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New Uses for Old Drugs: Insights on a Treatment Option for OIC

Dr. Turck:

Opioid-induced constipation, or OIC for short, can be a frequent side effect for patients receiving opioid analgesics. And while there are several pharmacological and nonpharmacological therapeutic options for our patients, emerging research may change the way OIC is treated.

Welcome to *Clinician's Roundtable* on ReachMD. I'm your host, Dr. Charles Turck. And here with us to share insights on the treatment of OIC is Dr. Frank Peacock. Dr. Peacock is a Professor of Emergency Medicine, Associate Chair, and Research Director for the Department of Emergency Medicine at Baylor College of Medicine.

Dr. Peacock, welcome to the program.

Dr. Peacock:

Thank you. Happy to be here.

Dr. Turck:

Let's start with some background. Dr. Peacock, what can you tell us about OIC? And what kind of burden does this side effect have on our patients?

Dr. Peacock:

Sure. So, OIC is what happens when lots of people, it's a common thing, when they take narcotics, for whatever reason, and the people who really suffer the most I think are those people who are chronically on it, like oncology patients. So, you know, they're taking this so their life can be a little bit better, and then the constipation, it becomes a real issue.

The thing about narcotics is if you take them for a while, you usually get used to a lot of the symptoms, like the sedative properties of it; you get used to that, and so you can function. And there's some nausea and some dizziness, and those things always are ascribed to narcotics, but those go away with time. The one that doesn't go away is the constipation issue, and it is frequently rated as the most annoying of the adverse events that you get with narcotics, so it's common in this population.

If you work in a cancer hospital, you're going to see these several times a shift in the ER. I work in a county hospital. I don't see it that often more like on a weekly basis. We don't really know how much OIC is out there because there's no diagnostic code, but what we can look at is the amount of patients presenting to the emergency department with constipation of generic causes, and that has been going up by about 5 percent a year, which is pretty amazing. So, it's not an insignificant issue, and it's a particularly difficult problem for cancer patients.

Dr. Turck:

Now let's focus on treatment. Dr. Peacock, what treatment options are currently available for OIC?

Dr. Peacock:

So, nobody comes to the ER the first time they can't have a bowel movement. What they do is they will try something at home. So they'll try an oral stool softener. That doesn't work very well. And they might try a laxative, and those are unpredictable. They might try a home enema, you know, and those are the same thing. They don't really solve this problem because none of that stuff is working at the underlying issue, which is the Mu receptor that is, you know, being affected by the opioid. So that's the secret sauce here with this new treatment is that it gets to the root of the problem where everything else is sort of working at it.

Patients come to the ER with this complaint, and they'll get an extensive workup. These patients tend to be older. They're fragile. They'll

get CAT scans and spend a lot of money on trying to figure this out. At the end of the day, you say, 'Well, it's constipation. Let's give you an enema,' or you try to manually disimpact them. And none of those are great successes, and nobody likes them on top of that. The patient doesn't like it. The doctor doesn't like it. The nurse doesn't like it. It's all a miserable thing to do in a crowded ER. And, you know, so at that point, patients either get hospitalized, and frequently that happens because they are sitting home. An old, fragile person with abdominal pain is, you know, fraught with error, so if they don't feel better, they're not leaving, and so they get hospitalized, and usually after four to six hours of messing around in the ER. So, the current treatment standard is not optimal.

Dr. Turck:

For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Frank Peacock about opioid-induced constipation, or OIC for short.

Now, Dr. Peacock, let's talk about your recent study on methylnaltrexone as a treatment option for OIC. Would you give us some background on this study and what your primary objective was?

Dr. Peacock:

Sure. So let me give you some physiology on methylnaltrexone. So, every emergency doc is familiar with naltrexone. It's called Narcan. Patients show up with overdose from narcotics, most commonly from an abuse scenario, but even can be done accidentally. They're not breathing very well, and sometimes they look like they're about dead, and naltrexone is one of the few category drugs where it's like you watch a miracle happen. You start an IV, and you push it in, and 30 seconds later they sit up on the bed and say, 'Hey,' and they look absolutely fine. It's amazing. And then 30 seconds after that they're furious and they get violent, and you have to tie them to the bed because they go through narcotic withdrawal immediately. And so every emergency doc always has a little fright potential of this drug because it works really well for doing what it's supposed to do, but it has the complications of immediate narcotic withdrawal. So emergency docs have been somewhat hesitant to use this drug because it's got that nametag to it.

But the key part here is this is not Narcan. This is methylnaltrexone. It's Narcan with a methyl group attached to it that does not go into the central nervous system. It can't get through the blood-brain barrier. So, while it causes immediate narcotic withdrawal of your colon, it doesn't do anything to your brain. You don't go into withdrawal, and the best part is they don't lose their pain effect of the narcotic because, you know, it would be really a miserable thing to take a patient who has metastatic cancer and is taking narcotics for pain and make their drug quit working. It doesn't do that. Their pain medicine still works. The only thing that happens is they have to get up and go to the bathroom, which usually happens in the majority within two hours, and in my experience, it's fairly immediate relief. And then they want to go home, which is a win for everybody, so we avoid an admission, and they get to go home.

Dr. Turck:

If we turn to the results of your study, would you share some of the key findings with us?

Dr. Peacock:

Yeah. So what we did is we took the three randomized controlled trials that had before been published on this, and they were all sort of small in size, and we put them into a larger trial and then matched them all into those who got placebo versus those who got methylnaltrexone, and the population, as you might expect, was about 60 percent cancer. We also matched them based on their functional status, and the majority of them spent more than 50 percent of their time in bed, or at least a chair, and so, what you're dealing with is a fairly fragile, pretty difficult patient to deal with who's got fairly advanced disease and is taking narcotics because it's the way they can deal with what they're having to go through.

And so we took those groups and simply divided them into the people who got methylnaltrexone versus those who didn't, and the people who got it had symptom relief usually within two hours, and we did pain scores on all of them. It's a 1 to 10. It's actually a 1 to 11 pain score because 0 is there, but it's a 1 to 10 pain score. The average pain was 3 when they started. It was 3 when they were done, so it did not change their pain scores at all. And as I said before, the majority of them got relief within two hours, so consequently, you know, from an efficacious point of view, compared to the placebo group it was 16 percent got relief in two hours, so it's a pretty profound effect to be able to manifest in the emergency department.

The adverse events associated with this is the folks who got methylnaltrexone had some abdominal cramping that the placebo group did not get. Somewhat expected. It was about a one in five patients on the methylnaltrexone had cramping. But if you can avoid a hospital admission, I think most patients were more than happy to do that because it's not persistent. It's not particularly painful. Their pain scores didn't change remarkably even though they said they had more cramping, but that's the end result here is that we solved their problem pretty efficaciously with minimal side effects, and I looked at that as a big success.

Dr. Turck:

Now, before we close, I'd like to give you the final word. Any key points you'd like to leave with our audience today?

Dr. Peacock:

Yeah. I mean, I think we ought to talk about contraindications when you don't want to use this drug. You know, elderly people with abdominal pain and cancer, they're fragile. They're scary. You have to be careful with them. You need to be pretty certain they don't have an obstruction. Giving this drug to somebody with an obstruction risks, you know, creating more problems, and that's the last thing you want to do, so you need to be pretty certain that they're not physically obstructed in terms of their bowels. As long as that's not the case, this is a pretty low risk intervention. And that's not a hard thing to do in the ER. You can just get some plain films very quickly, if you're at all concerned, and I find I don't do that. I probably do that in 50 percent of the cases, just to make sure that I'm doing the right thing. But that being said, there are not a lot of other contraindications for this drug. It's a pretty safe drug. And if you think about the Narcan experience, we've got a long history with this class of agent, so this is a new use for an old friend in the emergency department.

Dr. Turck:

Well, with those final thoughts in mind, I want to thank my guest, Dr. Frank Peacock, for joining me to share his insights on treating opioid-induced constipation.

Dr. Peacock, it was a pleasure speaking with you today.

Dr. Peacock:

Thank you very much for having me.

Dr. Turck:

For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit ReachMD.com/CliniciansRoundtable where you can be Part of the Knowledge. Thanks for listening.