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ECHO: MICRODOSING INDUCTION FOR BUPRENORPHINE

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[video transcript]

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Dr. Laila Khalid is an associate professor of medicine at Albert Einstein College of Medicine Montefiore Medical Center. She's board certified in internal and addiction medicine and co-directs a resident led chronic pain clinic. Dr. Khalid is also an e-consultant for opioid management of Ambulatory patients at Montefiore is a buprenorphine clinic site champion, and leads the buprenorphine micro dosing Working Group at Montefiore. Over to you, Dr. Khalid .

00:38
Thank you so much, Jeff, for the introduction. And I'm sorry for the technical difficulties. I'm trying to do the Zoom presentation through my phone, so bear with me. Next slide. So I've no disclosures. Next. So in this presentation, we're going to compare standard and micro dosing induction of buprenorphine. So those are two different techniques, and review some steps and micro dosing buprenorphine. And in the end, I'm going to share resources including protocols and patient educational handouts. And this is my Monti group that I want to thank next space. So background next, so what why do we need so little something about buprenorphine? So buprenorphine, as you know, is a partial agonist. If you look at the blue curve, which is for a full agonist, as the opioid dose increases, the opioid effect increases. However, for buprenorphine, the opioid effect increases until a certain point and then it plateaus. So let's say if somebody has a full agonist on board and I were to give them buprenorphine, there will be a shift from the blue curve to the red curve, which is going to produce withdrawal symptoms and those patients. Next slide, please. However, if you slowly introduce buprenorphine doses into the patient, which is called micro dosing, they will not experience those withdrawal symptoms. So if you look at the bottom half of this picture, the six pictures, they're literally displacing the opioid agonist, a few receptors at a time, so patients don't feel withdrawal symptoms. Next slide. So it's sort of this is another analogy to sort of understand it's a speed car and you suddenly stop next. That's why you have prodromal symptoms. On the other hand, next, if you slowly decrease the speed, or you slowly introduce the buprenorphine, you will not experience the withdrawal symptoms or the withdrawal symptoms would be much, much milder. Next, so in micro dosing, and that's like a wonderful part of it. You don't need to taper off full agonist completely, you can actually continue to take your full agonists while you're slowly introducing the buprenorphine doses. And at a certain point, you stop the full agonist and continue with the buprenorphine only. Now, why is this a good thing. So for example, if somebody is taking heroin, so heroin overdraw, you want somebody to be in virtual before you get buprenorphine. So that is up to 12 hours, six to 12 hours. However, if somebody is taking methadone, you have to be in sometimes the withdrawal can take up to 36 to 38 hours, I've had patients with even taking days before the withdrawal symptoms develop before I could give buprenorphine. So that's like an extended period of time where patients are experiencing withdrawal, and it's uncomfortable for the patients. And if patients experience withdrawal, there's a higher rate of return, you know, drop out rates, retention might be affected. So those are all things that you have to keep in mind, and it's destabilizing. Now, another thing we sometimes don't think about is lots of our patients also have been so if you tell somebody to stop taking a full agonist be in pain, as well as virtual

symptoms. While I'm trying to introduce buprenorphine, there will be very few patients who will want to go ahead with that. And precipitated withdrawal in the induction process, it has been found to decrease retention rates next place. There are other reasons to patients might have anxiety, you know, they might have had a prior of past experience of withdrawal. And they don't want to experience that again. And like I just said, if you have particularly long acting opioids such as methadone, and as we are finding out in today's time, that even the illicit fentanyl can hang around in your body for much more longer time, which I'm going to go into in detail, which makes transitions even more difficult. So there are four pathways that we're going to sort of like divide into. So for example, the first pathway that we're going to discuss is transition from heroin sentence to give an orphan. The second is what about patients who are in pain and I'm trying to transition them to buprenorphine transition from methadone to buprenorphine, and very brief We transition from full agonists in the hospital to buprenorphine next place. So how do we microdose so like I explained, it'll be very, very small doses of buprenorphine that we're going to give this patient. Now these small doses can be given in three ways. The first way is transdermal. The second way is a buccal film, which all are available in micrograms. And then the other way is cutting up a sublingual film into very small pieces. Now the smallest tools of a sublingual film comes as two milligrams and if I were to divide it into four pieces, each dose will be around point five milligrams, so it's much much lower than the two milligram cell. So in literature, people have done it in different ways. But like I said, you don't really have to taper the opioid agonist, but some people do that. The buccal and the transdermal buprenorphine are FDA approved for pain. So that's like the biggest challenge. If I start a buckle or buprenorphine transdermal patch, then I transition to sublingual, so lots of insurances might have issues with that. So we're going to talk about that in a little bit more detail towards the end, now transitioning from heroin fentanyl to keep in our vein. So as we all know, synthetic opioids are on the rise, and they're continuing to increase. Next slide. If you look at the epi next epi data that was just published this year, it is really humbling and very sad that the rates continuing to increase. So for a fifth year in a row fentanyl is the most common substance involved in overdose deaths, and 80% of overdose deaths in 2021 had fentanyl. So imagine that. And there have been studies that have been done in New York City. This is prior like many years ago, 2016 to 2019, where some patients were surprised to find that there was fentanyl in the urine. And so it's very essential, especially in New York City to test patients. If they're using fentanyl, our if their supply is, you know, contaminated with fentanyl. Next please. So buprenorphine induction in the era of illicit fentanyl. So when I first heard about this, I'm like fentanyl is short acting, would you mean why would buprenorphine cause precipitated withdrawal? You know, so there have been many studies that you can get precipitated withdrawal with fentanyl, which is very counter intuitive. There was a recent study, which was a qualitative study, in which they interviewed patients about withdrawal symptoms, and even 48 hours after last fentanyl news. When patients don't give in our fee, they went into withdrawal. So very counterintuitive, but we're gonna talk about that in detail next. So this was a study. So again, just to brief before we actually look at the studies, just looking at fentanyl, it has a really short half life. So 290 minutes, so maybe a few hours. But the other challenge is it likes fat cells, so it hangs around fat cells and is absorbed into fat cells, which slowly release the fentanyl over time. Next place. So when you look at this study, this I thought was really interesting. So just to orient everyone on the x axis, we have days. On the y axis we have the nanograms per milligram of fentanyl present. And then we have two things. One is the fentanyl and the other is Noor fentanyl. And when you look at this, it can

the fentanyl and nor fentanyl clearance can range from 7.3 to 13.3 days. And if you look at the outlier, 90 or 2060s. So that's like a really, really long time. And part of the reason is it hands around in the fat cells. The other is there might be other things that are added, which increase its lipo facility. And that's the reason why fentanyl almost acts like methadone in my opinion. Next. So this was the first study that looked at this was called the Bernice matters, the Swiss study. This was published in 2016. And the idea again is the patient continues to use heroin in varying amounts and the buprenorphine slowly increases next. So this was another study that was published in Canada 2020. And this is interesting, because if you can go back one slide. So on the left side, I have explained there were four patients who were switched from Central opioids. And this is very interesting. I'm going to slow down here they were switched to an opioid agonist. Okay, so let's say somebody was using heroin, somebody was using heroin. They were switched to prescribe opioids. Now this is happening in Canada. So I want to stress that and then they were microdose. Three of those patients in this study were not switched and they continue to use and this is what it's showing the three patients that continue to use illicit fentanyl and heroin in varying amounts, while this slowly increase the buprenorphine doses next place. So this is the case, I'm going to make you go through this slowly. So these are the seven case studies that was published and the precipitated withdrawal was not experienced in any of those patients. And in these seven patients, half, nearly half of them were switched again to prescribe opioids and half continue to use the fentanyl and heroin. And there was no best date for withdrawal next please.

10:36
Now, what about patients who have been and are prescribed opioids, I have a chronic pain clinic. So I see a lot of these patients. And I have to say patients who are on a really high doses of opioids have this something called complex persistent opioid dependence, which is not clear in the sense they don't have severe or moderate OUD, they probably have mild OUD, or they have this form of dependence in which they are in a lot of pain on those high doses of opioids. So the pain is not really well controlled on those high doses of opioids. And when you try to decrease these opioids thinking, is this opioid induced hyperalgesia. They don't do well. If you try to increase this, which I have done also, that doesn't help either. And so in those patients, sometimes not all patients sometimes transitioning to buprenorphine actually helps because it counteracts opioid induced hyperalgesia. And patients feel much better. Now, this is not I want to stress, you cannot do this for all patients, but some patients for sure. Next. So this is a very interesting study that just got published. I all I want to say is I encourage you to read this. This is like VA guidelines regarding opioids. And in this they actually recommend using buprenorphine for chronic pain. So as this gets more and more attention, people might think of switching patients to buprenorphine for better pain control, especially those who are on high doses of opioids, and don't have good pain control next weeks. So this was a study published by Dr. Becker, and I think this was in 2020, right in COVID. And if you look at it next. They weren't really high doses of opioids, which range from 105 to 360. Next, and they were transitioned to buprenorphine, and not even a maximum doses of buprenorphine, they were taking buprenorphine, four milligrams QID. And the least was two milligrams three times a day. Next. And this is the transition process that they use. So basically, they continued with the full agonist until day four, when the buprenorphine was increased to two milligrams DID. And then the full agonist was stopped, there was no almost no trade to bring, I would say, On the fourth day,

there were stapling next. Now, this is this I found really fascinating and interesting. So for control of chronic pain, even in sickle cell patients, using or switching them to buprenorphine sometimes can give you better pain control. And in these two young patients, this is a case study that was published very recently, I believe, 2022 patients were transition using the buprenorphine micro dosing induction process. And, you know, we're really looking at like 12.5 milligrams methadone, 37.5 milligrams oxycodone, and one and in the other group, 120 milligrams, long acting oxycodone, but 60 milligrams of short x acting oxycodone, so this micro induction can work really well, even with the high doses next. So what about transitioning from methadone buprenorphine? Personally speaking, I find this the most challenging. Next, there have been a few studies that have been, you know, published on this. And so the transition is really difficult. Sometimes people recommend, you know, decreasing to 30 to 40 milligrams, the methadone, and then once they go into withdrawal, then switching to buprenorphine, but this I find is the most difficult transition. Next. So this was a case study that was published again in 2020, where 60 year old male with history of OUD, he was taking 75 to 120 milligrams of methadone for the last 20 years from an OTB. So a methadone maintenance program. And he had this one episode of buprenorphine precipitated withdrawal, and he didn't want to go through that process again. And he eventually wished to transition care because of insurance issues. And he also had some endocrine side effects from long term methadone use next. So this was the protocol that was used next see If you look at it, the first thing I want to draw your attention to was it was done over 12 days. So typically if you want to transition from so don't you do it even more slowly next, and here they are sorry, go back. I forgot to mention. So here they use the buprenorphine batch. They use the buprenorphine patch to transition and they continue the high dose of 75 milligrams pure daily until data and then they switch to buprenorphine. And if you look at the cows, the cows was really low. And to manage some of the withdrawal effects, they use clonidine, loperamide buprenorphine ibuprofen to manage the withdrawal symptoms next. Now, I want to talk about this very briefly, because I know most of you are outpatient doctors, but you can also do this in the hospital setting. Next, and in the hospital setting it is you know, shorter, and you can even use IV opioids let's say somebody is coming in in pain and you want to transition them to buprenorphine, you can actually continue the hydromorphone, which is Dilaudid for three or four days depending on which protocol you use. And transition easily. Next.

16:22
Next, and I this these two articles, I'm just putting it in for everyone's reference there to review articles next, that sort of like look at the micro induction of buprenorphine in the literature. So now we're going to review the protocols that I use in my institution. So this is the protocol that I use, I typically if it's a short acting opioid, I do it over six days. And I'm an outpatient doctor. So when I'm outpatient, I tell patients to cut up films. So if you look at the comments in the comment section, I start off with a two milligram film, I cut it into four pieces, and how I tell them how I instruct them is the issue on the first day, for example, take one small piece on the second day, take one small piece twice a day. On the third day, instead of cutting your film into four pieces, cut your film into two pieces, and take half of the film in the morning and half of the film in the evening, and so on and so forth. Next, for the long acting, I'll use a start slightly longer protocol next. And all of these protocols will be shared. And this is what the patient handout looks like. And it has pictures so that they can imagine and know exactly how they're supposed

to cut this up next. Now, micro induction seems like this amazing thing that you can do. But I want to tell you the first time I did it, I was very anxious. I didn't know how it was going to go. I was like, Is this even going to work? What if I, you know, I'm telling my patient to continue opioids while I'm giving the buprenorphine. But one thing that I one question that I get from many providers is what if so if somebody is using an opioid, and I give up on our team, like I said, you can go into withdrawal. But if somebody is using an opioid agonist and I go give them small pieces of buprenorphine, they will not go into withdrawal. And that I have now I've done so many micro inductions. And there most of them have been successful. Obviously, there have been some I think, especially in the inpatient setting that you have precipitated withdrawal, it can still happen, especially in the time of illicit fentanyl. That is something you have to keep in mind. And patients might have anxiety too, because although we have this wonderful handout, patients still find it hard to follow. And they're worried about getting sick and what if it doesn't work? What are they going to do next? So these two things can sometimes act together and create issues next. Now how we can help is next. We can also we have to be very clear and educate the patients about what we are doing laid out as much as possible. Make sure that before they start anything prior authorizations are done. prescriptions are available in the pharmacy. So let's say if I'm going to do a micro induction, I don't micro induce on the same day just because I want to prepare all of these steps before I tell them to do it next. So again, making sure insurance by authorization and pharmacy make sure it is covered and they have it installed. That's the other thing that we've been experiencing is many pharmacies don't have the medicines in stock. The other thing that we have tried is we we have tried blister packing and what does that mean? next days. So blister pack, we actually will ask some pharmacies and not for all pharmacies will do this for you to cut up the phone for the patient, and prepare this for the patient, so they know exactly what to take on what day. Now, the problem with this is the micro dosing schedule is actually very flexible. So if let's say somebody is having some withdrawal symptoms, I have the ability to slow down. But if I have blister backing, you're sort of like stuck with that same protocol for the entire time. Next. So the other thing that has really helped us as we use standardized templates, we have smart phrases that we use. And again, I'm happy to share those with you guys. Next. So in order to alleviate my own anxiety, and also to alleviate the patient's anxiety, I do contact them by phone, sometimes every other day, but definitely, let's say if I'm starting a microdosing today, I will definitely follow up with the patient like the next day, and I also have an in person follow up in the next week or so. I also provide a contact number whether it's through my chart or it's an actual cell number. So, so does some take home points. microdosing is novel and an alternative option to standard buprenorphine induction in certain patients, clear instructions and close follow up is needed. Next, and these are other resources and that's my emails. If you have any questions, feel free to email me and I'm happy to take questions.

[End Transcript]