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Depression from Case to Clinic: Rethinking Partial Response with a Different Approach

Announcer:
You're listening to *Psychiatry Today* on ReachMD.

This medical industry feature, titled "Depression from Case to Clinic: Rethinking Partial Response with a Different Approach," is sponsored by Alfasigma.

Here's your host, Ashley Baker.

Ashley Baker:
A 41-year-old woman comes to your office for a follow-up visit. She has type 2 diabetes and is on metformin. She began taking a first-line SSRI eight weeks ago. Today, she tells you that her mood is a "bit better", but she feels that she's still struggling to focus at work, can't sleep, and "feels overwhelmed all the time." If you're like many clinicians, you've seen a similar patient before—someone who's had a partial response to antidepressants but is still struggling with the complexity of their depression. So what's the next step?

This is ReachMD, and I'm Ashley Baker. Today, we'll explore this clinical scenario to understand when patients with depression may need broader biologic support in addition to antidepressant therapy.

Ashley Baker:
Joining me today are Dr. Bradford Perkins and Ms. Kimberly Giberga. Dr. Perkins is board-certified in family medicine and obesity medicine, and is the Founder of Transform Wellness Clinic in Los Gatos, California.

Dr. Perkins, welcome to the program.

Dr. Perkins:
Thanks for having me. This is such a critical conversation.

Ashley Baker:
Also with us is Ms. Giberga. She's a dual-certified family nurse practitioner and psychiatric mental health nurse practitioner, and she serves as Founder and Clinical Lead of Salado Creek Mental Health in San Antonio, Texas.

Ms. Giberga, thank you for joining us today.

Ms. Giberga:
Absolutely, glad to be part of the discussion.

Ashley Baker:
So let's jump right back into this case. Dr. Perkins, when you hear this presentation—partial SSRI response, persistent cognitive symptoms, stress, sleep issues, diabetes, metformin use—what clinical patterns immediately stand out to you?

Dr. Perkins:
Well, there are several factors here that tell me this patient may benefit from a more comprehensive approach.

First off, we're seeing stress vulnerability—she's feeling overwhelmed, which suggests her coping mechanisms may be strained. In addition, we have complexity in symptom presentation—it's not just low mood, but also sleep disturbances. And she expresses clear cognitive concerns with the concentration difficulties, which often go hand-in-hand with depression.[1]

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The fact that she has diabetes with metformin use is also important, as we know that they can affect nutrient absorption and metabolism.[2,3] All of this suggests the biology of her depression may be more complicated than a monoamine imbalance.

What also stands out here is the partial response to the SSRI. She's had eight weeks on a first-line antidepressant therapy, yet she's still struggling.[4,5]

We know that response rates decline with each additional change in therapy, so to me, that's a signal that we may need to think beyond SSRI monotherapy.[6]

Statistically, polymorphisms in the *MTHFR* gene may affect up to 70 percent of patients with depression, reducing their ability to convert dietary folate into the active form that crosses the blood-brain barrier.[7] So, this patient might be someone who can't efficiently use the folate from her diet to support neurotransmitter synthesis.

Ashley Baker:
Turning to you, Ms. Giberga, let's dive deeper into possible reasons why this patient hasn't achieved remission. Can you walk us through what's happening biochemically here?

Ms. Giberga:
For sure. The stark reality is that less than 50 percent of patients respond to first-line antidepressants.[6] SSRIs and SNRIs do a good job of modulating monoamine neurotransmitter activity because they can increase serotonin and norepinephrine in the synapse.[8] But here's the thing: depression involves multiple biological systems, and sometimes we need to look beyond the monoamine pathway. So, in some patients, these therapies don't restore the full biochemical balance needed for optimal neurotransmitter function.[6,9-12]

And to Dr. Perkins' point, neurotransmitter synthesis requires specific nutrients as cofactors. When there are deficiencies in these nutrients, it can affect how antidepressants are metabolized, potentially reducing their effectiveness or increasing the risk of side effects.[13] In our patient's case, her metformin use and potentially her genetic makeup could create specific nutritional gaps which can limit her SSRI's effectiveness.[2-4,14]

Ashley Baker:
Now, let's build out this patient's risk profile further. As we dig deeper into her history, we learn that she works long hours at a desk job with minimal outdoor time. Her chart review shows that she's also taking an oral contraceptive and her BMI is 32. Ms. Giberga, how do these additional factors influence your thinking about her need for nutritional support?

Ms. Giberga:
In my experience, it's common to encounter patients who fit multiple risk categories, just like this one.

In her case, the oral contraceptive on top of metformin compounds the risk for nutrient depletion.[3,15] Her desk job with minimal sun exposure puts her at high risk for vitamin D deficiency, especially combined with her diabetes.[16] And we know that patients who are overweight may have different metabolic needs and could benefit from broader nutritional support.[4,16-18] We also haven't checked, but I'd be interested in her inflammatory markers, like high-sensitivity C-reactive protein, which can be elevated in patients with her profile.[19]

Ashley Baker:
Coming back to you, Dr. Perkins, what could comprehensive biologic support look like for our patient?

Dr. Perkins:
The key is addressing multiple functional domains that are relevant to her depression pathophysiology. I think about these as five main areas: mood regulation, neuroprotection, mental resilience, stress management, and cognitive function.[7,11,19-27]

For this patient, I'd want to provide targeted medical nutritional support that works alongside her SSRI to help restore the biochemical balance we are discussing. This approach recognizes that her depression is a multisystem condition that requires multisystem support.[11,19-23,25] Essentially, we're trying to optimize the biological foundation so that her SSRI can work more effectively.

Ashley Baker:
For those just tuning in, you're listening to *Psychiatry Today* on ReachMD.

I'm Ashley Baker, and today I'm speaking with Dr. Bradford Perkins and Ms. Kim Giberga about recognizing clinical patterns that may signal a need for broader biologic support in patients with depression.

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Now, with this comprehensive approach in mind, let's talk about DeplinPRO Mood Health™ as a targeted medical nutrition option for our patient. Ms. Giberga, can you give us an overview of what it is?

Ms. Giberga:
Absolutely. DeplinPRO Mood Health™ is a medical food specially formulated to meet the distinctive nutritional requirements for neurotransmitter imbalances in the clinical dietary management of mood disorders, including depression. It's for use under medical supervision in patients aged 12 years and older and is intended to be used with an antidepressant.

It contains four nutrients: 15 milligrams of L-methylfolate calcium, 25 milligrams of zinc from zinc bisglycinate, 50 micrograms—that's 2,000 international units—of cholecalciferol, or vitamin D_3, and 250 milligrams of gamma-glutamylethylamide, also known as L-theanine. This formulation can address multiple aspects related to our patient's presentation.

Ashley Baker:
And Ms. Giberga, how does this combination support the five functional domains Dr. Perkins mentioned earlier?

Ms. Giberga:
Great question. DeplinPRO Mood Health™ is designed for multi-action targeted medical nutrition to support those five areas: mood regulation, neuroprotection, mental resilience, stress management, and cognitive function.[11,20,21] These ingredients target multiple biological systems involved in depression to help restore balance in neurotransmission and support the biological foundation needed for effective treatment response.[7] It's important to note that biochemical processes require sufficient levels of key nutrients that may not be achievable through diet alone,[13] especially if you have multiple factors like genetics, medications, and lifestyle working against adequate nutrient status.

So, let's go through what this targeted medical nutrition means for our patient specifically.

L-methylfolate is the biologically active form of folate, and it's the only form that can cross the blood-brain barrier.[28] As Dr. Perkins noted, many patients with depression do have genetic variations that reduce their ability to convert regular folic acid or dietary folate into this active form. So its inclusion addresses the metformin and potential genetic variation that can affect the patient's folate status.[7] L-methylfolate helps balance neurotransmitters and promotes neuroplasticity.[11]

The vitamin D_3 addresses our patient's insufficient sun exposure and supports her metabolic health. It's not just a nutrient, but also a neurosteroid hormone that can reduce oxidative stress and modulates the inflammatory response to support neuroprotection.[19,20,24,29]

And the zinc can help manage oxidative stress and inflammation and support neuroplasticity.[21,30-32]

Finally, the L-theanine is a non-dietary amino acid that promotes cognitive resilience by modulating the stress response, and, for our patient, this could help with her sleep and stress symptoms.[23,25,33,34]

Ashley Baker:
This brings up an important practical question, Dr. Perkins. When you're considering adding targeted medical nutritional support like DeplinPRO Mood Health™ to a patient's regimen, how do you frame that conversation with them?

Dr. Perkins:
What I try to do in my practice is keep these conversations patient-centered and clinically grounded. So, for this patient, it's important to acknowledge that the SSRI has helped her mood to some degree, but we should address why she's still experiencing persistent symptoms with focus, sleep, and stress.

Then, I'd share how the brain needs specific nutrients at sufficient quantities to make neurotransmitters.[4,35] And given her other medications—the metformin and oral contraceptives—along with her limited sun exposure and the demands of her work life, she likely has increased need for these nutrients—levels that would be difficult to achieve through dietary change alone.[13]

It's critical to frame the addition of targeted medical nutrition as helping establish the biological conditions that allow her SSRI to work effectively, not as replacing it. With this patient, I'd emphasize that we're supporting the underlying biology that affects concentration, stress resilience, and sleep, essentially setting that stage for her SSRI to work as intended on neurotransmitter pathways.

And as you know, we have many patients who are interested in integrating nutritional strategies into their regimen, and that preference is something we should honor when it's clinically appropriate.[4]

Ashley Baker:

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We're just about at time for today, but before we wrap up, Dr. Perkins, what key takeaways would you like to leave with our audience?

Dr. Perkins:
As Ms. Giberga noted, this case represents patients we see every day in practice. And I think the key here is recognizing that she presented with multiple factors from the start—partial SSRI response, cognitive symptoms, stress, sleep issues, diabetes, metformin use, oral contraceptive use, minimal sun exposure, and elevated BMI.

Rather than waiting another eight weeks to see if she improves or cycling through different antidepressants with reduced effect, I'd introduce targeted medical nutritional support now to build that foundation we've been discussing. I'd continue her SSRI and add the multi-action targeted medical nutrition, then reassess in four to six weeks. The goal is to optimize her biochemical status and ensure adequate nutrient levels so we can achieve not just partial improvement, but sustained remission.

Depression is a complex biological condition, and when we address the various biochemical needs early on, we can offer our patients the best chance at meaningful improvement.

Ashley Baker:
Those are very valuable insights to consider, and as those final thoughts bring us to the end of today's program, I'd like to thank my guests, Ms. Kim Giberga and Dr. Bradford Perkins, for sharing their expertise on recognizing when depression requires broader biologic support through this case-based discussion.

Dr. Perkins, Ms. Giberga, it was great speaking with you both today.

Dr. Perkins:
It was great speaking with you as well. Thank you for having me.

Ms. Giberga:
Thank you so much for having me. I really enjoyed it.

Ashley Baker:
For ReachMD, I'm Ashley Baker. Thanks for listening.

Announcer:
This medical industry feature was sponsored by Alfasigma. If you missed any part of this discussion or to find others in this series, visit *Psychiatry Today* on ReachMD.com, where you can Be Part of the Knowledge.

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