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Transforming Schizophrenia Treatment: Advances in Medication and Therapy

Dr. Walker:
Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Robert Walker, and joining me to discuss future treatment options for schizophrenia patients is Dr. Deanna Kelly. She's a Professor in the Department of Psychiatry at University of Maryland School of Medicine and the Acting Director of the Maryland Psychiatric Research Center. Dr. Kelly, thanks for being here today.

Dr. Kelly:
Great. Thanks for having me.

Dr. Walker:
To start us off, Dr. Kelly, are there any new medications on the horizon that show potential for treating schizophrenia?

Dr. Kelly:
This has actually been an exciting year for us. We have a new medication that was approved at the end of September, which is our first antipsychotic on the market that does not directly block dopamine in the brain. It's made-up of the active ingredient xanomeline that has another compound with it called trospium. It really is a compound that acts on the muscarinic receptors, which are part of the acetylcholine-type receptors in the brain—the M1, the muscarinic 1, and then muscarinic 4—it serves as an agonist for. So it's the first medication that's come to market that hasn't been a dopamine blocker, and that's really exciting. And in fact, there are several other medications that are going to be similar to it, so this is opening up a whole new potential avenue for us to be treating our patients because, as you know and as the listeners know, mainly up until now we have only had medications that work very similarly, blocking dopamine. We did have another agent that was very similar to that new medication that just failed in its trials called emraclidine, which we were excited about. It's a very similar compound. It did not show benefits in the trial, but we also have other medications in the pipeline right now. We have medications that are targeting some of the domains like cognitive impairments and negative symptoms for which we currently have no treatments to date. Our antipsychotics that are on the market right now—their main effects are on psychosis, working to improve decreasing psychotic symptoms—but we don't have treatments to help with cognitive symptoms and negative symptoms as well. So we do have some in the pipeline. There's a medication called iclepertin that I believe is still in phase II but may be effective for the treatment of cognition, which would be exciting for us in the field.

There's also medications in the pipeline that target different transmitters like phosphodiesterase 4 inhibitors, et cetera. So coming behind this xanomeline, which was approved in September, there are several new medications that are potentially in the pipeline, so that's exciting.

Just a couple of other things worth mentioning—we are in a time right now where there are other options that are being explored. There are people looking at the relationship of the gut to the brain, looking at nutritional supplements, looking at how some food might decrease inflammation, and so there have been some exciting movements in the world of schizophrenia. We are not gold standard on these yet, but I think that it's worthwhile to point out when we talk about the excitement and the changes that are happening—to understand there's been a few clinical trials out there that have shown that a dietary intervention using a medical ketogenic diet where we replace glucose utilization in our cells with fat breakdown allowing our mitochondria to function a little differently has been able to show some really promising results. In fact, the few clinical trials that have been out there have shown really robust findings so far, so we need just to keep our eye on the area of ketogenic diets.

We also have had some prebiotic and probiotic studies that have been improving inflammation in the body and potentially might work for

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improving cognition, and we finished a recent double-blind clinical trial looking at the removal of gluten from the diet in specifically a subgroup of people with schizophrenia who have antibodies to gliadin. And so we see inflammation in the brain. We see inflammation in the body. We can improve that and improve some psychiatric symptoms. So it's a time with new mechanisms and potentially new strategies that could help us in other domains of the illness besides just positive symptoms of schizophrenia.

Dr. Walker:
So moving beyond medications, can you touch on the role therapy plays in conjunction with medication for treating patients with schizophrenia?

Dr. Kelly:
Sure. I do think this is an important point because we often talk about medications only when we start to talk about the treatment of schizophrenia, and this is actually a serious disorder that has a lot of impairment. People have a lot of impairments in a lot of areas of functioning, and so to think that just medication will solve everything is shortsighted. We have to really take care of people who have schizophrenia holistically, and so there are some very important pieces we need to always keep in mind, and that includes psychoeducation. We should make sure that we are talking with our patients and their families, make sure they understand their choices, make sure they understand what's going on, make sure they understand the hope we have for their recovery and their role in that with taking medications and participating in other therapies, so I think that shared decision-making, psychoeducation, are important.

We also have other strategies that have a good level of evidence associated with them. That includes cognitive behavioral therapy—and CBT is what it's called—really helps with other domains of the illness. It helps people with their distress and their coping, so it's thinking about, how can we catch our thoughts? How can we check our thoughts? And how can we change our thoughts to decrease distress and secondarily help our coping skills? It's not necessarily treatment that's going to help with positive symptoms per se, but it's important to help people function. They want to feel better and function better, and that's something that can help them.

Dr. Walker:
Diving a little deeper, in your perspective, how might emerging technologies like telemedicine or mobile apps change the way we treat schizophrenia?

Dr. Kelly:
We have really moved into a new era after COVID where people are using telemedicine, so I think telemedicine can really play a role in accessing care in rural areas—areas where there's not a lot of psychiatrists or other practitioners like nurse practitioners or psychiatric pharmacists or PAs, other people who can help prescribe and monitor them. So telemedicine is an important avenue, and I think that we're only going to see that grow for specialty care, especially in the area of psychiatry.

In terms of mobile apps, there's a couple of thoughts here. There is an explosion of apps out there so that people don't even know where to turn sometimes, because you can monitor your medications, you can monitor your symptoms or your sleep, and there's lots of things you can do, so I think helping to find technologies that can help you in the areas that you need help in is important. And as practitioners we can help people dig through and find different apps, and I think that we don't want to get lost in millions of apps out there. But there's this area called digital therapeutics, and digital therapeutics is actually different types of technologies and app-based approaches that will be cleared by the Food and Drug Administration. So they have a level of evidence associated with them that have been tried in clinical trials as opposed to a sleep monitoring app that hasn't been tested. And so there are emerging digital therapeutics. These are where a practitioner can write prescriptions for an app that has evidence to be part of your treatment plan. And there's apps out there that are digital therapeutics available for depression, for postpartum depression, for sleep, for PTSD. I think there's ADHD apps for both adults and children with different types of platforms.

In schizophrenia, we do have apps that are going to be prescription-based that are being tested currently, and from my knowledge there are some that are being tested for negative symptoms. But I think there's some apps that are going to help people deliver types of therapies where they could use the apps as practice spaces; they could be dinged and pinged throughout the day to test different strategies to practice on so that they could utilize these apps to be part of their care and part of the way doctors write prescriptions in the future. So these will be coming, and no doubt we will have likely in the next year digital therapeutics for schizophrenia available to us for prescription.

Dr. Walker:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Robert Walker, and I'm speaking with Dr. Deanna Kelly about emerging treatment options for schizophrenia patients.

We spoke a bit earlier about new emerging therapies, but now let's focus on potential roadblocks for improved treatments. So, Dr. Kelly, what challenges do you foresee in implementing new treatment options for patients with schizophrenia in the clinical settings?

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Dr. Kelly:
There's lots of challenges. One of these challenges is actually getting evidence-based treatments that we know into people's hands. There's certain medications that are very gold standard, like clozapine and long-acting injectable antipsychotics that are gold standards, have a lot of evidence, could really improve people's lives, and we just have trouble implementing those into treatment care. And sometimes it's because there's stigma associated with it; sometimes there's lack of training; sometimes there's actual barriers that are out there. So we are as a field trying to break down barriers, and that might be one of them that's going to be important and very exciting. There's many barriers potentially, but other barriers include costs. Some of the new medications that are coming to market are going to be very expensive, so there will be formulary decisions people are going to have to make around some of these new medications that are coming to market. And if people are paying out of pocket, sometimes the newer medications have cost barriers associated with them. And these are just a couple of the challenges. Our challenge as a field is to move the time from when we know something works to get it to people faster than we have before.

Dr. Walker:
On a similar note, how do you see disparities and access to mental health care affecting the treatment landscape in schizophrenia?

Dr. Kelly:
In schizophrenia, traditionally, we understand that some of our underrepresented minority patients have had less access to care, more trouble finding providers and sometimes less access getting good medications. In particular in our Black population, our patients have sometimes more trouble finding providers, and that's true for our Asian patients as well. So the providers become a more challenge to find. When we treat with antipsychotics, the literature shows us that Black patients often are less likely—and I've published a couple of papers on this topic, three or four of them now—Black patients are less likely to get the medication clozapine, which is a standard of care, topnotch, state-of-the-art first-line treatment for treatment resistance, and our Black patients are few and far between in the treatment there. We have been growing that and changing that, and new data is coming out, but it's partially because they have a lower white blood cell count, and that's a side effect, but it's also because we've done a poor job in making sure that we break down other barriers associated with stigma, associated with treatments. But we do know that patients who have depression even have more antipsychotic prescription if they're Black, so there are disparities, and there are challenges traditionally in our field. There is a growing parity on this, but we do know that access in Black patients to good treatment has been traditionally more of a challenge and a challenge for our field to overcome.

Dr. Walker:
Now, before we close, Dr. Kelly, do you have any key takeaways on how we can help and trust these challenges and ultimately optimize future treatment in schizophrenia?

Dr. Kelly:
I think as a field, as providers, and as educators, we need to be involved with lifelong learning. We need to pay attention to new treatments coming out. We can't have our backs to the world of change around us in terms of the new strategies that might include nutritional strategies and medications that might no longer affect the dopamine system. I think we need to pay attention and get educated. When we hear new mechanisms like acetylcholine and we hear TAAR1 or we hear PDE, different neurotransmitters in the brain that we're not used to, it could be a roadblock for prescribers to say, "I don't understand, and I don't know how to use these medications." But in fact, we need to be on the forefront as providers to pay attention, learn what we can, and make sure that we are developing, implementing, and making sure that our patients are receiving state-of-the-art new treatments.

Dr. Walker:
With those strategies in mind, I want to thank my guest, Dr. Deanna Kelly, for joining me to share her insights on future schizophrenia treatments. Dr. Kelly, it was great having you on the program.

Dr. Kelly:
Great. Thanks so much.

Dr. Walker:
For ReachMD, I'm Dr. Robert Walker. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.

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