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Diagnostic Hurdles: Recognizing and Addressing Treatment-Resistant Depression

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Goldberg:
This is CME on ReachMD. I'm Dr. Joe Goldberg. With me today is my friend and colleague, Dr. Manpreet Kaur Singh.

Welcome, Manpreet.

Dr. Singh:
Nice to be here, Joe.

Dr. Goldberg:
Good to be with you. So we're going to try to figure out what we need to know about recognizing and addressing treatment-resistant depression, or TRD. Some people prefer the language of difficult-to-treat depression versus treatment-resistant depression. We could talk about that, but whatever we want to call this phenomenon of depression that doesn't get better after adequate trials, how do you think about this, Manpreet?

Dr. Singh:
You know, words matter, Joe. And it is weird that we're trying to figure out how to label this thing that our patients experience that causes so much distress. And some of it has to do with the fact that they feel that they have not had an adequate complete trial or an adequate response to a particular trial. We have to play detective to sort out what's the etiology.

And one of the things that I really try to do before I reach a decision that this is a difficult-to-treat depression is I want to make sure did I get the dose right? Have I given enough time for a particular intervention to work? Have we addressed side effects that are of transient nature? Because these things can really be consequential before we label a patient with treatment-refractory depression or difficult-to-treat depression. And so many times I see patients that come in who actually have had subtherapeutic trials of medications, gingerly use of this and dabble of that. And when you have a difficult-to-treat patient, oftentimes, they've had several of those start/stops.

It's true that patients who experience more side effects tend to be more difficult to treat, but there is that business for us to really arrive at a diagnosis of someone who's had an adequate robust trial of a treatment and has not responded to it and then experiences residual symptoms, which can, of course happen, but one must operationalize that first. That's how I would define treatment-refractory or difficult-to-treat depression.

Dr. Goldberg:
And there's this notion of pseudo treatment-resistant, right, which we see all the time. Someone comes from a consultation, "Oh, I've been on a million things," and you go, "Well, actually, you've been on this thing for one day, and then you had a little bit of headache so you stopped it, and then you were on a microdose of something for 3 weeks, so you stopped it." So I think you make an excellent point,

which we want to really affirm the diagnosis is accurate, not confounded by something that we missed, like, oh, this is actually bipolar depression, or this is really psychotic depression, or major depressions that we know are just harder to treat, like anxious depressions, just much harder to treat. Substance use comorbidity can occur with major depression so that's going to be harder to treat.

So you kind of go through all that detective work, and then you cross your fingers and hope that your predecessors have documented adequate doses, adequate durations, with appropriate pharmacologies, and not doing the same thing over and over again. And then you get into this land of what I guess would be recognized by most people as true-blue treatment resistance, which is to say, the syndrome that we're trying to leverage is just not getting better. So if we go there, you know, what does it look like? I mean, it's depression that's not getting better and symptom scores, using a rating scale, will still be elevated; quality of life suffers. It's not hard to miss, right? What's hard to miss is, you know, you really haven't had adequate treatment. I hope the person I'm seeing with purported TRD is someone that has pseudo treatment resistance.

But for someone who's actually been on multiple things that haven't worked and the diagnosis is accurate and the adherence has been intact, etc., etc., it's a fairly short list of things that we can talk about that would be considered evidence based for treatment-resistant depressions.

Dr. Goldberg:
The intranasal formulation of the S enantiomer of ketamine, esketamine, also FDA-approved in treatment-resistant depression. And then we have, you know, device-based approaches, transcranial magnetic stimulation [TMS]. And let's please not forget about ECT [electroconvulsive therapy], which is still, I think, the most potent known intervention. Then we have a whole world of what might be called

more promising interventional approaches, things like the sync protocol for deep TMS. Some pharmacology – many of our younger colleagues don't even know about, like drugs like MAO [monoamine oxidase] inhibitors or, you know, cyclics and combinations.

So there are times where I think true-blue TRD actually can get tackled if one is being mindful of the size of the effect of a particular treatment and how well it works in the setting of prior nonresponses.

Want to add anything to that?

Dr. Sing:
Just that the therapeutic landscape is really open up for treatment-refractory depression, so lots of hope for the future.

Dr. Goldberg:
Absolutely. Tell patients we have things now we didn't have 5, 10 years ago. Can't wait to see what we have in a few years from now.

Well, this has been a terrific micro discussion. Our time is up, but thanks for joining.

Announcer:
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