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Live Expert Interview: Ketamine & Neuromodulation

Announcer Introduction:
Welcome to CME on ReachMD. This activity, titled “Ketamine & Neuromodulation”, is provided by Prova Education.
The following is a live interview recorded at Prova Education’s Guideline to Practice: Managing Challenging Cases in Primary Care.
Your host is Dr. Matt T. Rosenberg. Dr. Rosenberg will speak with Dr. Joshua P. Prager, Director of the Center for Rehabilitation of Pain Syndromes at UCLA.
Prior to beginning the activity, please be sure to review the faculty disclosure statements as well as the Learning Objectives.

Dr. Rosenberg:
ketamine is a medication used to induce anesthesia, produce relaxation and relieve pain. It’s approved for use in hospitals and other medical settings. We’ve just talked about that. It has hallucinogenic tranquilizing dissociative effects and is sometimes used illegally as a recreational drug. Ketamine has a good safety profile when it’s used appropriately in controlled medical settings. When used recreationally, it can have potentially adverse health effects and its prolonged use can lead to tolerance and psychological addiction. And I do a lot of work in urologic health, and I know we’ve seen some cystitis associated with that. Welcome to our program. Do you have any opening statements, Dr. Prager?

Dr. Prager:
You covered a lot of what I would cover, so thanks for the questions. Just to go over it a little bit, I’ve been practicing for more than 40 years, which is hard to believe.

Dr. Rosenberg:
You look 29.

Dr. Prager:
Right. And when I was in residency, ketamine was still being used from the 50’s. It’s what’s called a dissociative anesthetic and what dissociative anesthetic means is it doesn’t necessarily put you to sleep, but it separates your mind from your body. And so, you can see things happening to you, but you don’t necessarily feel them. And it went into disfavor around the early 70’s, because the patients, often for weeks after the ketamine, would suffer from hallucinations, which is one of the things that makes it attractive on the illicit drug market. Ketamine now, just before we get into its therapeutic effects, you touched on the fact that it’s an illicit recreational drug on the street with names like Special K, or going into the K-hole, Vitamin K, which is a different vitamin. And it’s used at raves. And the thing is, people can dissociate and not even realize they’re hurting themselves when they’re jumping around. When it was discovered around 17 years ago that patients could get relief from CRPS by ketamine, it caused a whole resurgence of the drug. In my practice, we’ve done now about 2000 infusions for pain. And what we find is that all the side effects that are described, including the hallucinations and the nausea, can actually be controlled with the right medications. And most of the time, we start off with a benzodiazepine, and if that’s not sufficient, we use low-dose atypical antipsychotics for several days. We’re talking about something like Seroquel 25, olanzapine 2.5; I mean, really miniscule doses so the patients aren’t suffering from the hallucinations. We’re actually in the process of writing a paper based on the first thousand patients, looking at the side effects of ketamine and how they can be managed. Since it was discovered in around 2000 that it could help pain syndromes, there have been several fairly large studies in the literature demonstrating efficacy. So,

there's no question in my mind that it's effective. One of the drawbacks is that about half our patients who go through a full course of therapy have to come back at 3 months for boosters, and about half don't. But the half that do, often are obliged for chronic therapy, coming back either once every 3 months for 3 infusions, or once a month for 1 infusion. But it winds up that about half the patients need about 12 infusions a year. But, what you're looking at is a patient population that otherwise would really have no life. So, it may seem drastic, but it's quite effective. More recently, the psychiatrists are interested in it for depression. I will not treat depression with ketamine unless a psychiatrist refers it to me, but many of the patients I get have been refractory to all medications and electroconvulsive therapy, and we get pretty decent results. We can give 1 infusion and get about a month of results, and the patient isn't stunned the way they are with ECT. I think there's more and more use of it for depression, and once there is a body of literature that's beyond the anecdotes that I'm describing, I think we'll see a lot more use of ketamine. No company will study the use of ketamine for the uses I'm talking about because the FDA requires such expensive studies that we're talking millions of dollars, and then anybody can make it; I mean any drug manufacturer can make it, so there's no financial incentive. There is one drug company out of Cambridge, Massachusetts that is using it in the battlefield because the advantage of it over morphine, number one, you don't have to establish an intravenous line. This was intranasal-metered ketamine, but the other thing is morphine lowers blood pressure and suppresses respiration, whereas ketamine has no effect on respiration and, actually, if it does anything to blood pressure, it slightly increases it. That may be more than you want to know about ketamine, but that's a little capsule on it.

Dr. Rosenberg:
Well, actually that's very helpful, and I think what you're saying is a drug that has had in the past some negative connotations is actually useful in the right patient.

Dr. Prager:
Correct.

Dr. Rosenberg:
It's like all the drugs we use in multiple classes. A drug can be bad in the wrong patient, but in the right patient it can be very helpful. Actually, this is more from a personal perspective, I had a patient who was working with a pain specialist in Detroit and this doctor was using ketamine for CRPS. The patient was moving to Jackson, which is where I live, and they had called for me to take over the ketamine care. It wasn't something I have a lot of experience with. You obviously do. My guess is most people in the audience don't. So, the question I have for you is, how do you feel about people using ketamine outside of a specialty center?

Dr. Prager:
I think it's a mistake. I do it actually in a surgery center, in the recovery room, with ACLS-certified nurses. That I would say the first 20 were quite bumpy with the hallucinations. I mean, we had patients jump out of the bed. Bladder problems, we don't see it that often, but we have seen it.

Dr. Rosenberg:
Right. It's more in the recreational group who are.

Dr. Prager:
Well, we actually saw it in one of our… we've only seen it in one of our patients, well, no, two. One who already had interstitial cystitis and it made it worse, and then one who never had a bladder problem and ended up with it and it did resolve, fortunately.

Dr. Rosenberg:
And developed it, right?

Dr. Prager:
We have to know all the things to watch out for and I attend these meetings of the 10 people in the country that are doing the most, and we look at how each other is doing it. One of the things that we discovered in the first thousand patients that we did, we had 3 patients develop deep venous thrombosis. Now, the drug itself doesn't cause it, but we have an hour of lying in the bed in preparation of infusion, where the patient is completely still, and then 2 hours recovery. So, it's 7 hours altogether, and during that time a patient, especially if they're on birth control pills, can develop a DVT, just like you can on an airplane by sitting in one position. So, all our patients now get a baby aspirin before we start, and we require everybody to put on support hose, except the depression patients who are only there for 1 hour; the others are there for 4 hours. But the thing is, you have to be set up with resuscitation equipment even if you don't need it. You have to be able to manage an airway, occasionally. And the other thing is, often to get to effective dosage; it's not something you want in the hands of somebody that isn't. Just the one other thing I'll add is that even though I'm an anesthesiologist, if I have more than 2 or 3 patients, I always have a certified nurse anesthetist with me, just to help. So, I mean, here's an anesthesiologist using a CRNA, and a guy who isn't used to dealing with the pharmacology of all these drugs that interact, including the antipsychotics, etc., I think it's a mistake to try to be doing it.

Dr. Rosenberg:
Well, I appreciate you saying that, because I was very uncomfortable and I said I won't do that. I found out later that this wasn't being done in a controlled setting. I don't think this was a specialist necessarily, using it. Unfortunately, the expectations of the patient were that anybody could do this, and you may have seen that. And then she was also on a myriad of opioids which will bring me to my next question. And to be honest, I thought her care was so detailed that I insisted that she stay with a specialist which she was very unhappy about, because her expectations had been any doctor can prescribe all of these meds. So, having said that, the use of…

Dr. Prager:
Well, can I interrupt you? Because I think you made a point that's really important: opiates and ketamine, okay? Our goal in using ketamine is to get the patients completely off the opiates. But the other thing is, we find with the combination of drugs that we use when we're giving the ketamine, opioids then cause the respiratory depression. So, we try to get our patients to, at minimum, get rid of half their opioids before we consider the ketamine, and our ideal is to get them completely off before we start.

Dr. Rosenberg:
Well, I appreciate that because I'm in family medicine, and what I would like to say in the real world, so here I am in a non-academic setting, a physician in a town several over from ours was prescribing ketamine, was prescribing a slew of opioids, none of which, to be honest, I agreed with, and I'm not a pain specialist. And the problem was that the expectations that the patient had were really, I don't want to say unreasonable, we had created those, not me, personally, but we as a medical profession. It was a primary care doctor in Detroit giving the patient ketamine, multiple opioids, as well as others, and she was very unhappy that the next primary care doctor wouldn't do that. Opioids in primary care are difficult. I sit on a medical malpractice board and we have to deal with this all the time with patients who are addicted, patients who overdose, have side effects with that. What is the role for primary care in opioid use now, and when should we be leaning on the specialists?

Dr. Prager:
Well, I think I covered some of that in my lecture, but the important thing is that you have an infrastructure in your office. So that you have to have an opioid agreement, you have to be able to do urine tox screens, and you have to have a firm hand and know when to make important decisions about saying no, and being able to pick it up. What I would say is that if you're getting into any kind of significant dosing, you either want to get a consultation from somebody who is more expert, or hand the patient over completely. The one other point I would make is that a lot of primary care physicians, the way reimbursement is set up these days, you really have to run through these patients. The problem is these patients; we spend a minimum of 15 minutes a patient, and that's even just for a refill. Because in California, the regulation is very clear, you have to provide a good faith physical examination in order to be able to prescribe that controlled substance. If the patient walks in and you just write the prescription, they walk out, that's not a good faith examination.

Dr. Rosenberg:
Right.

Dr. Prager:
The other thing is, if you're getting into the Schedule II's, you can't prescribe them over the phone, you can't mail them to a patient, because then you're actually in violation of the law. I think once you get into Schedule II, it really should be in the hands of somebody that knows what they're doing.

Dr. Rosenberg:
Right. I absolutely agree with that. And we have contracts in the office for the few patients that we do treat. What I've asked from my specialists is, I want to get an initial consultation, you prescribe a regimen that would work, and then once we get that regimen, I will control when it's stable. But if it's changing, then I need us to work together. And that's in a perfect world, but I'll tell you, one of the issues that I have, and it would be interesting from our audience if we see this as well, when a patient breaks a contract with a pain specialist, and the pain specialist says, "We can't see you anymore, because you broke your contract." They come back to me and… "Well, now the pain specialist won't see me. I've been fired from 5 pain specialties in your area," which I've seen multiple times. "You have to treat my pain, Dr. Rosenberg." And I'm like, "Actually, we have a problem here." But that's what happens, because you guys can sign off of the patient whereas I can't.

Dr. Prager:
Well, I would disagree on the fact that you can't. You can still choose not to prescribe opiates. In California, we have the prescription drug monitoring program which, any new patient comes in, we look at what they're story is. In California it's called CURES Version 2.1. Everybody has access to it. It shows any controlled substance that was written for a patient in the state of California, who wrote it, and what pharmacy filled it. And that's a great background before you start. What I can tell you is that since these regulations have become more stringent, or the guidelines have become more stringent, both nationally and within our own state. I have patients that show up that

never would have shown up before, because they've gotten kicked out of somewhere because somebody's following the guidelines a lot better than they used to be, and they decide it's time to fire the patient. Now, that doesn't oblige me, as a pain specialist, to accept the patient. But once you have relinquished the responsibility to prescribe opioids for that patient, even if that patient comes back into your care, you can leave it to whoever was prescribing before to find a referral for that patient which is what, when I fire a patient, which happens about 4 times a year, I have a list of physicians that I give them. I say, "I don't recommend any of these. These are just physicians that I know prescribe opioids, here's a 1-month supply. You're on your own."

Dr. Rosenberg:
That's good to hear. And it isn't impossible to discharge them in primary care, but it does become a little more difficult because of some of the quality metrics that we have to follow.

Dr. Prager:
Well, you don't have to discharge them. That's what I'm saying. You can just say, "I can't prescribe your opioids anymore."

Dr. Rosenberg:
Right. So, but here's my Friday afternoon scenario.

Dr. Prager:
Oh, Friday afternoon?

Dr. Rosenberg:
Friday afternoon.

Dr. Prager:
I don't practice on Fridays. That's how I'm …

Dr. Rosenberg:
You're smart. So, we've all seen this. The patient comes in at 4:30 on Friday afternoon. Your office was supposed to close at 4, but we're running late, and, "Oh, by the way, I'm running out of my Norco that I take 5 times or 6 times a day. My pain doctor has fired me. And you've been seeing me for this time. I need my meds." Right? How many have seen that scenario? I'll tell you what I do, but I'd like to know what you would recommend?

Dr. Prager:
Well, we have a sign in our office and it says, "Your lack of planning is not our emergency." (laughter) And it hangs up in our office. I deliberately decided that Fridays are my administrative day, my paper-writing day, my lecturing day, and that's it. I don't see patients on Friday and that's part of the reason, because these patients do show up. And they often show up saying, "Oh, your nurse said it was okay to come in." But the nurse has already left. And so, I'm a very compassionate physician. I don't know if that comes across, but I really am. And yet, at the same time, I can't get sucked into that. And what I have to explain to them is, "I have to give you the best care I know how to do, and giving you a prescription for this medication, when I don't really know what's been happening for you, is not a good care and I don't think I'm serving you well. If you feel that badly that you need medicine, you're going to have to go to the emergency room."

Dr. Rosenberg:
Right. That's really how we deal with it because what happens is you, as a specialist, you're closed, and we get the phone call at then 6 o'clock. Now we've actually closed. They call the on-call doc, you know the 6 o'clock call on Friday saying, "My specialist is out of town. I can't reach him. I had this, I had that, I need this." And we're uncomfortable. We go to the ER and we get the barrage of, "You are not a good doctor and you hate me" and well, "I'm trying to give you the best care I can." I don't think there is a great answer, because it's a difficult situation for both the patient and for us.

Dr. Prager:
We take our reviews on the internet very seriously and most of mine are 5's and then we get the 1's. And who writes the 1's? Those people.

Dr. Rosenberg:
Right. Those people.

Dr. Prager:
And you know what? You just have to, I mean, some people aren't going to like you. If you want to make an omelet which is good care, you have to break some eggs. And good care does not involve giving somebody opioids for the wrong reason or at the wrong time. One of our sayings, and what I do, "It's the right prescription for the right patient at the right time" and Friday afternoon at 4:30 is not the right

medication for the right patient at the right time.

Dr. Rosenberg:
That's great. Any final closing thoughts for us, although that last one was perfect?

Dr. Prager:
I think pain is challenging. We're living in an era where there truly is an opioid epidemic. We can contribute to that epidemic by not providing good care. We can contribute to that epidemic by continuing to provide opioids after the surgery's been weeks ago, and the patient shouldn't need them anymore. And we have to prescribe responsibly. And the biggest message I have to you, as primary practitioners, is don't take all the responsibility yourself. Use pain specialists when the patient needs a lot of opioids. If you want to prescribe opioids, get a consultation to see that it's the right thing and you're doing the right thing. It's not great for my practice to be prescribing lots of chronic opioids. So, there are quite a few physicians that I have this deal with them: That they write them, but I see the patients every 3 months to just take a look and not even prescribe, because only 1 physician should be prescribing.

Dr. Rosenberg:
That's a great point. That's a great take-home for that. So, Dr. Prager, I want to thank you for this, talking about ketamine and talking about chronic pain.

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