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### Addressing Fibromyalgia: From Timely Diagnosis to Individualizing Treatment

Narrator:

Welcome to CME on ReachMD. This segment, Addressing Fibromyalgia: From Timely Diagnosis to Individualizing Treatment, is provided by Prova Education.

Your host is Dr. Jennifer Caudle. Dr. Caudle will speak with Dr. Paul Christo, Associate Professor in the Division of Pain Medicine at The Johns Hopkins University School of Medicine. He served as Director of the Multidisciplinary Pain Fellowship Program for 8 years, and the Blaustein Pain Treatment Center for 5 years at the Johns Hopkins Hospital.

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Dr. Caudle:

Fibromyalgia is a common disorder characterized by widespread chronic pain, fatigue, sleep disturbances, headaches, and cognitive impairment. Symptoms of fibromyalgia overlap with many other conditions which may complicate its diagnosis. Although diagnostic criteria are available, many physicians do not effectively utilize, or are not fully aware of the criteria, and many are not confident in their diagnosis of fibromyalgia. Combination treatment with pharmacotherapy and non-pharmacologic therapy is often necessary to provide more optimal outcomes. But repeated therapy switching and complicated polypharmacy remain as barriers to more optimal patient outcomes. These issues are the core focus of our program. This is CME on ReachMD, and I am Dr. Jennifer Caudle and with me today is Dr. Paul Christo. Dr. Christo, welcome to the program.

Dr. Christo:

Thanks so much for having me.

Dr. Caudle:

Well, this is a really important topic and I really wanted to first start with talking about how we diagnose fibromyalgia.

Dr. Christo:

Fibromyalgia, as you mentioned earlier, affects somewhere around 4% of the population, and is the second most common rheumatologic disorder, actually. It's more common in women who are middle-aged, and it is the most common cause of musculoskeletal pain in women who are between 20 to 55 years old. It's now thought to be a part of an entity called the central sensitivity syndrome. Those are things like chronic fatigue syndrome, interstitial cystitis, restless leg syndrome. We've also learned that fibromyalgia isn't a discrete disease entity. Rather, it exists on a continuum with multiple types of symptoms. In the past, we used a tenderpoint exam to make the diagnosis. But in 2010, the American College of Rheumatology proposed new criteria that has removed the tenderpoint exam altogether. Part of the reason for the change is our growing understanding of the relationship between fibromyalgia and clinical symptoms, like fatigue and cognitive changes. Instead, a scoring system has replaced the tenderpoint exam. One system is geared for a physician assessment and the other is a self-administered patient questionnaire. The scoring system combines a widespread pain index and a symptom severity scale for making the diagnosis. The widespread pain index measures the

number of painful body regions, like the shoulder girdle, hip, jaw, arms, legs, and back. There is a defined list of about 19 areas. Now, the symptom severity score includes an estimate of the degree of fatigue, waking up tired, trouble thinking, and abdominal pain, for example. The symptoms need to be present for at least 3 months, too. We make a diagnosis then of fibromyalgia if the widespread pain index and the symptom severity scores add up to specific numbers.

Dr. Caudle:

You know, I think that that's a very helpful description of the criteria, not only as its changed from years ago, the 1999 criteria, but also the new criteria. And I also think it's really interesting how common fibromyalgia is. I'm glad that you mentioned statistics about how common it is, because I think a lot of physicians and patients may not realize this. How do patients typically present when they see their doctor and come to the office?

Dr. Christo:

Well, fibromyalgia is, unfortunately, pretty disabling and it presents with generalized musculoskeletal pain that can vary in severity and anatomical location. The pain involves both sides of the body, above and below the waist. I've had patients say for example, "I hurt all over," or "It feels like I have an unending flu." The discomfort is mainly in the muscles but many report pain in the joints and some patients report joint swelling. They also describe an increased sensitivity to pressure and light touch. In fact, there is often allodynia which is pain due to a non-painful stimulus. You can think of it as a bad sunburn. And they also report hyperalgesia which is amplified pain to a painful stimulus. It's like experiencing 10 times the pain of an ordinary pinprick. By the way, these clinical features are hallmarks of neuropathic pain, and that's why fibromyalgia reflects the process known as central sensitization. Some have viewed it as having the volume control dial stuck in high position. So, patients commonly experience depression and sleep disturbances too. They wake up un-refreshed even after sleeping 8 to 10 hours, have daytime somnolence, and may also have insomnia. There's just an overall fatigue that they experience. The majority of patients talk about cognitive problems as well. In other words, they struggle with attention and doing things that require rapid thought changes. Fibro fog is the term often used for these symptoms. Tension-type headaches and migraine occur in, I think, more than 50% of patients, and patients often report paresthesias, numbness, burning in both arms and legs, but the neurologic exam and formal testing is usually negative. Other poorly understood symptoms can manifest as well, things like abdominal pain, chest wall pain, pelvic pain, and bladder symptoms.

Dr. Caudle:

I'm a family physician myself and as I'm listening to the symptoms that you're discussing, they're so wide ranging, and potentially widespread, and I'm sure you've encountered this, but I feel like it can be overwhelming for physicians, and it may be difficult to really be able to pinpoint and understand how these symptoms may play a role and how they relate to fibromyalgia. And along those lines, how do you rule out other conditions? How do you make sure that some of these symptoms are not attributable to other conditions?

Dr. Christo:

Yes, that's a great question. The many symptoms of fibromyalgia can mimic other conditions. History, physical exam, as well as a limited laboratory test usually are enough to differentiate fibromyalgia from other similar disorders though. What are those disorders? Well, as you might imagine, there are many of them. For instance, rheumatoid arthritis, systemic lupus, polymyalgia rheumatica, myopathies, hypothyroidism, multiple sclerosis, for example; even myofascial pain syndrome and headache disorders. So, there's a lot of potential overlap. Keep in mind that there is no definitive lab test or radiologic findings that establish the diagnosis of fibromyalgia. Sometimes a referral to a rheumatologist is more cost-effective than ordering multiple tests, if you suspect another condition. Now, that all being said, consider a basic workup to exclude conditions that mimic fibromyalgia. First, a complete blood count and erythrocyte sedimentation rate, or C-reactive protein. Normal values provide confidence that no underlying inflammatory disorder is present. If you suspect some type of inflammatory or systemic rheumatic disease, though, then consider getting antinuclear antibody and rheumatoid factor tests. But, bear in mind that these are often positive, even in healthy people. They are more predictive, though, if there is a strong sense of systemic rheumatic disease. And, if you suspect thyroid disease or inflammatory muscle disease, order thyroid function tests or creatine kinase. If patients present with symptoms like obstructive sleep apnea and restless legs, then refer to a sleep expert, or for some type of sleep evaluation. If they have an undiagnosed or uncontrolled psychiatric disorder like depression or anxiety, refer them to a mental health professional.

Dr. Caudle:

I think that's a really great, almost like an algorithm that you've provided for physicians and clinicians to approach these symptoms and our suspicion of fibromyalgia or concerns about other conditions. Let's turn to pharmacological treatment of fibromyalgia. Once we've done our physical exam, we've interviewed our patient, we've maybe done a little bit of a workup, how do we really approach the pharmacological side of the care plan?

Dr. Christo:

I start with centrally-acting agents such as the serotonin norepinephrine reuptake inhibitors, antiepileptic drugs, and tricyclic

antidepressant medications. Those are shown to be the most effective. The 3 drugs that are FDA approved are: pregabalin, known as Lyrica; duloxetine which is known as Cymbalta; and milnacipran, known as Savella. Two antiepileptic medications, the pregabalin and the gabapentin, which is known as Neurontin, have shown positive results in clinical trials. These drugs work by binding to the alpha-2 delta subunit of calcium channels in the central nervous system. Duloxetine is a serotonin norepinephrine reuptake inhibitor along with milnacipran. These have both demonstrated the ability to improve pain and fatigue. . All the clinical guidelines recommend the tricyclic antidepressants, and, specifically, amitriptyline, known as Elavil. This drug has been thoroughly studied and found to reduce pain and sleep disturbance in fibromyalgia patients. In fact, a recent metaanalysis showed that amitriptyline out-performed duloxetine and milnacipran in areas related to pain, fatigue, and health-related quality of life. Keep in mind that there is some data to suggest the value of combining medications; that is, using milnacipran along with pregabalin to provide more benefit than one drug alone. You may have some patients asking about antiinflammatories or opioids, but neither is recommended for fibromyalgia. I've sometimes used tramadol which is a weak opioid, and cyclobenzaprine which is a muscle relaxant, in patients that don't respond to more conventional medications. Low-dose cyclobenzaprine has shown to improve pain in several trials, as a matter of fact.

Dr. Caudle:

That's very helpful and also, I think, a really important note that you made which is that typically antiinflammatories and opioids are not considered first line, so I think those are very important points. If you're just tuning in, you're listening to CME on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Paul Christo, and we're talking about fibromyalgia. So, Dr. Christo, , let's talk about maybe the value of integrative therapies: exercise, acupuncture, and things like that.

Dr. Christo:

I'm glad you mentioned those. Exercise, I mean, aerobic exercise, resistance training, or flexibility training have been shown in clinical trials to provide benefit. In larger scale analyses, aerobic exercise alone improved global well-being, physical function, and pain. If patients prefer water, and some of mine do, then they should engage in aquatic exercise, because another metaanalysis showed improvement in pain, stiffness, muscle strength, and overall well-being with water-based therapy. Now, let's look at acupuncture, because that has the ability to reduce pain and improve stiffness in fibromyalgia, and also calm the mind. It often requires like 8 to 10 sessions. And interestingly, Qi Gong, which is type of meditative movement therapy, may also provide benefit in all domains of fibromyalgia, based on recent trials. Another mind-body technique, called Tai Chi, has shown benefits in pain and sleep quality. Massage therapy was controversial in the past and some patients, even today, feel like they just don't want to be touched, but if you look at some of the studies on massage, you'll see that they've shown substantial improvements in pain, anxiety, and depression for more than 5 weeks or so. Myofascial relief may be the most beneficial among all the techniques. And then, finally, I think yoga is worth considering too.

Dr. Caudle:

That's very interesting. I guess, I'm actually curious about your thoughts about the role of pharmacologic and non-pharmacologic therapy. Do you feel that they're equally as important as one another? Is it important to employ both? And maybe what are some barriers or some difficulties with therapies that we might prescribe for our patients?

Dr. Christo:

Well, I think that incorporating the pharmacological therapies along with the integrative therapies is key, and I do both for patients that I see. Some patients, for example, will only want to try the pharmacological therapy. So, I think that's good, and that's fine. Others will just say, "Look, I want to avoid medications altogether, and I just want to focus on holistic treatments." And, again, I feel like that's appropriate. My overall feeling and experience, though, is that combining them can achieve the best effective. I think the key, in terms of some of the difficulties, with respect to persuading patients to adhere to therapy, is validating the diagnosis and letting patients know that you're going to work with them to help make life better. Adherence is a common problem and often is the cause of continued symptoms. Patients tend to forget to take their medications or exercise, which contribute to a lack of effectiveness of these particular strategies. If you can make patient visits positive and supportive it will really enhance patient compliance. And there's an increasing emphasis on the need for patients to shift their treatment expectations to greater acceptance of pain and the need for ongoing self-care. It doesn't imply withdrawing care on the part of us, as physicians, but it does ask patients to be more active in their quest to improve how they feel and what they can do.

Dr. Caudle:

Those are really excellent points and I think great reminders for us clinicians out there. The idea of making visits positive. Kind of also managing expectations and being very clear about what can be expected and what not. I think those are very important things that we need to be integrating into our office visits with patients that maybe we don't always focus on as physicians. I want to turn a little bit back to medications and very quickly, are there any new drugs that are in the pipeline that may improve symptoms and may change the landscape of fibromyalgia?

Dr. Christo:

There absolutely are. One drug that's shown promise is called mirogabalin. This is a drug that binds to similar calcium channels to pregabalin, that is, the alpha-2 delta channel, except that it binds to a specific subunit of that channel that's thought to be involved in pain generation. Because mirogabalin preferentially binds to this one subunit, it may offer pain relief with fewer side effects than similar medications on the market. It's being studied for fibromyalgia and neuropathic pain currently. Now, there's another drug called naltrexone and that drug, in a pilot study, found that it reduced pain, enhanced satisfaction with life and improved mood. The drug may work by blunting inflammatory processes and antagonizing immune cell receptors in the central nervous system. Microglia serve as the immune defense in the brain and spinal cord. Once these microglia are activated, they produce pro-inflammatory factors, like cytokines. Now, naltrexone may act to block microglial activity and thereby reduce symptoms of fibromyalgia, since activated microglia may account for the symptoms of fibromyalgia. Nabilone is another medication that may be helpful. That's a synthetic cannabinoid that could help patients with fibromyalgia get to sleep, but it's not clear how much pain relief it actually offers yet. And then, finally, something called transcranial magnetic stimulation has shown positive effects on quality of life one month after starting therapy. There are some preliminary trials on this and on the use of occipital neural stimulation and C2 stimulation that have shown benefit as well.

Dr. Caudle:

So, it sounds like there's a lot of potential medications that really may be coming down the pipeline to help patients with fibro and that's very encouraging and very interesting. Before we close, is there anything else you'd like to discuss that maybe we haven't touched upon in this interview?

Dr. Christo:

I think that reassuring patients that fibromyalgia is a real illness, and not an imagined one, is critical. Let patients know that it's not life-threatening, and that there's no evidence of sort of ongoing or persistent infection. Let them know that managing stress helps to lessen the impact of the illness, and that any co-occurring mood disorders can be and should be treated. Sleep hygiene and exercise are important to integrate into therapy. And, finally, the majority of patients live normal and active lives despite the waxing and waning symptoms.

Dr. Caudle:

Dr. Christo, this has been a great discussion. Thank you so much for joining us today.

Dr. Christo:

My pleasure. Thank you.

Dr. Caudle:

I'm your host, Dr. Jennifer Caudle, for ReachMD. Visit us at [ReachMD.com](https://ReachMD.com) where you can be Part of the Knowledge.

Narrator:

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