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CARTER:**

Hello. My name is Jonathan Carter and I'm an MS neurologist here at the Mayo Clinic in Arizona and today I'd like to talk a little bit about symptomatic therapy and MS. This is an area that sometimes is overlooked because we spend a great deal of time talking to our patients about disease modifying therapies, treatments that might affect the actual course of MS. Some types of MS are not particularly amenable to disease modifying therapies and there are many complications of MS that arise that can be treated with symptomatic approaches.

Today, I'd like to pick a couple of key areas of MS symptomatology that I'd like to address and this is by no means going to be comprehensive. The first area I'd like to talk about is the area of actual MS walking impairment. And this is an area that we've never really been able to treat before, but just recently about a month ago, the US Food and Drug Administration approved a new drug called Ampyra, also called dalfampridine. And this is a medication that actually blocks the potassium channels in the membrane and helps improve the conduction in the nerves where the myelin has been damaged. So it's a first-in-class drug, meaning it's the first drug of its type approved.

This drug previously was available as a formulated preparation that you could get from certain specialty pharmacies, but the drug had problems in terms of safety. There were high blood levels seen in some patients that led to generalized epileptic seizures. As a result, another sustained release compound called dalfampridine was developed and this drug has now been approved by the FDA. In the clinical trials of this drug, somewhere between 33 and 40% of patients who take the drug seem to respond to it. And the response is defined as an improvement in time walking of a certain amount over their baseline performance.

The patients who have responded well to this drug have shown improvements in walking speed in the order of 20 to 25% and they've also shown improved leg strength, which has also led to functional improvement. This drug is now available on the market. It's given as a dosage of 10 milligrams every 12 hours and the side effects of the drug are generally fairly mild. There is a small risk of seizures still, even with the new formulation, but that's estimated to be less than 1%.

The nice thing about this drug, and others in its class that may follow it, are that this is something that can be used at any stage in MS where there's significant walking impairments. So it can be used in relapsing remitting types of MS. It can be used in progressive types of MS. And you don't have to be at a certain stage of the disease or with a certain type of MS to respond to it.

Another area of MS symptoms that we commonly deal with is the area of spasticity. Spasticity is a result of damage, usually to the spinal cord, from MS lesions. And it's characterized by stiffness in the legs, jerking movements, and sometimes spasms. Now, we have fortunately fairly good therapies for this.

We have a drug called baclofen, which has been the mainstay of therapy for a number of decades, and this drug can help reduce the muscle stiffness in the legs or in the arms, and the number of spasms. It's usually given three to four times a day at doses anywhere from 10 to 80 milligrams a day for the total daily dose, and sometimes we can go a little bit higher than that in certain cases.

Another drug in that same category, as far as an anti-spasticity agent, would be a drug called tizanidine. That drug works through a different mechanism than baclofen, and sometimes we can combine those two drugs together very effectively. Tizanidine causes a fair amount of drowsiness, so we usually start it at night at a low dose of two to four milligrams at bedtime, and then gradually increase it, and sometimes introduce it during the daytime as well on a three to four times a day dosing schedule. The dose range for the tizanidine can range anywhere from 2 to 36 milligrams per day, divided up into three to four doses.

There are also other non-pharmacologic measures to treat spasticity and that can include things like physical therapy, stretching exercises, and also getting moderate aerobic exercise can help quite a bit with spasticity. So that's a very treatable complication of MS.

Another area I'd like to mention, just because it's so common in MS, is the area of MS-related fatigue. And some studies have estimated that up to 80% of people with MS have some degree of fatigue related to MS. Now this fatigue is a little different than the ordinary type of tiredness or sleepiness that we all experience from time-to-time. And the reason it's different is that MS-related fatigue tends to peak later in the day, usually in the mid to late afternoon, and many patients that I speak to tell me that it's as if somebody was pulling their plug at that point in time.

They get very tired. They feel like they can't do one more thing, and oftentimes, have to take a nap. There are, fortunately, some good treatments for MS-related fatigue. There's a drug called amantadine, which originally was used to treat influenza and also it's been used in Parkinson's disease, and this drug was incidentally discovered to help MS-related fatigue in about a third to a half of patients who take it. And usually we give amantadine at a dosage of 100 milligrams in the morning and 100 milligrams at noon.

A newer drug that's available, which is not approved for MS fatigue, but has been used for other conditions, such as narcolepsy, it's a drug called Provigil or modafinil. And that drug is usually given, again, as 100 milligrams or 200 milligrams once in the morning and once at noon. And again, it's not FDA approved for this purpose, but at least in our experience, it's been oftentimes quite helpful to treat MS-related fatigue.

Mayo investigators are also currently studying something as simple as aspirin because we have some preliminary data that aspirin, at a dosage of two 325 milligram tablets twice a day, may help with fatigue. And there's currently a Mayo study ongoing, looking at different doses of aspirin, to see if that effect holds up in a larger, randomized trial. So even something simple like that may prove to be effective.

Also occasionally, we will use or see patients come in on drugs that are used for other indications like attentional deficit disorder. These might be drugs like Ritalin, or Strattera, or various derivatives of dextedrine. Generally speaking, we find these drugs to have a lot more side effects. They can cause excessive sedation. They can cause significant sleep problems, and there is a tendency for dependency and possible abuse of these medications, so we tend to not use them very often in MS fatigue.

And then, finally, there's non-pharmacologic measures in this area as well. Especially important is looking at sleep quality. So if a person is having spasms at night with their legs that are awakening from sleep, if they have to get up frequently to go to the bathroom, if they have something like restless legs syndrome, or if they have obstructive sleep apnea, all of these conditions can disrupt sleep and make the MS fatigue during the day that much worse. And we find that if we can treat these conditions successfully, usually the MS-related fatigue is a lot easier to treat.

Now I could go on and cover quite a few other areas in the symptomatic therapy realm including treatments for MS-related pain, bladder and bowel dysfunction, depression, cognitive issues, et cetera. And really, in the interest of time, there's not enough time to go through all of those. But I think the point I would want to make is that an MS-trained neurologist can really help sort through all of these different treatment options and create a personalized treatment program that may be very effective. And this is true regardless of what type of MS you have, how severe it is, et cetera. I think there's always room for improvement in symptoms and some of these medications are very effective in doing so.

So with that, I'd like to just direct you then, in conclusion, to our website, which has a lot more information about these different symptomatic therapies and other resources for you to get further information.