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Beyond Monotherapy: Augmentation Strategies to Combat the Residual Symptoms of MDD

Announcer:
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Dr. Goldberg:
Hi, everyone. 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:
Thank you, Joe. Great to be here.

Dr. Goldberg:
Likewise. So we're going to talk for just a few moments about augmentation strategies to combat residual depressive symptoms. You know, it's often been said, if you've got a partial response in major depression, there may be value, especially if the patient has the desire, to augment and make something out of something rather than to switch altogether. We don't really have wonderful guidelines for what to augment with; we've got a lot of options, though. Can you make sense of some of that chaos for us, Manpreet?

Dr. Singh:
Yeah, absolutely. Certainly, the extant guidelines suggest, you know, augmentation when it comes to addressing hypothyroidism with thyroid replacement, or second-generation antipsychotics have been used adjunctively and studied in that way, similarly to psychostimulants. You know, it's interesting to me that when we feel a sense of failure with our patients, we are very quick to jump to maybe adding to the existing treatment. I would caution us to make sure we've optimized the primary monotherapeutic first before we move to adjunctive, with the appreciation that it's completely reasonable that a patient might benefit from more than one treatment, because depression is so heterogenous, and it's very likely that a single agent doesn't cover it all. And with limitations in time, we may not be able to adequately get to a precision-based treatment match for a patient.

Joe, do you have some specific examples that you could describe for us?

Dr. Goldberg:
Yeah, I think you make some very good points around how would you choose from among, say, an atypical antipsychotic or a stimulant or adjunctive thyroid hormone? How about adding a second antidepressant to the first that has a complementary mechanism? So my gripe with guidelines is they give you lists of things to do, and here are the first line and second line and third line, but they don't really help you tailor it to the patient. So I might, for instance, be especially interested in an adjunctive stimulant if someone has a history of ADHD, or even if there's just impaired attentional processing, which can come with the territory in major depression, lethargy, sluggishness, I probably favor that over a sedating drug. On the other hand, someone who's wound up and keyed up and anxious, distressful kind of depression, I'm not going to use a stimulant there. I might think about the value of a second-generation antipsychotic. I

might think about the value of an adjunctive treatment like mirtazapine, commonly not used enough augmentation, which a very nice meta-analysis a couple of years ago in *The New England Journal* showed a pretty large effect size as an augmentation treatment, especially in anxious depression.

Dr. Singh:
Can I just interject here and just say something about lithium? Lithium is an interesting adjunctive treatment that people say, and guidelines, to add. But then I have to ask myself, am I treating bipolar depression? Have I adequately addressed a mania that may be the primary problem altogether? So adjunctive treatment is all well and good, but it gives another opportunity for us to really explore the differential diagnosis and make sure we have the right diagnosis, because what ends up happening sometimes is that the adjunctive treatment ends up becoming the primary monotherapeutic choice. So that's also within the realm of consideration. So what you just said just sparked that thought in my head.

Dr. Goldberg:
Yeah, and you just sparked in me the thought, you know, so lithium is not a diagnosis-specific drug. It can have adjunctive value in MDD, but some would say it's got particular value when there is suicidal features present, when there's high impulsivity present, or high recurrence. So some people describe lithium as an anti-recurrence drug. You're depressed, you're not, you're depressed, you're not, you're depressed, you're not. You may never ascend into a mania or hypomania, but that ON/OFF, ON/OFF quality, you know, a mood stabilizing antidepressant, full compound like lithium might have value for that niche.

So in a way, we're kind of inviting our colleagues out there to sort of really think with great curiosity about what's the nature of the symptoms that a patient's presenting with? What are you trying to target by way of residual symptoms? And how can you craft, hopefully, a regimen that would be synergistic, non-redundant, non-contradictory, and where the benefits outweigh the risks?

Dr. Singh:
Exactly my point. Thank you so much.

Dr. Goldberg:
Well, thanks for joining us today, and we will look forward to seeing you again next time.

Announcer:
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