MIGRAINE WORLD SUMMIT

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TRANSCRIPT

COULD YOU HAVE MEDICATION OVERUSE HEADACHE?

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Introduction (00:05): I sometimes see patients who are 60 or 70 years of age, and they've taken this medication for 10 years, so they have 10 years of medication overuse headache. And if you take out this medication, then it turns out that the migraine actually is already resolved. Because we know from natural history studies that in many patients, luckily after the age of 60, 65, the migraine diminishes and can even disappear. So, I've often seen that in these elderly people: There's no headache at all after the withdrawal of the medication.

Wendy Bohmfalk (00:40): Have you ever considered whether your migraine attacks are due to the medication you are using? Many people with medication overuse headache don't even know they have it, but it could be the case if you are suffering with daily migraine attacks that start in the early morning. One study found that a majority of all patients visiting a headache clinic have medication overuse headache. Dr. Gisela Terwindt is joining us today to talk about better treatment options and how to break the cycle for those living with medication overuse headache. Dr. Terwindt, welcome to the Migraine World Summit.

Dr. Terwindt (01:16): Thank you, and thank you for [the] invitation. I'm happy to join you today.

Wendy Bohmfalk (01:21): Great. We're so happy to have you. Thank you. Well, let's just start with, what is medication overuse headache?

Dr. Terwindt (01:28): I think that's a very important question, and I always start with explaining to people that there are two types of headaches. So, in the classification system of headache disorders that we use in our clinical practice, we decided to divide people [into] those who have a primary form of headache — for instance, migraine, tension-type headache, cluster headache. So, for this, the causes are partly known but it's intrinsic. It's an intrinsic problem of yourself; for instance, you are genetically more prone to have migraine. So that's what we call primary headache disorders. And the other types of headache disorders: We call that secondary headache disorders. So you, for instance, when you have a flu, and the flu gets more severe, and you get meningitis, you get also headaches, so this is secondary headache caused by an infection. Or for instance, when you get a severe stroke, and you get a headache, it's a secondary headache.

Dr. Terwindt (02:32): And medication overuse headache is also a form of a secondary headache, and it's caused by taking too much medication. So, with this, it's not blaming people, because sometimes people think, "Oh, medication overuse headache — it's my fault that I have this headache." No, that's not what we are trying to do with this classification system. We're just trying to see that there is a cause for these secondary headaches, and that's the overuse of acute pain medication. And often these two types of headaches — for instance, migraine and medication overuse headache — goes hand in hand. Because people take medication because they have — they suffer from a primary headache disorder — they have severe migraine attacks that are frequently becoming more and more severe. There is much more need to take acute pain medication. And with this, people end up in a kind of vicious circle where they have — there's a need for medication, which helps, in the beginning, their migraine. But in the end, the medication itself also provokes headache, because when you are not taking this medication — for instance, when you wake up in the morning and you did not take your pain medication — yet the headache that you might experience is caused by the absence of the intake of the pain medication.

Wendy Bohmfalk (03:59): Are there a certain number of days per month you need to have headache for it to be classified, potentially, as medication overuse?

Dr. Terwindt (04:06): We have set some guidelines when we think this overuse might be a real problem. So, it's not when you take one paracetamol, or one triptan, once a week, then you will not develop medication overuse headache. So, for medication overuse when you take a triptan — we decided that if you take 10 days per month (a triptan) or more, then a medication overuse headache might be a problem. And for normal painkillers it's 15 days per month. And if you combine this kind of medication, again, 10 days per month or more, then you are above the level where we think that medication overuse headache might be a problem.

Wendy Bohmfalk (04:47): OK. And does it also matter how many actual headache days that you're recording per month, like does it line up with chronic migraine, for instance?

Dr. Terwindt (04:56): Yeah, so of course, if you take, on a daily basis, painkillers and you don't experience headache, then you [do not have] medication overuse headache, by definition, because it's not a problem for you. And interestingly, there are people with other pain conditions who take, each day, a painkiller but do not develop a headache. And then, there is of course no medication overuse headache. The problem is that people with an underlying primary headache disorder like migraine are more vulnerable to develop this medication overuse headache; therefore, it's often a combination. And in migraine, for instance, it's often a combination of having chronic migraine — which is defined with at least 15 headaches per month, of which eight are fulfilling the migraine criteria — and this goes hand-in-hand with this medication overuse headache, where also people have, most of the time, more than 15 days per month of headache. And in practice you see that many of these people experience 20 or even more headache days per month. So it's a great burden for patients who suffer from this type of headaches.

Wendy Bohmfalk (06:05): Absolutely — and hard to separate, probably, if it is truly medication overuse headache, or chronic migraine, or even something else. I'd like to come back to this, actually. Before we do, can you tell me, is there a term that you prefer perhaps more so than medication overuse headache? Like you said, that sometimes can feel like it's blaming the patient?

Dr. Terwindt (06:26): Yeah. I think the term "medication overuse headache" is quite clear, because there is overuse, and I think we should use this term and explain to our patients that we're not blaming them at all. And trying to find another term, I think, is not very helpful because, as a doctor, I always also think that being clear in the definition, and what you mean, or what's the problem that's going on, is very important.

Wendy Bohmfalk (06:55): Just for simplicity during this discussion, I'm going to refer to it by the abbreviation — MOH — just to kind of keep things simple. But we certainly understand there's no blame involved, and it's just to be specific. I just want to actually dive right into, get to the punchline and really talk about the medications and treatments that do not cause MOH. Can you please spend a little time and walk us through them?

Dr. Terwindt (07:20): In my opinion, I think many of the medications that we are currently using for the acute phase of the migraine, for instance, they all cause medication overuse headache. So, I'm not convinced that there are medications currently that we're using in clinical practice that are not doing that. So, painkillers, NSAIDs, triptans, ergotamines, opioids — they all will cause medication overuse headache. It might be that in the future we will have a new kind of medication which is coming up, and is I think already available in some countries, which are called the gepants — which are more related to a specific protein, CGRP. And the new thing

about this kind of medication is that there seems to be [the] claim that [this] kind of medication will not cause medication overuse headache, because they can be used both as preventive and acute treatment, which would be, of course, great.

Wendy Bohmfalk (08:23): OK. And also, ditans.

Dr. Terwindt (08:25): Yeah — so both the gepants, which are working on the CGRP, and the ditans, which are aiming for the serotonin 1F receptor, are now brought into clinical practice with the idea that these medications will not lead to medication overuse headache. But we should be aware that in — worldwide, these medications are not available in many countries yet. But they are potentially very interesting, especially for those who had medication overuse and are resolved, again, in the more less-frequent types of migraine and tension-type headache — for tension-type headache, this kind of medication doesn't work, but for migraine it does.

Wendy Bohmfalk (09:14): OK, so, in the pipeline in many countries, but hopefully coming soon. I know in the United States we are fortunate that we do have some of these medications available now to use.

Dr. Terwindt (09:23): Yeah.

Wendy Bohmfalk (09:24): What about devices? I guess that could be another kind of class of treatment that would be available that does not result in MOH, obviously.

Dr. Terwindt (09:32): Yeah, and especially these neuromodulation devices are extremely interesting. Also, from the point of view — from the pathophysiological point of view — because we think that when the migraine patient develops chronic migraine and medication overuse headache, we think that there are processes going on in the brain which we call central sensitization — which means that apart from the mechanisms that are playing a role during the migraine attack, also deeper structures in the brain and connectivity between brain regions are influenced by this chronification process, and that's what we call sensitization of the brain. And it could well be that, especially, neuromodulation can be important to bring the sensitization back to the normal state of the brain. And that's why I think these kinds of new treatment options are extremely interesting, especially for those who suffer from medication overuse headache.

Wendy Bohmfalk (10:36): That's great. Yes, I thought it was really interesting what you said earlier — that other people with pain conditions don't necessarily go into MOH. It could be something to do with our brains — those with migraine — or this, like, the sensitization that you mentioned.

Dr. Terwindt (10:50): So, I think there could be a very simple explanation why migraine patients accept, also, medication overuse headaches: Because as a patient, you were so happy that you got rid of these severe migraine attacks, you accept this other headache as a side effect.

Wendy Bohmfalk (11:10): I can personally relate to that 100%. I lived with a very low-grade headache for a couple of, you know, many years, actually. So I think that could be related, but that low-grade headache allowed me to function, right? So, before we finish up on the treatments that don't cause MOH, what about preventatives too? I know that might be the optimal solution is to get on the right preventive, you know, to keep MOH from developing or to

stop it. What are some of the preventives that you recommend that would definitely not lead to MOH?

Dr. Terwindt (11:41): OK. I think the very simple answer is: None of the preventive medication will lead to MOH. The problem is, when you have MOH, what should you do? And this is a large international debate going on, because in the Netherlands, when a patient comes to us with MOH, we say to this patient, "You should stop the medication first, so you have to withdraw from the medication acutely." So it's a kind of "cold turkey" method. Many people in the Netherlands, although they might be reluctant at the first sight, they are very willing to try this — and they are very ... and I notice that very many migraine patients are very strong, actually, and are very well in control — try to get into control of their own attacks again.

Dr. Terwindt (12:34): So they're willing to try this. And they are able to withdraw from this acute medication without any other support. And the only support that we provide them is we give them guidance with our headache nurse, and this can be discussing with them, how could they cope with this migraine attack? So, it's a kind of behavioral intervention on short notice. And we also showed in our studies that this short behavior intervention by our headache nurse is very effective to make people stronger, to be able to withdraw from this medication. And so, we do not start preventive medication during this withdrawal process. Because we did a study in the Netherlands where we had a randomized controlled blind trial where all patients were withdrawn from the medication — half of them received Botox and the other half didn't receive the Botox, but just the placebo. And finally, we found no differences between those groups. So, the withdrawal itself was so effective that there was no additional effect of the Botox support supplementing this withdrawal process.

Dr. Terwindt (13:44): And we published this paper, but there were many people from other countries [who] were very reluctant to accept this finding, because they said it's not what they call a patient-centered approach; you need to provide people with preventives before starting the withdrawal process. And although I understand the logical reasoning behind it as well, I think it's very good to have a strong debate whether withdrawal alone, starting a preventive medication, starting behavioral therapy — what would be the best approach for the patients on a national, but also on an international, level. And that's the strong debate that is currently going on and which is not resolved yet. But that's for those people who are already experiencing medication overuse headache. That's a different approach than when you — when patients come to my clinic, I always warn already for medication overuse headache, and that's why we start, as many other doctors, very early in the process already, preventive medication.

Wendy Bohmfalk (14:51): OK. So just to, kind of, back up for just a second, it sounds like that there's still some debate about whether you're going to immediately put somebody on a preventive if you're also trying to get them out of MOH. And, probably, people differ in their opinion on what to do in different countries, but of course, preventives might be the solution regardless — the long-term solution.

Dr. Terwindt (15:11): So it is. So, I think you should never withdraw a patient and then just stop. I think you — at some point you need to add preventive medication for people — and I think we — and there will be new trials coming up also on the monoclonal antibodies with CGRP, where there will be a large studies trying to show whether adding this kind of medication to the withdrawal — or not only the withdrawal itself, but maybe taper down the medication overuse — might be more helpful than just saying to people, "You have to stop the medication." And I think it's great that we are doing these kinds of studies, because in the end, you want to do

something which is best for the patients and makes them have a nice life without having a tough time for weeks, because you have to withdraw for the medication.

Wendy Bohmfalk (16:02): So, certainly, work with your doctor to figure out what the best approach is for you, given your circumstances where you live. How long does it usually take, you know, for the patients that do go cold turkey? I'm sure it varies by individual, but how long does that process typically take until you start to feel better?

Dr. Terwindt (16:21): Yeah. So, we know from some studies, and from clinical experience, that the withdrawal headache itself for triptans is quite short — it's only one or two weeks — and for painkillers it's much longer. And if you have taken opioids, when there is opioid overuse, it will take much … longer, and you cannot do that in an outpatient fashion, I would say. So, actually, the first weeks are — the first two, three weeks — I always warn my patient that [those] will be the most terrible weeks. After that it will go up, and we often see that. So, normally I would say, after eight weeks — then you are completely withdrawn from your medication. And then I say the last month — so the last four weeks — is especially to look: What is my natural frequency of my migraine? And we look at this last month of a three-month period to see what's the natural frequency of my migraine currently, and is preventive medication needed? Because ... sometimes we are surprised that people, after these eight weeks of withdrawal, the last four weeks, they don't have any migraine attacks at all.

Wendy Bohmfalk (17:35): You would certainly think if their migraine attacks were bad enough to start taking all this medication, then once they weaned themselves off, you know, that natural baseline would still be pretty bad? But you're saying that you might even be better off than you were before, is that right?

Dr. Terwindt (17:51): Yeah. I sometimes see patients who are 60 or 70 years of age, and they've taken this medication for 10 years, so they have 10 years of medication overuse headache. And if you take out this medication, then it turned out that the migraine actually is already resolved. Because we know from natural history studies that in many patients, luckily after the age of 60, 65, the migraine diminishes and can even disappear. So, I've often seen that in these elderly people: There's no headache at all after the withdrawal of the medication.

Wendy Bohmfalk (18:26): Wow. Wouldn't that be wonderful? I mean, yeah, that alone is worth kind of trying, in case your migraine, like you said, has evolved to the point where it's not as severe or maybe gone. That would be a great outcome, obviously. So, for our viewers that are watching and wondering if they may have MOH, I'd like to talk about what the symptoms might be. In fact, Diane, one of our viewers, would like to know if the symptoms are different from chronic migraine?

Dr. Terwindt (18:51): Actually, that's a very good question [from] Diane, and I think she will probably see, if she has ever suffered from chronic migraine medication overuse headache, she will have noticed that it's quite difficult. If you wake up with a headache, you're not sure whether this headache will develop into a migraine or just stay as a mild headache. And that is actually the problem that migraine patients have, and that's why they take this pain medication or triptans: because there is also a lot of anxiety of developing a migraine attack and being too late. And you want to go to your work, so you don't want to miss your work, or other social activities, so you are going to take the medication, and then you are ending up with asking yourself, "Ooh, would this have been a migraine attack or would it have stayed with just a mild headache?"

Dr. Terwindt (19:38): So, I think it's quite difficult for patients to know whether the headache that they're experiencing, whether it's medication overuse headache or migraine; I think it's impossible to know. And the only way to get a grip on this is to try to get rid of this medication overuse headache and then look what kind of migraine is remaining: Is this still chronic migraine or is it episodic migraine, and how can I get a grip on my migraine attacks?

Wendy Bohmfalk (20:08): OK. Well, you touched on a very popular question that we received and that is: How do we reconcile the guidance to treat at the first sign of migraine, but don't overuse acute medications? Is there effective spacing that we should use? You know, for instance, should we wait a couple of days between using triptans? But I'd love to know your thoughts on this for our viewers.

Dr. Terwindt (20:30): Yeah. I think what we are using in our clinical practice now is what we call "e-diaries." So electronic diaries is just an application — it's an app, and with that an algorithm is calculating whether your day was a migraine day or a headache day, and this is shown not only for the patient but also for the doctors at the hospital, so we can immediately see what's going on within the patient. And also, the patient herself, he or she, can see: "How many medications did I take this month?" And with that, I think that's extremely important to see what you filled out — to count the dates on which you take medication. You can actually see whether you took a triptan, or whether it was effective, or whether it came back the next day.

Dr. Terwindt (21:14): And one of the interesting things we discovered by using this e-diary and doing our research is, for instance, that what women already told us is actually really true: That attacks surrounding the menstruation period — which we call that pure menstrual-migraine attacks — are of longer duration; they're more severe. A triptan will work, but there will be a recurrence of the migraine attacks. So there is a need [for] another intake the next day and maybe thereafter, also another day, to have a triptan. And with that, you are more prone to medication overuse headache. So that's a great explanation of why women are more prone [to] medication overuse headache.

Wendy Bohmfalk (21:58): Yeah, that brings me to another question we received from Jamee — and I think you just touched on this — but she asked: When taken properly, do triptans actually abort a migraine or do they just mask the pain? She said her attacks last for multiple days, so when the pain returns after a day or two, she struggles to know if it's MOH or just the recurrence of the same migraine attack after the triptan has worn off. Is there any way to tell?

Dr. Terwindt (22:24): No, I think there's no way to tell. But I can tell you that in episodic migraine patients with no medication overuse, we can see the same pattern. And then you know, "OK, my migraine is of longer duration because of my menstruation period, and it's logical that I have to take three or four days [in a] row, a triptan." Whereas if you have medication overuse headache, you are not sure what's going on anymore, and the only way you can get a grip on this is to get rid of the medication overuse headache. I think that's the easiest and quickest answer to these kinds of questions. But we should be aware that, especially in women, a migraine attack can be of long duration, and with that, it's clear that a triptan in itself — it doesn't resolve the entire migraine attack.

Dr. Terwindt (23:12): Indeed, it treats the symptoms that are occurring [during] an attack. And sometimes, if you take it early, it seems to abort the whole cascade that is going on, but sometimes you are a bit too late, and a cascade in your brain is already running. But also, when there is an activation of what I mentioned before, central sensitization — so other neurons ...

and regions in the brain, are activated. People experience this as what we call allodynia. And what's allodynia? People express that they have the feeling, and point to, when touching the head, or when taking a shower, or when wearing glasses or contact lenses, or wearing a ponytail, during a migraine attack, it's very painful." So, touching the head is normally not painful, but during an attack it might become painful, and that's called allodynia.

Dr. Terwindt (24:06): And when this process is going on, then we know that there is central sensitization of the brain — so there is activation of the whole brain — and on this mechanism, triptans do not work anymore. So if you can explain it to a patient, you know, that "You shouldn't take a triptan too early because then it's already faded out before your full-blown attack occurred." But most of the patients don't take triptans too early. If you take it too late, you are already in the allodynia phase with the central sensitization, and triptan doesn't work as well. So, there is a small window where you have to decide as a patient, "OK, I'm not too early and I'm not too late. Now I should take my triptan." And that's extremely difficult for some people: to know this window.

Wendy Bohmfalk (24:49): I've actually never heard that before, that when allodynia sets in, it's almost too late to take the triptan. That's really interesting. You know, one thing you did mention that made me think is: OK, so if we know we are a female that has a lot of problems with migraine attacks during our menstrual cycle, and it's going to go on for several days, well then, what do we do if we can't continue to take a triptan every day, you know, but it's a five-, six-day event we're dealing with. How do we handle that?

Dr. Terwindt (25:14): So normally I advise my patient: Don't take a triptan longer than — or other pain medication — longer than three days [in a] row. So if you are still in a need of pain medication after three days of treatment, then nothing will work anymore, because then the central sensitization process is running and running in your brain, and you cannot work on that anymore. So, you have to accept the attack." And what we often see is that when people stop after three days, the attack resolved more quickly than when taking the medication, on day [four, five, six, and seven]. Then this process is ongoing and ongoing and ongoing. And then, actually, we think there is medication overuse headache going on, and not the migraine attack itself. So that's why in practice I say to people, "If you take medication, not longer than three days [in a] row, and then you really have to stop — lie in your bed, just wait until the attack resolves."

Wendy Bohmfalk (26:20): Well, that's good motivation to have a stop at the end of that three-day period, but I know for some it can still be excruciating when you're still in so much pain.

Dr. Terwindt (26:29): I know. Of course I always say to my patient, "This is very easy advice for me to give, but it's really difficult and tough for you to do what I advise. So I understand if you're not able to do that at some point; I completely understand, because it's really easy to say." But from a pathophysiological point of view, and also experiencing what people are telling us, I think this would be the best advice for patients.

Wendy Bohmfalk (26:55): Got it. Well, one last question from a viewer that's again, kind of related, I would believe. Elin asks: If you have daily headache anyway, why bother restricting acute medications if they do continue to bring relief?

Dr. Terwindt (27:10): If you have no problem with it, just do it. I don't mind. So, I think it's up to a patient to decide what will be the best approach for him or her. So, if you think you are only

able to function taking this medication, and you are relieved from your migraine, and you accept taking these painkillers all day and a mild headache each day, but it's not a migraine, and you think, "This is the way I would like to approach my migraine," it's fine with me. I think it might be a very good approach. And sometimes patients come to my clinic, and they say, "I fully understand that I have medication overuse, but in order to function in life I need this." And I say, "OK, that's fine with me."

Dr. Terwindt (27:52): But the problem is, some of these patients, even though they take this medication, they still suffer from very severe migraine attacks, and these migraine attacks, they just break through this wall of medication, and then there is no resolvement [other] than to attack this medication overuse headache. But I fully accept that in some patients, it might be the best approach just to stick to your daily pain medication.

Wendy Bohmfalk (28:19): Interesting. OK. So again, work with your doctor. But that brings me up to one of my last questions for you and that is: Is MOH discussed very often in the doctor's office? I feel like it was never asked of me. I think a lot of patients don't discuss it with their physicians. If you have chronic migraine, should you be bringing this up with your physician?

Dr. Terwindt (28:38): Yeah, I think it's extremely important to bring it up with your physician.

Wendy Bohmfalk (28:42): What are the first steps our viewers should take if they are watching this right now and they are concerned that they are in medication overuse? If they have medication overuse headache, what are some first steps they should take?

Dr. Terwindt (28:54): I would recommend not to start with [blaming] yourself. That's the first recommendation I would give. So, just use a diary, whatever diary you want, you can have just a written diary. Just make — look at the one month — how many headache days did you have? How many days did you experience migraine? How many days were you in need of taking acute medication? And then discuss it with a doctor first, before you [take] any actions. And then you — it's important to discuss what would be the best personal approach for you as a patient to tackle this problem.

Wendy Bohmfalk (29:32): Great. I think also from what I've heard you say during our discussion, whether or not the migraine attack resolves after taking medication could also be a really big clue.

Dr. Terwindt (29:41): Yeah. Sure.

Wendy Bohmfalk (29:43): Well, great. Any final thoughts for our viewers today?

Dr. Terwindt (29:47): I think what I find extremely important is the patient empowerment. I think that's extremely powerful. So, I think we need to empower our own patients to be aware of the problem of medication overuse but also have a shared decision-making in what would be the best approach for these patients.

Wendy Bohmfalk (30:09): Great. Well, thank you for this very informative discussion. I know our viewers are going to appreciate it very much. Where can we learn more about you or follow the work that you're doing?

Dr. Terwindt (30:20): We are currently working on our website, but as you might understand, it's — most of our work is in Dutch — but we're currently working on a translation of our website, and there you can find more of our work. And also, if we publish, we try to do it in an open-access publication so it's accessible also for patients to look at our work.

Wendy Bohmfalk (30:42): That's great. I know I was able to pull up several of your studies myself. Well, we'll definitely link your website below this interview. But thank you so much for joining us today on the Migraine World Summit.

Dr. Terwindt (30:52): OK. You're welcome.