disorder? Do you employ these at your clinic?

Dr. Diamond: Yes, sure, so there are a couple of neuromodulation therapies that are approved by the FDA. There is a transcranial magnetic stimulator that is approved for migraine with aura, and a non-invasive vagal nerve stimulator that has been shown to work in acute cluster headaches. So, these are devices that can impact an acute attack. Preventatively, there is a transcutaneous electrical nerve stimulator, a device that you sort of put around your neck and that has also been shown to be effective in episodic migraine.

So, I think these devices are good, unfortunately today they are not reimbursable by insurance companies. And so, I think we need to help to navigate this process for our patients so that they can have access to these stimulators, because right now some of them are fairly expensive. They are also
in investigation. An SPG stimulator for cluster headache and then preventatively a vagus nerve stimulator for migraine and chronic cluster. So there’s a lot of different stimulators being looked at.

Dr. Wilner:
Well, with that, I’d like to thank my guest, Dr. Merle Diamond, for speaking with me and our ReachMD audience about primary headache disorders and their treatment.

Dr. Diamond:
Thank you so much. I appreciate the time.

Announcer Close:
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