Removing Barriers to Clozapine Use

Clozapine is the only effective medication for treatment resistant schizophrenia, with response rates in the range of 40%-60% compared to <5% for other antipsychotics. Although data indicate that use of clozapine increased prescribing more than 2-fold. Moreover, healthcare systems in New York and the Netherlands showed that supporting prescribers facilitates greater clozapine use. Knowledge is indeed power, and clinicians in the U.S. have two new resources to facilitate clozapine prescribing: one is a handbook that I co-authored inspired by the lack of clinically oriented published resource on clozapine; the other is a web-based educational site that (importantly) also provides clinical consultations to registered users (https://smaiadviser.org). This initiative is free, and is sponsored by the American Psychiatric Association and the Substance Abuse and Mental Health Services Administration.

For patients, monitoring burdens may be lessened by a newly approved point-of-care (POC) device that uses a small drop of blood from a finger stick. The first of these devices (http://athelas.com) not only provides results from a finger stick. The first of these devices (http://athelas.com) not only provides results and medication dispensing, and the quantity dispensed matches the interval to the next blood draw. For those on weekly testing, a delay of 24 hours in going to the lab or transmitting lab results places the patient in jeopardy of running out of clozapine.

Yet, there is hope. At the state hospital system to which I consult, a regular lecture series on clozapine increased prescribing more than 2-fold. Moreover, healthcare systems in New York and the Netherlands showed that supporting prescribers facilitates greater clozapine use. Knowledge is indeed power, and clinicians in the U.S. have two new resources to facilitate clozapine prescribing: one is a handbook that I co-authored inspired by the lack of clinically oriented published resource on clozapine; the other is a web-based educational site that (importantly) also provides clinical consultations to registered users (https://smaiadviser.org). This initiative is free, and is sponsored by the American Psychiatric Association and the Substance Abuse and Mental Health Services Administration.

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the impact of delays in receiving the next prescription. Clozapine dispensing is tightly tied to pharmacy notification of blood results, and the quantity dispensed matches the interval to the next blood draw. For those on weekly testing, a delay of 24 hours in going to the lab or transmitting lab results places the patient in jeopardy of running out of clozapine.
Lauren Kennedy
Living Well with Schizophrenia

Lauren experienced a normal childhood, free from trauma. But as a teenager, she struggled with mood problems and apathy. She also experienced thought broadcasting, believing that others could hear her thoughts. Though symptoms caused her to skip classes, she maintained decent grades. These early warning signs went unnoticed.

After high school, Lauren began studying political science and psychology part time at the University of Alberta. A few months into college, at age 19, her boyfriend noticed something was wrong, and convinced her to see a family doctor. She was diagnosed with depression. At that time, she also experienced highs which led to higher productivity, and she embarked upon “adventures,” such as traveling and running in the mountains. For years, she never discussed these elevated moods with her doctor.

In 2011 Lauren decided to pursue a career in social work and transferred to the University of Waterloo in Ontario in order to complete her Bachelor of Arts degree in Social Development Studies. She won several scholarships and awards, and successfully graduated in 2013.

At age 22, Lauren decided to pursue a second bachelor's degree in social work. However, at this time, she began to experience her first thoughts of suicide and sought counseling at the university. Her diagnosis was changed to bipolar disorder, type two.

A few months later, in winter of 2014, she overdosed, which lead to her first hospitalization. On her release, she experienced hallucinations, hearing someone in the distance saying her name. She also sensed terrible smells, which were olfactory hallucinations.

A year after her first hospitalization, Lauren overdosed again. This was a more serious attempt and she was placed on life support for several days.

Following her final hospitalization, Lauren began looking for her “new normal.” She found it especially hard to deal with the stigma of schizophrenia and mood disorder. Lauren benefitted from the Schizophrenia Society of Alberta, where she met others who were thriving despite a psychiatric diagnosis.

Today, Lauren is a successful student in public health and psychology graduate program and once again enjoys working as a research assistant. She lives a meaningful and productive life and has not been hospitalized since October of 2016.

Lauren maintains a YouTube channel called “Living Well with Schizophrenia.” She shares the message that there is no shame in having severe mental illness, and that with medication and treatment, it can be overcome or managed. Although her road to recovery was at times very challenging, today she is thriving. Lauren is living proof that recovery is possible.
Tardive Dyskinesia (TD) was first described in the early 1960s, but we don’t have a clear understanding of why it happens despite nearly 60 years of research. TD does seem to have a clear relationship with dopamine, which regulates a vast number of functions in our bodies, including attention, pleasure-seeking, and motor function. Some psychiatric disorders, including disturbances of mood, sensory perception, and thought processes are believed to be associated with an excess of dopamine stimulation in certain pathways, or “circuits” of the brain.

We often use antipsychotic medications for these symptoms because they are dopamine receptor blockers (DRBs), and thus prevent dopamine from completing the circuit. In hyperactive dopamine circuits, this normalizes function, but DRBs are unable to discriminate between overactive and normal dopamine pathways. Sometimes blocking dopamine can reduce function in pathways it should not, and cause unintended consequences.

The basal ganglia is the part of the brain that is responsible for controlling movements, and is also dependent on dopamine to conduct its signaling. Prolonged use of DRBs can stimulate the basal ganglia to produce too many highly sensitive dopamine receptors. In an attempt to rebalance its diminished dopamine signals, the process may overcompensate for some. The motor system becomes hypersensitive, and dopamine now overstimulates it, resulting in the involuntary movements, or “dyskinesia” that give TD its name. “Tardive” comes from the French word for “late” because it generally takes months or years of exposure to a DRB before the symptoms develop.

Imagine you’re listening to music with a friend, and you think the volume level is normal, but it’s too loud for him. He gets out ear plugs, but puts them in your ears as well. Now you can’t hear the music at all, and you find the ear plugs won’t come out, so you turn the volume way up to compensate. Eventually the ear plugs may malfunction and fall out, and the music sounds unbearably loud. Unfortunately, you find that the volume button is broken, and you can’t turn it down.

The real problem with TD isn’t that it’s delayed after the start of a DRB, it’s that it’s generally irreversible. Not everyone taking a DRB gets TD, but those who do can’t get rid of it by stopping the medication. While some risk factors are known, we don’t yet have a very good way of predicting who is going to get it before it happens. Or in the terms of the analogy above, we don’t know whose earplugs are going to malfunction.

Therefore, we shouldn’t consider TD a “side effect” of DRBs, because side effects go away if you remove the medication that cause them. Rather, we should think of TD as its own syndrome that is cause by exposure to DRBs in vulnerable people. Just like cigarette smoking causes lung cancer in some people – those who get cancer don’t go into remission just because they stop smoking. Improving Tardive Dyskinesia at that point requires its own additional treatment, which I’ll discuss in my next column.

The hippocampus is one of the most critical components of the human brain. It is involved in multiple psychiatric disorders and its volume is smaller due to atrophy in depression, PTSD, Alzheimer’s Disease, and chronic alcoholism but is developmentally hypoplastic (smaller) in schizophrenia. Its functions include:

- Neurogenesis: the dentate gyrus within the hippocampus is a “neurogenic region” where progenitor cells (stem cells) are created throughout adult life, and replenish the brain. In young adults, the hippocampus generates 250,000 baby neurons/month!
- Memory: the hippocampus is the “grand central station” of autobiographical, spatial and episodic memory in the brain. Hippocampal injury can lead to serious amnesia and poor navigation skills. Chronic stress is toxic to the hippocampus and shrinks it.
- Learning: the acquisition and retention of new information.
- Emotions: the hippocampus is a component of the “limbic system” which is associated with emotional regulation, and a dysfunctional hippocampus can disrupt emotional stability.
Long Acting Injectables (LAIs) are an intramuscular formulation of antipsychotic medications which are already available in pill form. These injections were first developed in the United States in the 1970s to ensure continuous delivery of the antipsychotic medication to the brain of a person with schizophrenia who often is unable to take their oral medication regularly, and ends up relapsing and getting re-hospitalized.

There are several reasons why nonadherence with medications is common in schizophrenia:

1) Over 80% are unaware that they are sick and refuse treatment because they believe they do not need it.
2) Memory is impaired in most individuals with schizophrenia, so they actually forget to take their tablets.
3) The paranoid thoughts make them think they are being poisoned if they have a side effect.
4) Alcohol and substance abuse is very common among persons with schizophrenia living in the community, and that interferes with taking prescription medications. Relapse is serious because psychotic recurrence destroys hundreds of millions of brain cells, eventually leading to brain atrophy and permanent disability.

In addition to being very useful in preventing relapse, LAIs are a convenient option because they eliminate the need to take pills every day. Today, several newer antipsychotic medications are available as LAIs that can be given by injection every 4, 6, 8 or even 12 weeks.

VIDEO HIGHLIGHT

Dr. Henry Nasrallah and Bethany discuss LAIs in this four-part video series.

Please consider making a donation to the CureSZ Foundation online at CURESZ.org

Your contribution will help provide education and referrals to persons with schizophrenia, their families, and those who work with the seriously mentally ill. CURESZ informs the general public to better understand this serious brain illness, and to provide scientific advances showing that there is hope for recovery, and a return to a fulfilling and normal life. The CURESZ Foundation is a 501(c)(3) nonprofit organization. All contributions are tax deductible.

“We are committed to helping individuals to cope with and recover from schizophrenia.”

You can now also support the CURESZ Foundation by signing up with Kroger Community Rewards and Amazon Smile.