The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Treating anxious syndromes with pregabalin in patients with psychosis

Nicolas Garel, MD; David Bloom, MD; Ridha Joober, MD, PhD

A 32-year-old woman was admitted with overwhelming auditory hallucinations and suicidal thoughts, with plans to immolate herself to "get rid of the devil living inside her." She had a schizoaffective disorder that had started 4 years previously in the context of a cannabis use disorder. During most of her illness, she experienced religious delusions and auditory hallucinations concomitant to subsyndromal depressive symptoms. She was hospitalized on 2 occasions, each time for many months. She did not tolerate several antidepressant trials and had 1 manic switch after starting sertraline, which led to modifying her diagnosis from schizoaffective disorder depressive type to bipolar type.

Since the onset of her disease, the patient had experienced psychotic symptoms resistant to medication. She initially developed a metabolic syndrome while taking olanzapine 25 mg/d for 5 months. She was then switched to a long-acting antipsychotic. She had partial responses to intramuscular administration of aripiprazole (400 mg every 28 d) and paliperidone (150 mg every 21 d) but did not tolerate flupentixol decanoate. She finally responded to zuclopenthixol decanoate, and her psychosis was controlled at a dose of 200 mg IM every 14 days, but the dose was eventually decreased to 150 mg IM every 14 days owing to bothersome extrapyramidal symptoms. She was also taking lithium 900 mg/d and quetiapine 25 mg/d to promote sleep when she was admitted.

Prior to the current hospitalization, the patient did not use drugs, was compliant with her medication and had normal blood work. She reported that her psychotic symptoms had gradually increased in the last few months as well as concomitant increased levels of anxiety, tension and irritability secondary to ongoing anxious ruminations. She mentioned experiencing anhedonia, sadness and guilt but not changes in her energy level, sleep pattern or appetite. She denied experiencing racing thoughts, increased self-esteem and increased energy toward specific goals.

The patient was diagnosed with a comorbid generalized anxiety disorder (GAD). Given her psychiatric history, antidepressants and benzodiazepines were contraindicated to treat her GAD. Pregabalin, an α2δ subunit agonist of voltage-dependent calcium channels, reducing neurotransmitter release,[1] was started and gradually increase to a dose of 250 mg twice daily. The patient responded after 3 weeks, and her anxiety level decreased significantly. Concomitantly, her psychotic symptoms and her suicidal ideation also decreased significantly.

Pregabalin has been shown to be effective in treating GAD[2] and is a first-line option for GAD in Canadian clinical practice guidelines for anxiety disorder.[3] Pregabalin is not approved for the treatment of GAD in patients with psychosis but has been reported to have a potential role as an off-label add-on treatment for anxiety in schizophrenia.[4,5] Englisch and colleagues[4] showed in an observational case series that pregabalin could significantly reduce anxiety in patients with schizophrenia, leading subsequently to improvements in positive and negative psychotic symptoms. In 2018, the only randomized controlled trial investigating the use of pregabalin for anxiety in patients with schizophrenia found no statistical difference between the pregabalin and the placebo groups in the overall score on the Hamilton Anxiety Scale (HAM-A), but found a significant difference (effect size 0.57, $p = 0.04$) between the groups on the psychic factor of the HAM-A (no difference was seen on the somatic factor) and a greater reduction in the Positive and Negative Syndrome Scale total score.[6] Most common adverse effects were weight gain, dizziness, sedation and increased duration of sleep.[6] Intentional overdose and abuse risks also need to be taken into account when pregabalin is prescribed.[7,8]

Anxiety can elicit significant burden in patients with psychosis and is associated with sleep disturbances, reduced quality of life and increased risk of suicide.[9] It is estimated that between 30% and 62% of patients with schizophrenia experience anxious syndromes.[10] Treating these conditions with pregabalin can be an effective option and could lead to improvement in psychotic symptoms.

Affiliations: From the psychiatry residency program (Garel) and the Douglas Mental Health University Institute (Bloom, Joober), McGill University, Montreal, Que., Canada.

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