SCOPE of PAIN: Safer/Effective Opioid Prescribing Education

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Episode 6

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Ilana Hardesty: Thanks for listening to Boston University Chobanian & Avedisian School of Medicine's Safer and Competent Opioid Prescribing Education: *SCOPE of Pain* Podcast Series. I'm Ilana Hardesty.

This series has eight episodes. If at any point you want more information on receiving credit, please visit our website, scopeofpain.org. There are also resources that accompany this series. All of it can be found at scopeofpain.org.

In this episode we'll speak again with Dr. Daniel Alford and Dr. Erica Bial. Let's go back to our case. Michelle had been doing well on her pain treatment plan for her painful diabetic neuropathy and chronic hip pain for 11 months. Then her PCP was notified that Michelle was seen in the emergency room of a local hospital requesting an early refill of her oxycodone prescription. The ED physician noted that she was in moderate to severe opioid withdrawal and gave her a prescription for enough oxycodone pills to last until her next PCP appointment in one week.

At the follow-up appointment, Michelle noted that her foot pain had worsened in the last month and is a ten out of ten most days. She started taking an extra pill every day and ran out early. She's concerned that she's become used to the current dose and says her husband thinks she's addicted. She has trouble going to work and trouble sleeping and requests an increase in her dose. Her PCP reeducate her about the serious risks of self-escalating her dose.

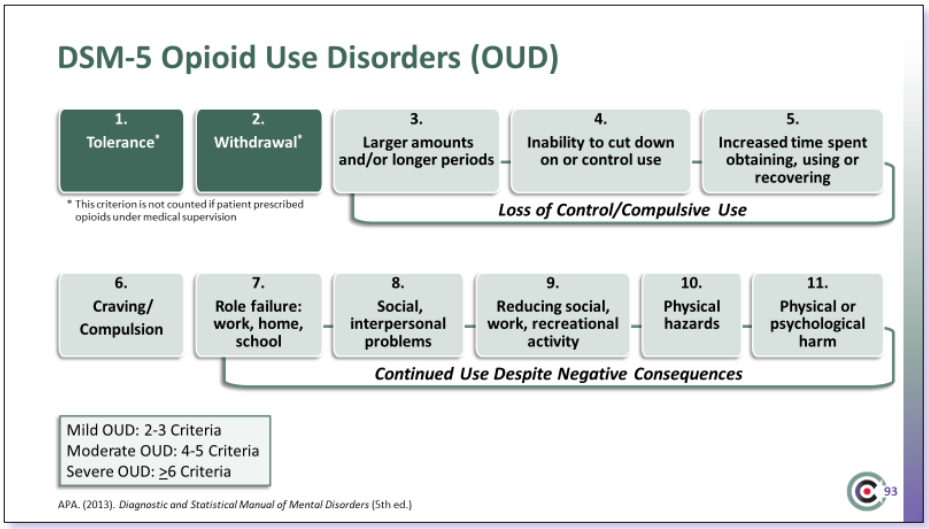
Dr. Alford, what do you think is happening with Michelle and how would you respond to this recent worrisome behavior?

Dr. Daniel Alford: So, it's certainly worrisome. And I think the important thing is to think about it in a differential diagnosis. Is this behavior because she's substance seeking? That is, does she have an opioid use disorder? Has she developed an addiction? Maybe she's self-treating other symptoms. We know that opioids make people feel better. So maybe she's treating an anxiety or insomnia. Maybe there's some diversion, which could be sharing or selling her opioids.

But on the other side, maybe it's all pain relief-seeking. Maybe her disease, her neuropathy has worsened. Maybe she has some new painful condition that she's self-medicating. Maybe her pain is actually not very opioid responsive, and we didn't realize that initially. Maybe she has developed opioid analgesic tolerance. Maybe she has withdrawal-mediated pain, or maybe she's developed something called opioid induced hyperalgesia.

Let me just take a step back for a moment and say, remember that someone who's on opioids around the clock will develop physical dependence. There may be times during the day where their opioid level drops to a point where they actually have some withdrawal that's experienced as worsening pain. They take their opioid, their pain feels better. Are they treating withdrawal or are they treating their pain? That is part of the rationale for thinking about using long acting opioids to prevent that up and down and potential for withdrawal-mediated pain.

We talked about substance-seeking and pain relief-seeking as potential explanations for this worrisome behavior. But maybe it's a combination of all the above. Maybe she has worsening pain. Maybe she's developed an opioid addiction, and maybe she's diverting some for income.



Now, I keep referring to opioid use disorder. And let me just remind everybody, what is it? And it's really based on the diagnostic criteria of the DSM-5. It includes 11 symptoms. The first two are tolerance and withdrawal. And remember that when a patient is on chronic opioids for chronic pain, they're going to have tolerance and potential withdrawal or physical dependence. And so the DSM-5 says we can't use those two criteria in making the diagnosis of an opioid use disorder in someone who's being prescribed opioids. But that leaves us with nine other criteria, three of which are really talking about loss of control and compulsive use. Is the person taking it more than expected, or are they just having a hard time controlling their use? Then there are five criteria that deal with continued use despite negative consequences. That is, as a result of being on opioids, is this person performing poorly at home and school or work? Are they having some interpersonal social problems? Is the opioid use basically worsening their function and worsening their quality of life? Yet they still want more. And then finally, the last criterion would be craving compulsion. That is, is the patient describing this urge to take an opioid every single day beyond their pain? And based on the number of these criteria, you could diagnose a mild, moderate, or severe OUD depending on the number of criteria.

Dr. Erica Bial: You know, it's really hard to talk about possible OUD with our patients. And so when we recognize opioid use disorders, what I might suggest is that we give really specific and timely feedback. So don't wait to talk to your patient about concerns. You want to give specific and timely feedback about behaviors that are raising your concerns for possible or OUD. You know, "I noticed you seem to have a loss of control," or that they're meeting the criteria for compulsive use; talk about their demonstration of continued use

despite evidence of harm. And you know, it's important to remember that patients may suffer from both chronic pain and OUD. Ultimately, patients might just really disagree with us and we might need to agree to disagree with the patient. But at the end of the day, the conversation really needs to focus on the idea that the benefits are no longer outweighing the risks. And that on balance, and I sort of suggest to providers that are uncomfortable talking about this with their patients, that they just practice like a mantra saying aloud, "I cannot possibly responsibly continue prescribing opioids because I feel it would cause you more harm than good." Right? Or some other way to say it would be unconscionable for me as a person who cares about you to continue prescribing a medication that is causing you more harm than good. And you should always feel comfortable to offer a referral to addiction treatment when you think addiction exists, even if the patient disagrees.

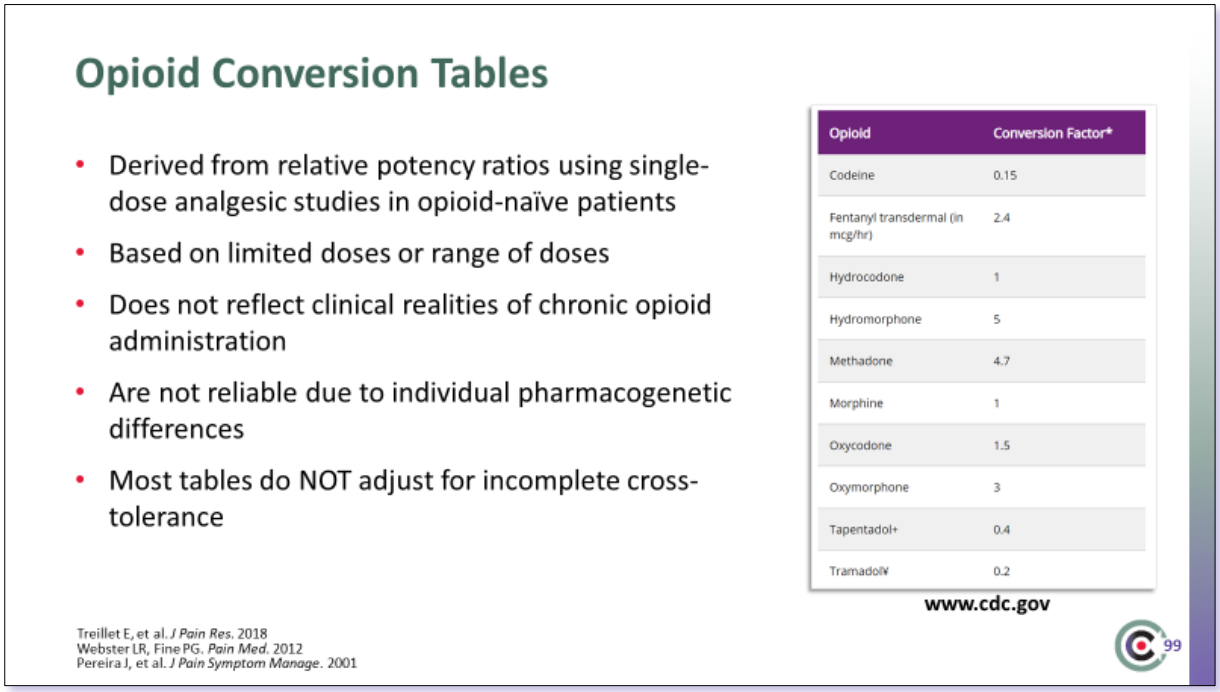
Dr. Daniel Alford: I also realize that we've used the term opioid induced hyperalgesia. It's this strange, paradoxical enhancement of pain sensitivity in a patient who's taking opioids chronically. It doesn't happen to all patients on chronic opioids, but it happens to some. Unfortunately, the underlying pathophysiology and how common it is – what's the true incidence – are unknown, and unfortunately there are no official criteria or guidelines for diagnosing it. But what do I see clinically? I see kind of a generalized, diffuse, ill-defined pain that's not necessarily located at the source of the original pain. Some patients have a really hard time appreciating that this might be their problem. That is, they're saying, "I have terrible pain and I need more opioid." And I'm thinking, well, maybe it's opiate induced hyperalgesia and we need to decrease the dose, which seems very counterintuitive to patients and can be a very challenging discussion to have with them. But if I'm convinced that the patient isn't benefiting and this is a possibility, I'm going to try to educate them about it and then move in that direction, which would be to taper your opioids. And unfortunately, there's also no standardized approach on how to taper opioids to manage this. But I would start to decrease the dose and start to increase other treatments for their pain.

Dr. Erica Bial: I agree it's such a leap of faith for patients when I try to explain that on the basis of this diagnosis that I think that your medication might be paradoxically making you more sensitive to pain.

But I think we need to have a really open and honest conversation with our patients when we're recognizing a lack or loss of benefit. So, you know, what are the next steps? We want to reassess factors that are affecting the patient's pain and try to re attempt to treat underlying disease and co-morbidities. And sometimes those co-morbidities might be seemingly unrelated to the pain generator. So if the patient has high stressors at home, if the patient's nutrition is poor, if their sleep is poor, if they are suffering from depression or symptoms of anxiety, for example, all of these things can kind of magnify the pain experience, and treating them will improve the patient's global level of function. So we want to consider adding or increasing non-opioid and nonpharmacologic treatments. Let's not forget about those. We could add breakthrough medications. We could switch to a different opioid, so thinking about what we used to call opioid rotation. But we want to avoid dose escalation, if we can, to high dose opioids.

So in considering breakthrough medication, the first choice, which can be surprising to many, is a non-opioid. So if a patient is maintained on a chronic opioid medication, like our example patient, we might consider adding a nonsteroidal anti-inflammatory medication or even acetaminophen. Sometimes exploiting that synergy gives us some added benefit. We could consider adding in a short acting opioid, either the same molecule or a different molecule, or we could consider adding a dual mechanism agent like tapentadol or tramadol that we talked about before.

Dr. Daniel Alford: There are three potential reasons to consider switching from one opioid to another. One is to restore analgesic efficacy, that is to try to get some benefit when the other opioid is no longer benefiting the patient or didn't benefit them in the first place. Two, to limit any adverse effects. So maybe the opioid they're currently on is causing them some intolerable adverse effect that a new opioid might not. And then three, finally, is to try to decrease the overall opioid dose that is, decrease the overall morphine milligram equivalent. It's important to remember that the rationale behind switching from one opioid to another is based on the large intra-individual variation in response to different opioids. We talked about this earlier, but not all patients respond to the same opioid in the same way. And remember, it's based on variants of the mu opioid receptors and how opioids are metabolized. But this concept of opioid rotation is really based on limited evidence, as most trials looking at it, have been retrospective and have studied small numbers of patients.



Now, if you're going to go that route and switch to a different opioid, you're going to need to go to a conversion table or an equal analgesic table. What does equal analgesic mean? It means it's the dose at which two opioids at steady state provide the same pain relief. These tables are derived from relative potency ratios using single dose analgesic studies in opioid-naive patients. And they're really based on limited doses and ranges of doses, and they don't reflect the clinical realities of our patients on chronic opioid therapy for chronic pain.

And they're often not reliable because of the individual pharmacokinetic differences between patients that we talked about earlier.

And one of the most important take homes here is that most tables do not adjust for incomplete cross-tolerance. Cross-tolerance is the development of tolerance to the effects of pharmacologically-related drugs, particularly those that act on the same receptor site. In this case, we're talking about opioids acting at the mu opioid receptor. So what's meant by incomplete cross-tolerance? Well, when switching from one opioid to another, you need to assume that cross tolerance is incomplete, which means that the starting dose of the new opioid needs to be reduced in order to prevent overdosing, like sedation or respiratory depression.

Dr. Erica Bial: So why don't we do some math? If we think about our sample patient. Where would you start if we're going to convert her away from her current oxycodone?

Dr. Daniel Alford: All right, so let's remember that she's on long acting oxycodone, 15 milligrams twice a day or 30 milligrams of oxycodone, which is the equivalent of 45 morphine milligram equivalents. So that's our starting point. And I would go to – there are various sites to make these conversions – but I like globalRPH.com, which is a fancy calculator that allows me to put in that oxycodone 30 milligram total daily dose then allows me to make a reduction due to that incomplete cross tolerance that we talked about. And it's a totally inexact science. The recommendations are to decrease by 25 to 50%. So let's pick something in the middle: a 33% reduction. And then I put in the opioid that I want to switch to, let's say, for example, morphine. And I say calculate. And it says the dosage for morphine based on that 33% reduction would be 30 milligrams total daily dose. So I'm going to dose it as long acting morphine, 15 milligrams twice a day, which is the equivalent of 30 morphine milligram equivalents, which is 15 less than we started.

So again, I'm trying to achieve three things. One, hopefully with this morphine dose will get improved analgesia. Two, we'll get rid of some adverse effect that she was suffering with the oxycodone, for example. And then three, we've already made the reduction in the total morphine milligram equivalents just by making this conversion.

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Ilana Hardesty: Thank you, Dr. Alford and Dr. Bial. Over the next 18 months, Michelle's pain improved on a stable morphine dose of 15 milligrams twice per day, and she had no recurrent, worrisome medication-taking behaviors. Along with the morphine, her acetaminophen was continued and her gabapentin was titrated up, and low dose nortriptyline was added at night for her neuropathic pain. Michelle attended acupuncture therapy and a monthly chronic pain support group. Her individual PEG scores remained between five and six on the ten-point scale. She remained employed and remained adherent with treatment and monitoring. She continued with her regularly scheduled follow- up visits.

Next time we'll look at some other possible scenarios for how this case might go, including what happens when the opioid rotation doesn't help and the patient doesn't improve. We'll discuss what the next steps might be.

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I'm Ilana Hardesty. Thanks for listening.