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Clinical Considerations for the Treatment of Schizophrenia

Dr. Wilner:
Schizophrenia is a chronic mental disorder characterized by symptoms that negatively affect a patient's mental and emotional behaviors. And although there are current treatment options, including first- and second-generation antipsychotics, therapeutic challenges still persist. So which clinical strategies should we consider in order to optimize outcomes for our patients?

Welcome to *NeuroFrontiers* on ReachMD. I'm your host, Dr. Andrew Wilner. Joining me today to share clinical considerations in the therapeutic landscape for schizophrenia is Dr. Craig Chepke, a psychiatrist with Excel Psychiatric Associates and Adjunct Assistant Professor of Psychiatry at the University of North Carolina School of Medicine.

Dr. Chepke, welcome to the program.

Dr. Chepke:
Thank you so very much for having me today. I'm excited to be here.

Dr. Wilner:
Well, it's definitely our pleasure. And to start us off, Dr. Chepke, can you give us an overview of the current treatment patterns that are available for schizophrenia?

Dr. Chepke:
Sure. I'd say that we could break it down probably into a couple different ways. We could go by route of administration. We've got oral medications, which include sublingual as well. There is one transdermal formulation available for treatment of those with schizophrenia and then long-acting injectable antipsychotics. And then amongst those, we've got many different options within those subcategories. As you mentioned at the top, we've got first-generation and second-generation antipsychotics, as sometimes categorized as typical or atypical antipsychotics, many different ways of talking about it. But we have a lot of different options to treat schizophrenia, but unfortunately, not all of them tend to work out that great for many patients.

Dr. Wilner:
Right. It sounds like there's a very diverse armamentarium for the treatment of schizophrenia, but we still need more and better therapies. Is that correct?

Dr. Chepke:
Absolutely. Schizophrenia is a very severe brain disease and one of the most difficult conditions that we treat as psychiatrists, and despite the plethora of different options, honestly, I don't think we're still doing a great job of treating people with schizophrenia.

Dr. Wilner:

What's the biggest challenge?

Dr. Chepke:
Well, there's a myriad of challenges. The first-generation antipsychotics very often come with a large liability of movement disorders, both acute like dystonia, Parkinsonism, akathisia and then more chronically potential for tardive dyskinesia. Second-generation antipsychotics tend to show a reduced risk for the movement disorders in many cases but carry often greater liability, many of them for metabolic side effects and weight gain. And we know that the physical health of people with schizophrenia is also impaired by this disease. It's not just a brain disease. It affects the entire body. People with schizophrenia have a dramatically increased mortality rate compared to healthy controls and have a much shorter life expectancy, so we really need to be cautious about that as well. Those are definitely some challenges that we see in terms of the tolerability, but also the efficacy is often not fantastic for people. The efficacy is usually pretty decent for the positive symptoms of schizophrenia—the hallucinations and delusions—but schizophrenia is so much more than that. There's also the cognitive and the negative symptoms of schizophrenia, and those are 2 symptom domains that the current antipsychotics that we have tend to not do a very good job of treating.

Dr. Wilner:
I understand that adherence is an issue. Can you explain that to me?

Dr. Chepke:
Of course. I'd say, honestly, adherence is a human condition of any chronic illness. If you look at rates of adherence in things like asthma or heart disease, they're not great either. And who hasn't had the experience of having a few extra pills at the end of a month even when you think that you're trying to take them the best you can? But schizophrenia does present some other challenges on top of just the difficulties that anyone with any chronic condition faces. There's a facet and symptom of schizophrenia called anosognosia in which the person doesn't realize that they have symptoms. They believe that they're totally healthy and have no insight or awareness, and that could happen in many different illnesses but is very prominent in schizophrenia unfortunately, and so if the person doesn't realize they need medications, they don't think they have a problem, they're not going to take it. But then on top of that, I mentioned those tolerability issues that even many of the newer atypical or second-generation antipsychotics have, and so pair the fact that people with schizophrenia might not realize they need treatment for their symptoms and then the fact that many of them can be extremely intolerable for many people, that's not a very good combination, and so it leads to very high rates of nonadherence in this condition.

Dr. Wilner:
What I remember from medical school is that it's very important to form a therapeutic alliance with the patient and that psychiatrists, in particular, try and do this with their patients. But how do you form a therapeutic alliance when the patient, as you say, has anosognosia and doesn't think they have a problem?

Dr. Chepke:
That definitely can present some challenges, and having a person-centered approach I think is really critical to getting good outcomes. So in my private practice I run with my wife, who is a social worker, those kind of notions of person-centered care and shared decision-making really have been baked into the DNA of how we practice from the beginning. So the main thing with anyone is to just get to know who they are as a person. And certainly, when someone is coming and maybe doesn't realize they have symptoms or isn't convinced that they're as severe as the outside world believes they are, that becomes one of the most important things in keeping them coming back for treatment. That's showing that we care about them as a human being, that they're not just someone that we're writing some scripts to. So for me, I just get very curious. You know, "Tell me about your life." "What do you do on a daily basis?" "I want to know about what your hobbies are, your interests." And if you get to know them as a person and show genuine concern and genuine care, then I've found that people with schizophrenia who have no belief that they need to take medications, they'll come back to appointments, and many times they'll take their medications. They have said things like, "I don't think I need this med, doc, but you've never led me wrong before, and I trust you, so I'm going to take it anyway," because they see that I care about them, so it really to me does underline the importance of having that kind of person-centered approach and showing the genuine concern and care for that individual.

Dr. Wilner:
So you're really putting the emphasis in the therapeutic relationship on the relationship part in order to get to the therapy part. That sounds like a terrific strategy.

Dr. Chepke:
Yeah. It certainly in my experience has helped, and there's also research to back that up. And also, I think it's very important to engage in shared decision-making. And instead of us as the clinicians just telling the patient "Do this because I say so," I mean, that doesn't work great for my kids. It's certainly not going to work well for adults with schizophrenia or any other illness. So involving them in the decision-making process really helps because if people have a hand in making a decision about the treatment option that they're undertaking, they're going to be more likely to follow through with it because "Hey, I chose it. I may as well follow through with it." It's a type of mindset. So even if it might be something that may not have been our very first choice but is a reasonable and appropriate option, if that's what they choose, I'd rather go with that than what my first choice would have been because no medication works if they don't take it, and I'd rather them take something that might have been my second, third, or fourth choice than take nothing whatsoever.

Dr. Wilner:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and I'm speaking with Dr. Craig Chepke about clinical considerations in the treatment of schizophrenia.

So with all that being said, Dr. Chepke, about forming a relationship with the patient and trying to improve adherence with shared decision-making, what does the future of schizophrenia treatment look like?

Dr. Chepke:
Well, I'm kind of an optimist by nature, and I think it looks pretty bright. I think we've got a lot of hope that there could be future treatment options that might be meaningfully better for our patients with schizophrenia. I've always been excited about long-acting injectable antipsychotics. We do have a number of those that are woefully underutilized, unfortunately. I think that that's one area that we could do better with, and there's future long-acting injectables that might help to change that. Certain LAIs that are in development have longer durations of ability to go between injections. They started out being every 2 weeks, every 4 weeks. Then we've been able to use some every 2 months, every 3 months. There's one out there even every 6 months, and so increasing the duration and then also hopefully some options of new molecules. Most of the LAIs that we have currently are based off either aripiprazole or risperidone and paliperidone, and some new antipsychotics with new molecules in the future could be coming out, and that could broaden the diversity there.

And then most exciting to me though is that there are some clinical trials, and some of them should be showing results within the next year have a completely different mechanism of action, which is, I think, what we really need to move the needle forward. Every treatment we have today for schizophrenia is basically based off of either completely blocking or partially blocking the dopamine D2 receptor more or less, and I think we've kind of hit a dead end with that. We haven't seen anything with a measurable increase in efficacy over any other antipsychotic other than clozapine several decades ago, which that's another story. Clozapine is also woefully underutilized in my opinion. But the medications in clinical trials now work on completely different non-dopamine pathways. Now some of them will intersect with dopamine downstream, but there are TAAR1 agonists that are being studied currently that do not directly interact with dopamine receptors, and then another category of muscarinic acetylcholine receptor agonists. Both of those in phase II studies have shown very promising results with outstanding tolerability and really good efficacy. That, I think, could really change the game and give us a big step up in our ability to treat people with schizophrenia.

Dr. Wilner:
Well, that's pretty exciting. Now before we conclude, Dr. Chepke, are there any additional thoughts you'd like to share with our audience today?

Dr. Chepke:

Well, I would just say for anyone out there listening who does serve people with schizophrenia, I would just like you to raise the bar. Don't just look at someone as being out of the hospital and that's your measure of success. "Oh, yeah, they haven't been hospitalized in 2 years. They're doing great." Well, that doesn't mean they're doing great. We need to look at the person's function and their quality of life. And it's usually the positive symptoms that puts someone in the hospital, and so that's what we focused on in treating schizophrenia, but it's the negative and cognitive symptoms that really are underlying the deficits in function and quality of life for a person living with schizophrenia and their family. So to raise the bar, expect more because if we don't expect more from our treatment, why should our patients expect more from ourselves. We need to get people with schizophrenia back to work, back into relationships, and back into living fuller lives, and to do that I think it starts with looking in the mirror and raising our own expectations of what they are capable of.

Dr. Wilner:
Well this has been an insightful look at how we can optimize outcomes for our schizophrenia patients. And I want to thank my guest, Dr. Craig Chepke, for a great discussion. Dr. Chepke, it was a pleasure speaking with you today.

Dr. Chepke:
Thanks so much. It's been delightful being here.

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