Steroid Dependence

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[00:00:02] **Announcer:** "ABCs of MOGAD" is an education podcast series to share knowledge about MOG antibody disease, or MOGAD, a rare neuroimmune disorder that preferentially causes inflammation in the optic nerves and spinal cord. "ABCs of MOGAD" is hosted by SRNA, the Siegel Rare Neuroimmune Association.

[00:00:26] SRNA is a non-profit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our web site at wearesrna.org. This episode is made possible in part by the generous support of Amgen; Alexion, AstraZeneca Rare Disease; Genentech; and UCB.

[00:00:59] **Krissy Dilger:** Hello and welcome. My name is Krissy Dilger, and I moderated this episode, "Steroid Dependence." For today's podcast, I am pleased to be joined by Dr. Eoin Flanagan. Dr. Flanagan is a professor of neurology and consultant in the departments of neurology and laboratory medicine and pathology at the Mayo Clinic in Rochester, Minnesota. You can view his full bio in the podcast description.

[00:01:27] Welcome, and thank you so much for joining me today, Dr. Flanagan. We're here to talk about steroid dependence and MOG antibody disease. To start us off, can you begin by talking about how steroids work and also how they are specifically used to treat MOGAD?

[00:01:49] **Dr. Eoin Flanagan:** Thanks so much, Krissy. It's great to be here and to be on the podcast here with the SRNA. Steroids are commonly used and many of our patients will talk about steroids and they tend to work very well for acute attacks for people but then have some challenges in the long term in terms of risk of side effects. The steroids themselves, the way they work is that they dampen inflammation in the brain. They do this in a few different ways. They can reduce the amount of swelling associated with the lesions within the brain.

[00:02:21] They can kind of tighten up your blood-brain barrier to prevent those immune cells getting across. They reduce some of the signaling molecules that we call cytokines in the brain that tend to be pro-inflammatory. It kind of reduces a lot of inflammation. They have a kind of a very broad effect and are really useful actually in the acute setting of attacks of MOGAD.

[00:02:44] Most of our patients who present with an attack or a relapse will undergo treatment with a high dose of steroids, and then afterwards there may be more of a prolonged course which we can discuss. Yeah.

[00:02:58] **Krissy Dilger:** Great. Thank you. And you mentioned most patients who are diagnosed with MOGAD will receive steroids in that acute setting. Are, is that all people who are diagnosed with MOGAD receive steroids? Or are there reasons someone might not receive steroids?

[00:03:17] **Dr. Eoin Flanagan:** Most of the time people will receive steroids for their first attack. Sometimes we don't know that it's MOG antibody disease because the antibody test can take a while to come back.

[00:03:26] So we usually don't wait for the antibody to come back to start the treatment. And this treatment is similar for other demyelinating conditions like multiple sclerosis or NMOSD. So, people will often start steroids right away. In some people we have to be a little bit more cautious with steroids.

[00:03:42] For example, people who are diabetic. That can sometimes raise their blood sugar and cause some issues. If you've got high blood pressure, that can be another issue. Most of the time we will use steroids, sometimes traditionally in milder attacks. For example, with multiple sclerosis, if you have a little bit of numbness, sometimes we might not use steroids. Most of the time for an acute episode, if you're having an attack of the condition, we would use steroids as our first treatment to kind of dampen things down.

[00:04:11] And that can be in a variety of different ways. It can be through the vein or by mouth, and we can maybe get more into that as we go forward. Yeah.

[00:04:18] **Krissy Dilger:** Great. So how is dosage determined by care providers?

[00:04:25] **Dr. Eoin Flanagan:** In general, when we see inflammation and when somebody's having an attack, we really want to dampen that down quite quickly. We use a very high dose. One of the doses that we use in adults is a thousand milligrams or one gram of intravenous methyl prednisolone. We're also called Solu-MEDROL. We give that usually once a day for three to five days. I would say most of the time we give it for five days. There is an oral equivalent, so we can give the same amount orally, which is 1,250 milligrams, so 1,250 milligrams of oral prednisone.

[00:05:00] The only problem with that is that the largest tablet is a 50-milligram tablet, so you need to take 25 tablets at a go. That's a bit of a challenge for people, but it is helpful in that it reduces expenses of going to the infusion center and it can be taken right away, which means that you can get in and get these attacks treated early because it seems like the earlier you treat an attack after it starts, the better people do, the more vision they recover and the better they recover from the attack. We like to get in early, so that's one way we can get in early. In children, it's a little bit different and they dose based on weight.

[00:05:38] I think 30 milligrams per kilogram is a dosing that they would use in children. So there needs to be some slight adjustment for the pediatric dosing. So that's also important. Yeah.

[00:05:51] **Krissy Dilger:** Awesome. Thank you. We're here to talk about steroid dependence specifically, which is something that has come up in our community of MOGAD patient, quite a bit. What is steroid dependence?

[00:06:07] **Dr. Eoin Flanagan:** Yep. Great question. We talked a little bit about when we use those acute high dose steroids, and then afterwards we'll often put people on a bit of a steroid taper, particularly after the first attack of MOG. We would kind of go down and wean the steroids over many weeks to sometimes even a few months.

[00:06:27] During that time sometimes as we're reducing the dose of oral prednisone sometimes people will notice that their symptoms return or they may have an actual relapse in the setting of that steroid weaning and therefore they become more dependent. And then each time we try to come down on the steroids, they can have another attack.

[00:06:45] Now it is a very important that if you are coming down and you do feel you're having a flare up, that you contact your doctor and that they do the MRIs and different tests to make sure that it is indeed a flare up. Because the steroids, we know steroids are used for weightlifting and other things.

[00:07:00] They do boost your energy and sometimes as you taper down, the energy levels can go down, particularly if you taper down too quickly. That can be a challenge. And then people can just have low energy levels, and it might not be that they're having an actual relapse. But in some people, they become quite steroid dependent, particularly with optic neuritis.

[00:07:17] And we sometimes call that chronic relapsing inflammatory optic neuritis or CRION, which is a term that you'll hear the doctors mention where people, Each time they come off the steroids or try to come off the steroids, their vision, the optic nerve gets inflamed and then they have to go back up on a higher dose of steroids.

[00:07:36] And the challenge with that is steroids have lots and lots of side effects. So, they can cause weight gain, insomnia. They cause thinning of the skin, bruising. They can cause your blood sugar to raise up. They can cause the bones to thin. They can affect the blood supply to your hip, and some other bones.

[00:07:52] So they are quite a challenge. They can cause confusion in older people. What you'll hear a lot of people use the term steroid sparing agents is trying to get people off of the steroids and onto something that has less side effects. Those medications will often also reduce the immune system but may not have all those other side effects that steroids have. Because when people are on steroids long term it does cause a lot of side effects for people. Yeah.

[00:08:19] **Krissy Dilger:** Okay. Thank you. That makes sense. You mentioned someone who is coming down off of weaning off of steroids might feel fatigued or just not feel as much energy. Are those the only markers that someone would know that they're experiencing steroid dependence or how would someone know that they're experiencing that?

[00:08:48] **Dr. Eoin Flanagan:** Well, I think, yeah, I think the steroid dependence, I suppose we think of more in terms of the disease becoming inflamed. So, the optic nerve getting inflamed, otherwise, I suppose we try to slowly go down on the steroids to avoid, because when you go on high dose steroids, your adrenal glands kind of go to sleep and stop working and you need to kind of wake them up slowly or else they won't kick in. And then you'll have low blood pressure, and it can be quite dangerous actually.

[00:09:15] We usually try to go down slowly. If people are experiencing some of those symptoms, then they can try a more gradual reduction over time. That can be one way of still trying to get off the steroids because it is important to try to continue to wean down and get off of the steroids. A lot of times there are other treatments that we can use that are much safer and better in the long term. We should still be trying to do that rather than remaining on the steroids. Long term is really not a good idea.

[00:09:45] **Krissy Dilger:** Is there any research or any ideas into why some patients become steroid dependent while others can taper off without issues? Any research being done?

[00:10:02] **Dr. Eoin Flanagan:** We don't know fully. Sometimes we know that the MOG antibody disease can be a one-off episode, what we call monophasic, which means you just have one attack and then you never have another attack.

[00:10:11] And then that can happen in up to half of people. And then otherwise people will go on to develop future relapses. We don't fully understand why that is, but it may be that there's some people where they're just more prone to develop inflammation and more, have more active MOG, and then as you come down on the steroids, they can flare up.

[00:10:32] We also know that the frequency of attacks tends to be highest early on. So sometimes it's a phenomenon where you come down on the steroids, you have an early attack, but then you might be able to get off them down the line because the frequency of attacks tends to reduce over time. There may be potential for the attacks to kind of lessen over time as well.

[00:10:57] **Krissy Dilger:** Got it. One of the things that you've already mentioned is there's other drugs that are similar to steroids but aren't, don't have maybe the same side effects, that people can use. Is that the only way that steroid dependence can be managed or are there other strategies?

[00:11:18] **Dr. Eoin Flanagan:** I suppose we talked about one is, going slower on the steroid wean and that's one way of doing it and then trying to get off the steroids. You can add in other medications like we sometimes use something called IVIG or immunoglobulin to boost things up. We can do that through the vein, which is IVIG, or subcutaneously under the skin, which we call subcutaneous immunoglobulin. There are other oral medications, azathioprine, mycophenolate, and there's IVIG medications.

[00:11:46] There's one called Tocilizumab. And then sometimes we'll, if patients are eligible, they may enroll into a clinical trial for MOGAD. And in that situation, sometimes we'll use the clinical trial medication, and they would come off of the steroids as part of the trial and then we'd see if those medications work because we don't have any proven medications yet for MOG.

[00:12:07] Clinical trials will be a way of us developing proven medications so we can get something FDA-approved and then covered by insurance because we often get into issues around insurance coverage and that.

[00:12:18] **Krissy Dilger:** Got it. And are there any risk factors for someone experiencing steroid dependence?

[00:12:25] **Dr. Eoin Flanagan:** Yeah, there are. Yeah. I suppose if you go too quickly, then people will often get symptoms and become dependent. And then I suppose in terms of not so much risk factors, but risks of the steroid dependence are a bit of a challenge. Again, you're gonna get into those side effects of blood pressure elevation, diabetes, weight gain, lower extremity swelling.

[00:12:53] And people can come become what's called cushingoid, where some of the body habitus changes and they get fatty deposition in different regions and it's very difficult. It can also be important for children because children are growing and steroids can impact growth and growing bones and things like that.

[00:13:11] So, in children in particular, we also try to get people down on lower doses of steroids quickly. Now, sometimes the side effects are a little bit less with lower doses of steroids. So, if we can get them down from those high doses, sometimes people will remain on a low dose of steroids in the medium term, and that might not be so detrimental as being on a high dose. So that might be another way you could manage it. Yeah.

[00:13:34] **Krissy Dilger:** Great. If someone with MOGAD experiences a relapse and they've previously experienced steroid dependence, should they avoid using steroids as an acute treatment on this new relapse?

[00:13:50] **Dr. Eoin Flanagan:** No, a quick burst of steroids is completely fine for people, even if they've become steroid dependent in the past. But then after the attack, then we can try to get them off the steroids quickly and probably get them onto a different type of medication that also targets the immune system but has much less side effects. Yeah.

[00:14:08] **Krissy Dilger:** Great. And so how do you balance the need to control inflammation with the risks of prolonged steroid use, especially in young patients?

[00:14:20] **Dr. Eoin Flanagan:** Yeah, that's a big challenge for us and we usually talk to patients about that because we don't want them to keep having attacks and losing vision or developing additional disability. But on the other hand, we know that the steroids can affect their growth and other aspects. So, we have to manage that carefully.

[00:14:36] And if you are on high doses of steroids, it's important to talk to your doctor. One, to make sure that you're on the preventative agents that you need to be on. So usually, we'll have people on calcium and vitamin D. We'll monitor them for osteoporosis because that's a potential risk factor. And we often have them on an antibiotic, one called Bactrim or trimethoprim–sulfamethoxazole, which prevents against a particular type of lung infection.

[00:15:00] So that can also be important, and we'll monitor their blood sugar and blood pressure and so forth. It's important to monitor all those things when you are there. And then we have to balance up kind of the risks and benefits and then see if we can bring in one of those other medications potentially.

[00:15:17] If people are truly steroid dependent, can we get them onto something else that will work? But some of those medications take a while to work, so then we have to keep the steroids going and we know that we can't stop the steroids all of a sudden. If people are having a lot of side effects and the steroids, they say "I want to stop it right now," we can't do that.

[00:15:33] We have to go down slowly. Because if we do that, the adrenal glands won't wake up and then people get into, you can even have life-threatening issues. It's really important not to stop the steroids all of a sudden, but just to come down very slowly. And that should be done in conjunction with your doctor.

[00:15:48] But I will say that we often use a multidisciplinary approach. We might involve our endocrinologists because many of the steroid side effects can affect the endocrine system. So, we'll work on that and get their help in terms of how quickly we can wean off, what sort of things we need to watch out for.

[00:16:06] And in some people, they have very bad side effects. Like it can affect the blood supply to the hip. And if that happens, then we would really have to get people off of steroids completely. So, we would work to get them down. But again, can't suddenly stop and have to go down slowly, but we can kind of do that in a managed situation over many weeks, kind of thing. Yeah.

[00:16:27] **Krissy Dilger:** Got it. Ok. So how do you approach situations where a patient feels better only while on steroids, even after inflammation appears controlled on imaging?

[00:16:40] **Dr. Eoin Flanagan:** Yeah, we do encounter this where people really feel they need the steroids and there's a fear of coming down, rightfully of coming down on the steroids and what that's gonna cause.

[00:16:50] So we try to work with them carefully, kind of adjust the taper and see if we can still start to wean down on the steroids. Because in most people, we're successful at doing that, but sometimes people feel a little bit worse as they go down on the steroids because their energy levels are down, but it might not necessarily be inflammation or the MOG antibody disease coming back, but just those steroids sometimes boost the energy and then you reduce it down and you notice you have a little bit less energy. But usually as we come down, we can get people kind of back to normal, get their adrenal glands waking up. It is really important to try and come down and then get those adrenal glands back up. Yeah.

[00:17:35] **Krissy Dilger:** Ok. Great. Thank you. So that is the end of my questions, but I did want to open the floor in case there was anything else you'd like to mention about steroid dependency that we haven't discussed.

[00:17:49] **Dr. Eoin Flanagan:** I suppose just to reiterate that the steroids are a double-edged sword. They're super helpful for relapse, so if you have confirmed relapse, get in with the steroids, try and get in as early as you can, get them treated. They're really gonna help you and they will reverse your symptoms. But the long-term steroids are problematic.

[00:18:08] So you've got to work with your doctor to see how you can come off of them safely and make sure that you don't come off them too quickly. If you're on steroids for a short time, like a week or two, it doesn't matter. Stopping them right away is okay. But if you're on them for a prolonged period of time, like more than six weeks or so, then you really need to come down on them slowly.

[00:18:28] So I think just reiterating, don't be afraid of the steroids. They'll really help you with the relapse. But then in the long-term work with your doctor and see if you can come down on those steroids and, you may need other medications, but a lot of times those medications are safer and easier to tolerate over time. But it can take some time so it can't really adjust the steroids overnight. You have to kind of be patient with the doctors as we wean them down and work on other treatments in the background.

[00:18:56] **Krissy Dilger:** Great. Well thank you so much Dr. Flanagan, and we appreciate your time and expertise joining us today.

[00:19:03] **Dr. Eoin Flanagan:** Great. Thanks so much. Pleasure.

[00:19:10] **Announcer:** Thank you to our "ABCs of MOGAD" sponsors, Amgen; Alexion, AstraZeneca Rare Disease; Genentech; and UCB. Amgen is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare, autoimmune, and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Amgen believes science and compassion must work together to transform lives.

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