It's Time We Took Chronic Pain in Rheumatology Seriously

Transcript

Don L. Goldenberg, MD (Guest): What I want to stress there is pharmacologic management is part of a multidisciplinary approach to centralized pain. As itself, pharmacologic management is not that effective.

Deeba Minhas, MD (Guest): One factor that would be helpful in the populations that have unaddressed pain control is first acknowledging our implicit biases.

Meghna Rao (Host): Welcome back to season 2 of the *Rheumatology Advisor* podcast, Rheum Advisor on Air. I'm Meghna Rao, the senior editor of *Rheumatology Advisor* and the host of this podcast.

In this series, we will be joined by expert clinicians and researchers to discuss emerging and compelling topics in rheumatology. These perspectives may be related to the management of rheumatic disease, guideline updates, patient care, data from conferences and scientific meetings, and much more.

We're also excited to announce that Rheum Advisor on Air was shortlisted as a finalist in the Best Podcast category for the 2022 Jesse H. Neal Awards, one the most prestigious editorial honors in journalism. We thank you for your continued support.

Let's dive in!

Meghna: Pain – the main manifestation of many rheumatic diseases, but also the most underappreciated, leads to worse disease outcomes and affects the quality of life of patients.

Animal models and modern technology have highlighted the complex mechanisms that underline chronic pain in rheumatology.

Now to get further insight into the prevalence of pain and its mechanisms, I'm speaking with Dr Don Goldenberg, emeritus professor of medicine at Tufts University School of Medicine and adjunct faculty in the Departments of Medicine and Nursing at Oregon Health Sciences University in Portland.

Welcome and thank you for joining us today, Dr Goldenberg.

Dr Goldenberg: Oh, it's my pleasure.

Meghna: Based on your vast experience as a rheumatologist and your expertise in areas of chronic pain, let's talk a little bit about potential mechanisms involving pain.

Now, pain in rheumatic disease has typically been characterized as nociceptive but, of course, due to the heterogeneous nature of many of these diseases, understanding and managing rheumatic pain is probably much more complicated, right?

So, I wanted to ask you – what are the various aspects in the pathophysiology of chronic pain?

Dr Goldenberg: Well, I think the biggest change in my long career in rheumatology has been the introduction of the concept of centralized pain or central pain or central sensitization as an important factor in all types of rheumatic pain.

Traditionally, in the way I was taught, and the way most rheumatologists were taught 20, 30, or 40 years ago was that rheumatic disease pain was either related to inflammatory/immunologic disorders, [t]he prototype would be rheumatoid arthritis, or more structural disorders, the prototype being osteoarthritis.

Around 1980 or so, people started talking about what was called then fibrositis or fibromyalgia as a model of an illness where neither inflammatory [nor] structural problems could be detected, and that led to more interest in the concept that it was the central nervous system independently causing the pain in that condition. One of the problems with that is a lot of people thought that [it] meant that since there were no structural inflammatory or immunologic causes of the pain, it was "all in your head."

So, for a long time, I think, psychogenic pain or psychogenic rheumatism was equated with fibromyalgia. It's been very, very difficult to get physicians, including rheumatologists, out of that idea that if you can't see it structurally, if it's noninflammatory, it's more of a psychogenic *[inaudible]*. I think in the last 20 or 30 years a lot of sophisticated techniques have demonstrated that this central pain is [indeed] a disease in itself.

The other big issue is that we now know that central pain, centralized pain, is important in our traditional rheumatic conditions, certainly in inflammatory disorders, such as in rheumatoid arthritis, while at least 20% or 30% of people would meet the criteria for fibromyalgia. The same is true with structural disorders.

So, I think rheumatologists now are better accepting of the fact that we like these neat categories, where first of all the standard, prototype rheumatologic condition is rheumatoid arthritis – clearly an inflammatory condition, clearly has immunologic basis, does do structural damage. Then there's the more structural conditions like osteoarthritis. We used to think that many types of low back or neck pain would fall in that category; that's probably not true. And then, we have this centralized pain, which is, sort of, out there and poorly understood.

Now, I think everybody understands that this centralized pain is important in both structural diseases and certainly in inflammatory pain.

Extending that the biggest thing recently or in the last decade, I'd say, would be how this plays an important role in therapy. Because we know that if a person has fibromyalgia – or let's call it centralized pain – [it] may markedly interfere with how we treat the patient. We might think that a person's doing very well with rheumatoid arthritis on methotrexate and/or a [tumor necrosis factor] (TNF) inhibitor. After a couple of years, their pain levels increase significantly, their exhaustion increases significantly, [and] their arthritis doesn't seem to be more active. Rather than increase that person's biologic medication or switch to another medication, [t]hat's the time to think about centralized pain and adjust the medications in that regard.

So, that's been a big switch in how rheumatologists think about even our traditional inflammatory pain disorders.

Meghna: I've also been noticing that many experts, like you mentioned, have recently commented on their preference to use the term "central pain sensitization" to fibromyalgia owing to the fact that it's probably the most common central sensitivity syndrome, right?

Dr Goldenberg: That's correct. Let's just talk for a second or a minute about labels. Labeled "fibromyalgia" is a clinical label; I usually link it with the term "syndrome"; it doesn't meet criteria, basically, for a disease. The term "central pain" or "centralized pain" [is] a pathophysiologic description; it's not a clinical definition. So, I think people get mixed up in how we use these terms. Even the [*International Statistical Classification of Disease*] (ICD) codes want you to use the term "fibromyalgia."

The description I think that's more difficult is when people use "fibromyalgia" or say, "chronic widespread pain," meaning the definition nowadays of fibromyalgia [i]s you have to have chronic widespread pain for at least 3 months, and that's the clinical description, and at the same time we should be excluding other disorders that would cause that. And that's really the criteria for fibromyalgia.

If you apply that criteria, fibromyalgia probably occurs in 3% to 5% of the general population whereas the broader description of chronic widespread pain occurs in like 10% to 15%. What's the difference in those 2 groups? There probably isn't any difference; there is probably just different in severity and duration of symptoms. So, many people with chronic widespread pain don't meet the exact criteria for fibromyalgia because they're not having the severity that we talk about when we see people in the office with fibromyalgia.

Meghna: I think that makes sense. [Because] we're on the topic of fibromyalgia, would you also be able discuss how fibromyalgia, as chronic pain condition, can

be used [a]s an example to study other rheumatic diseases with severe pain manifestation?

Dr Goldenberg: Yeah, again, I think, we have to keep in mind this bidirectional categorization; so, as rheumatologists we always need to look for central pain.

The example being if a person has rheumatoid arthritis and, as clinicians, we examine the patient, we see that they're very actively having a lot of joint inflammation [and] their biomarkers all suggest inflammation, to think about fibromyalgia in that situation is probably moot because our design has to be to treat the rheumatic disease.

It's more in the patients [for whom] we're scratching our heads and trying to figure out, why is this patient really doing so poorly? And when there is a mismatch of what our traditional biomarkers or x-ray evidence of joint damage, etc, that's when we should think about central pain.

But we also have to be aware of the fact that both disorders might be going on at the same time.

It might be even more difficult in osteoarthritis. Some people with very minimal x-ray damage have very severe, ongoing knee pain, whereas other people who have a fairly damaged knee with marked joint space narrowing, they are doing very well, and most of the time that has to do with the centralized pain aspect.

Meghna: I think this is a great segue to the next part of our discussion about diagnosis.

To get a perspective on this from a practicing rheumatologist, I'm speaking with Dr Deeba Minhas, a rheumatologist in Ann Arbor, Michigan, practicing at Michigan Medicine.

We're finally here after much back and forth and availability, but I'm glad you could join us today.

Dr Minhas: Yes, it's great being here, thank you.

Meghna: I wanted to draw our attention to the manifestation of pain in rheumatic disease. Maybe you could talk us through the case of a patient who first presented to your practice with severe joint pain and how a differential diagnosis of the condition was made based on this.

Dr Minhas: Yes. I recently had a patient, a young woman, 19 years old [who] came in with multiple areas of joint pain, and then on her lab work, she was also noted to have a really high [cyclic citrullinated peptide] (CCP) antibody, which is a marker of rheumatoid arthritis. But when I was examining her, I noted that she had pain in multiple areas besides just where we would think about for rheumatoid arthritis, which would be mostly like the small joint of your hands and wrists. I just made sure to do a thorough physical exam and made sure to identify other areas that could be pain generators for her.

She also ended up having hypermobile joints in a lot of areas of hypertonic – so really tensed muscle spasm – and so we did some trigger point injections on her upper back to release some of the tension there, which you can often get from just being on our computer all day and doing these kinds of things. But, in her case, it was exaggerated. I think it's really helpful when you're seeing a patient to look for all of the different areas that generate pain. Oftentimes, there's more than 1 thing going on that needs to be treated.

Meghna: Now, Dr Goldenberg, since pain is an overlapping symptom, like you mentioned, in many, many rheumatologic diseases, how [do you think] an accurate diagnosis of the related condition be made? Now, I'm sure there's no one-size-fits-all answer to this, but it may be valuable to our listeners if you could describe the typical approach and how it can incorporate patient perspective as well.

Dr Goldenberg: That's an interesting question. We started doing the diagnostic classification criteria – the first one we wrote was back in 1990 and, I think, subsequently in the last 20 or 30 years, those criteria have been redesigned maybe 6, 7, [or] 8 times.

The issue is that we, clinicians, [r]eally understand now what fibromyalgia is, and it is still an illness of exclusion. I think most of us are [quite] good at examining and diagnosing rheumatoid arthritis, lupus, [and] conditions like that. It's in those patients where there is a mismatch of their symptoms; that's where we're really looking at fibromyalgia. That could be in people who have an ongoing disease, like rheumatoid arthritis, and that sometimes becomes a little tricky.

But to answer your question specifically, the diagnostic criteria are all clinical. It's a diagnosis based on widespread pain, involving both sides of the body, upper and lower torso; it should be the neck, shoulders, upper back, etc, and it should be for at least 3 months. Furthermore, almost everybody with fibromyalgia have these other symptoms particularly chronic fatigue or exhaustion. Many people also have sleep disturbances; there are a lot of cognitive disturbances, mood disturbances, etc.

So, you're looking for those other symptoms to help you with a diagnosis. There's no laboratory tests. The only use of a laboratory test is to exclude the other conditions. So, if the [erythrocyte sedimentation] rate or the [C-reactive protein] (CRP) is elevated, that's not part of fibromyalgia; then you might want to think about polymyalgia rheumatica.

Meghna: Hmm, I think you're right. I was also reading that, I think, it was in 2018 that the World Health Organization released a preliminary version of the 11th revision or the ICD-11, which will be effective from this year. This update also includes a systematic classification of clinical conditions associated with chronic pain. So, this is an exciting development for clinical practices, right?

Dr Goldenberg: It is, it is! And the other thing that's been very important [is] the noninflammatory rheumatic conditions. So, chronic widespread pain, centralized pain, where people meet the exact criteria for fibromyalgia is very important in all types of musculoskeletal disorders in chronic neck and back pain; they're probably the most common chronic pain disorders that primary care physicians see in conditions that typically have been very difficult to figure out, [such as] benign hypermobility syndrome [and] Ehlers-Danos syndrome.

That whole concept has allowed us to look at these in a more unified fashion.

Meghna: Dr Minhas, many studies that have indicated that women may be at a higher risk for arthritis mostly due to their biological nature, but it's not just the risk, right? Women have also reported worse pain scores and quality of life related to their rheumatologic condition. This is, of course, concerning, as we were both talking about earlier, but how can chronic pain be identified and addressed in a timely manner in this population?

Dr Minhas: So, I think 1 factor that would be helpful in the populations that have unaddressed pain control is first acknowledging our implicit biases; if data [are] showing that certain populations of women who are [African American] are having their pain taken less seriously or not being addressed, we need to keep that in our minds. So, when we're getting a history and physical exam, we are trying to address those implicit biases that everyone has.

The other thing that I think is helpful is just understanding that there are a lot more things besides just structural causes for pain. When you're examining patients and getting their history, a lot of other risk factors for pain need to be considered.

A big one is assessing patients' sleep. In almost all patients who have the nociplastic type of pain, they will report that their sleep is very poor. If patients are not sleeping well that's a huge thing that needs to be addressed, [and] that just putting a patient on a [disease-modifying antirheumatic drug] (DMARD) or a biologic is not going to be enough to cover.

There's also a lot of other factors that can be involved. [Research has] shown that patients who have greater social support will have less severe pain intensity and pain-related disability [and among] patients who have more difficult life stressors, such as tenuous housing situations.

Other things that have been associated with higher levels of pain are patients who have higher levels of depression, anxiety-negative affect, which we define as emotional distress, along with a cluster of other negative emotions, thoughts, [and] behaviors.

Environmental stressors and trauma have been associated with higher levels of pain, so that's another important thing to address with patients. Sometimes pain

can be triggered in people with history of certain viruses, if they've had physical trauma, like car accidents, childhood physical, sexual, or emotional trauma.

[Research has] shown that patients who have a history of childhood abuse [h]ave a 97% increased risk for having chronic pain in the future.

Meghna: I think you made some excellent points in how clinicians and clinical practices can address these systemic biases, especially with respect to race, ethnicity, and sex. I've seen so many studies lately about Black women with lupus having reported that their pain has historically "not been taken seriously" by providers and things like that.

[Now], Dr Goldenberg, let's shift our focus to pharmacologic treatments. So, what are the typical goals when addressing rheumatic pain? Although, I'm sure this is probably dependent on type of pain, whether neuropathic, etc, and developed on a case-by-case basis.

Dr Goldenberg: So, again, back to our [previously mentioned] 3 categories. If it is an inflammatory disorder, of course, [a]s rheumatologists, we've seen a huge turnaround in the ability to treat conditions like rheumatoid arthritis and seronegative spondyloarthropathy. So, we treat the inflammatory immunologic characteristics of those conditions first with medication.

In osteoarthritis, medications are certainly less effective, but surgery can be extremely useful. But, in regard to the centralized pain, [it] always should be thought about, as we talked about, in treating all of these conditions because it will play a role, particularly in people who may not be doing well and may not be responding as well as you thought they should be.

What I want to stress there is pharmacologic management is part of a multidisciplinary approach to centralized pain. As itself, pharmacologic management is not that effective. It's much more effective when it's combined with a multidisciplinary therapy, which traditionally would include things like cognitive therapy, education, physical therapy, exercise, etc.

The medications, in some people with centralized pain, can be quite effective; however, in the many, many randomized clinical trials that have been done in fibromyalgia and chronic widespread pain, certainly, mediations are not as effective as we'd like them to be.

The other thing that's changed a lot in the last 20 years has been the idea of trying to stay away from opioids in chronic pain management, both because of the opioid epidemic, but also the fact that chronic pain management hasn't really improved much with even the good use of opioid therapy.

So, we would traditionally say that, other than in exceptional circumstances, opioids should not be used in the treatment of [c]hronic central pain.

Meghna: Yeah, I think any conversation about chronic pain warrants a discussion about opioid use, especially in light of the imminent "opioid epidemic" you mentioned.

I mean, even before [COVID-19], I think almost 150,000 individuals were dying from opioid use and that number has reportedly increased by 50% during the COVID-19 pandemic.

Dr Goldenberg: That's right; absolutely.

The other thing I would point out since you mentioned [COVID-19] is its interesting, as you're probably aware, [of] so-called "long COVID," [which a] poorly understood illness in many individuals, particularly individuals who really do not have any evidence of significant organ damage. About 30% or 40% of patients with "long COVID" do have chronic widespread pain. And in a number of studies, including one from Italy, which was quite well done, those patients did meet criteria for fibromyalgia.

So, the 2 things that's happened with the pandemic is this realization that "long COVID" and the association with chronic pain and chronic fatigue are probably [w]hat happens in individuals with fibromyalgia and so-called chronic fatigue syndrome.

Also, [b]ecause of the opioid issue and even more difficulty with stress and mood disturbances, etc, in the general population, we're probably seeing more people with chronic widespread pain since the pandemic has occurred. The rheumatologists throughout the country have told me that.

Usually what I try to do is the look and see which factors are associated with a person's pain. For example, if somebody has really significant sleep disturbances, we would often use a medication such as amitriptyline in low-doses at nighttime or a medication such as pregabalin at nighttime or gabapentin. Whereas if a patient has more energy issues and possibly associated with what seems to be some depression, we might use a serotonin reuptake inhibitor or a dual reuptake inhibitor, such as a duloxetine, in the morning. Often we combine low doses of both of those.

You'll notice that I didn't mention analgesics or anti-inflammatory medication because they haven't been that effective in pain reduction in patients with centralized pain.

Meghna: I think this was such a wonderful conversation, Dr Goldenberg, that I hope we can all continue to have in the future. I thank you for taking the time to speak with me today.

Dr Goldenberg: My pleasure, Meghna; it's been nice to talk to you. Thank you.

Meghna: Please stay tuned for more episodes in this series. For more information on *Rheumatology Advisor* and this podcast, you can reach out to us at editor@rheumatologyadvisor.com.

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