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Is It Bipolar Depression or MDD? Treatment Strategies

Announcer:
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Dr. Singh:
Alright, so MT got a bunch of treatment trials. And I think that because she had such an interesting presentation, somebody early on actually thought not to start her on another antidepressant to treat her depression symptoms, but to actually start her on a second-generation antipsychotic or combination thereof. But her depression was hard to treat. So she was even given a combination of SGA plus an antidepressant. Unfortunately, most of these were poorly tolerated. She was also tried on a number of antianxiety medications, which often co-occur, and she was again re-trialed. And with some slight improvement.

The trials really suggest that we may have had somewhat of a poor understanding of the diagnosis or best practices where maybe polypharmacy just got into the mix, because we didn't have a discernible treatment strategy.

What I can say is that we're beginning to understand more personalized treatment options for patients who are experiencing certain cardinal symptoms and noticing that some of our existing treatments actually do better or perform better for certain kinds of symptom clusters. For example, lurasidone seems to work really well for people who have very significant sleep disturbance and irritability presentations. These are overlapping depression and mania cluster symptoms that present both in the depressed phase of illness as well as a manic phase of illness. So you get that broad coverage. It makes sense then that lurasidone would be approved for Bipolar 1 Depression down to age 10, for that reason. Similarly, we have data in adults to demonstrate the, again, coverage of both depressed phase and manic phase of illness that are with now, not just approvals for Bipolar 1 Depression, but also for Bipolar 2 Disorder.

Do you want to comment more on that, Joe?

Dr. Goldberg:
Yeah, I want to ask a contrarian question. If this is her first presentation of diagnosis of probable Bipolar Disorder, and there have been more than one suicide attempts, and there's a sense of trait impulsivity, you know what I'm about to ask you.

Dr. Singh:
You bet.

Dr. Goldberg:
No lithium?

Dr. Singh:
You are right on it. And after confirmed diagnosis of Bipolar Disorder was made, and we discussed and psycho-educated about the course and treatment, we switched MT actually, took her off of all of these other agents that had only partial responsiveness to lithium monotherapy. Her episodes were so clear, she was able to get titrated to a therapeutic dose. She tolerated lithium very well, and had

marked reduction in suicidal thoughts, anxiety, irritability, and impulsivity, along with hypersexuality. She didn't want to drink any more. She didn't want to go out to do the kinds of things that she readily felt she could do, and have control over when she was manic.

We did augment her pharmacological management with some psychotherapy, and though she had some breakthrough of suicidal thoughts and hypersexual behaviors, with ongoing adjustment of her lithium, we were able to bring her to more euthymic phases of illness, and frankly, she's been euthymic with only moderate degrees of relapse and related to nonadherence. So that's the ongoing story there for her.

Dr. Goldberg:
You know, lithium is an interesting drug that's got a pretty narrow spectrum of activity. But as we might say to MT, you'll never be 18 again, and you'll never be this close in time to the initial onset of your illness as now. And one of the problems with lithium is it seems to work better sooner than later in terms of the initial onset of symptoms. So if somebody decides to save that for the last possible thing, wait till she's 40, she may have missed the window. So really, any early onset, really Mood Disorder patient with impulsivity and suicidality, but especially with a high index of concern for Bipolar Disorder, such as MT, you have to bring lithium up in that context without saying, 'yeah, we'll wait, let's do seven more things and then see if it works,' because that that window that's been shown to be really important to proximity of symptom onset to get the best effect.

Dr. Singh:
I couldn't agree more, Joe. I think that we underutilize lithium, in part because we may be very concerned about its side effect profile and the narrow therapeutic window, but its efficacy is second to none in my view. Though, we need to do more direct comparative effectiveness trials to really understand for which patients, lithium makes a sense as a first-line agent. We do have to develop a culture where we understand both its neurocognitive benefits over the long term and potentially disease modifying benefits of lithium over the long term. And also the fact that perhaps we can keep patients well for longer periods of time on this medication, early in the onset of illness.

Dr. Goldberg:
And a couple of related things here. So in the world of polypharmacy, which I fear awaits this young lady, she'll be on seven drugs by the time she, you know, finishes college, if things don't go well, really only two things have been studied as polypharmacies for Bipolar Depression. As you know, one is combining lithium or valproate with lurasidone, or combining lithium or valproate with lumateperone. So if one is going to use an atypical antipsychotic with the antidepressant properties, and I noticed that she didn't really get much better with lurasidone alone or with cariprazine alone, one could make an argument for considering lithium as a foundational treatment. And then if she's partially better, you have a very logical augmentation, it's possible that one of those agents may work better in conjunction with lithium and as monotherapy.

Dr. Singh:
I couldn't agree more, especially when you worry a little bit about the evolution of her neurodevelopmental, self-regulatory problems, and potentially feelings of brain fog, where if there is an evolution towards psychosis, having an SGA on board in conjunction with lithium, might make a great deal of sense.

So thank you so much for this excellent conversation, Dr. Goldberg, and I hope this was informative to our audience.

Dr. Goldberg:
Interesting case, tough case, it illustrates a lot of the key questions that we want to ask about such patients so that we can formulate a rationale for why we think what we think and what we want to propose as treatments. I'll tell my own patients, 'the one thing I can guarantee you is a rationale. Whether it's going to work or not, we'll find out,' but we don't have a good rationale and reasoning for what you're going to propose so it doesn't feel random.

Dr. Singh:
You got it. Thank you.

Dr. Goldberg:
Thank you.

Announcer:
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