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The Tragedy of Schizophrenia and Suboptimal and Poorly Tolerated Treatment

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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Dr. Citrome:

Hello, I'm Dr. Leslie Citrome, Clinical Professor of Psychiatry and Behavioral Sciences at New York Medical College in Valhalla, New York. Let's talk about The Tragedy of Schizophrenia and Suboptimal and Poorly Tolerated Treatment.

First off, let's take a look at schizophrenia and the disorder itself. We know it's a severe chronic and disabling disorder. And it's characterized by symptoms that are positive, negative, and cognitive. What do I mean by that? Well, the positive symptoms we're most familiar with, those are the hallucinations and delusions. They occur in exacerbations generally. And we often see these symptoms remit at least partially with the use of antipsychotic medicines. But we often also encountered negative symptoms and cognitive symptoms. These can actually emerge before the positive symptoms first become apparent in someone with schizophrenia. Negative symptoms include a deficit from normal behavior and functioning. This includes a lack of interest in everyday activities, and this can certainly impair functioning. Cognitive symptoms include problems with memory as well as attention. People in the prodromal phase of the illness of schizophrenia often have some cognitive and social deficits before they have positive symptoms.

When we take a look at the typical time course of the disease of schizophrenia, we see in the prodromal phase, variable onset of mood symptoms anxiety, there may be substance use. Eventually, there may be an exacerbation that is apparent, but typically we encounter positive symptoms, and that's when the diagnosis of schizophrenia is generally made. Negative symptoms and cognitive symptoms do continue.

With every relapse, patients are at risk for further irreversible lifetime functional impairment. So we know that there's a certain degree of functioning in the prodrome that is a little less than what is anticipated in someone of that age. During the first episode of psychosis, the level of functioning goes way down. Typically, someone will respond to antipsychotic medication, and their level of functioning will improve, almost reaching their baseline. But with each subsequent exacerbation, the ability to return to the prior level of functioning is diminished. And eventually, over time, patients have what we call a chronic relapsing or residual symptom phase where their level of functioning is not very good. And sometimes patients become treatment resistant to the antipsychotics that have worked in the past. This is attributable to progressive brain tissue loss that occurs with every relapse.

We also know that patients with schizophrenia can experience a range of common physical comorbidities. Typically, we think about metabolic abnormalities such as diabetes, metabolic syndrome, but there's also a high risk of hypertension, and respiratory illnesses as well. Patients may be more prone to infectious diseases, perhaps due to lifestyle issues and risks that they engage in. So HIV, certainly a possibility, as well as hepatitis B and hepatitis C. These physical illnesses and disease categories of infectious, respiratory, cardiovascular, and metabolic disorders are consistently more common in people with schizophrenia than the general population. This results in a higher risk of mortality over 2.5 times higher risk of mortality than the general population. And this is based on a meta-

analysis of over 100 studies. It's been estimated that people with schizophrenia have a lifespan that is 10 to 30 years less than people in the general population.

Let's take a look at side effects of treatments for schizophrenia, and see how much of an overall burden is experienced by patients. In a study of about 2,000 participants with psychosis, about 80% reported medication side effects, and about 60% reported impairment in their daily lives as the result of these medication side effects. Roughly a third reported moderate or severe impairment in their daily lives as a result of these medication side effects.

So side effects can be disabling, markedly affect quality of life, and if not addressed early can lead to long-term distress and health complications. We want to do our best to shift their functional status as best we can in order to have these effects on quality of life in the positive direction.

So we have treatments that are not optimal. And we have a disease that is relentless. So we have limitations. And the limitations of our current antipsychotic treatments can be summarized as follows: Treatment resistance which may emerge over time. We do know that a certain percentage of people will no longer respond to the antipsychotics that are based on direct dopamine D2 receptor antagonism, that is, all the antipsychotics we have available so far. Roughly a third to two-thirds of patients have partial response or intolerance to the medications that we use. And a very small percentage of patients actually achieve recovery, that is long-term remission and good functional outcomes. Perhaps this is due to our lack of ability to address negative and cognitive symptoms in a way that we want to. Our medicines are pretty good at reducing hallucinations and delusions, at least their intensity and frequency. They're not as robust in addressing negative and cognitive symptoms, and many of our patients have prominent or predominant negative symptoms.

Comorbidities are a problem, and this is part and parcel of the disease, perhaps because patients with schizophrenia have an underlying disease course that actually makes them more vulnerable for all these comorbidities, and our medicines sometimes make them worse. The adverse effects of medications we certainly can improve upon, discontinuation due to side effects is alarmingly high, and it contributes to reduced life expectancy and stigma as well, and to treatment noncompliance.

Thank you for your attention.

Announcer:

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