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 gave informed consent for the publication of the column.

Add-on lithium for the treatment of unipolar depression: Too often forgotten?

Fabrice Jollant, MD, PhD

A 61-year-old man presented in the emergency department with increasing fatigue and irritability, which had started 2 months prior in the context of urinary retention due to benign prostatic hypertrophy. One month later, he was successfully operated, but his anxiety increased sharply in association with low mood, anhedonia, lack of motivation, poor concentration and decreased sleep and appetite. He had no suicidal intent. A severe major depressive episode was diagnosed.

The patient's history showed more than 10 untreated and undiagnosed episodes of depression lasting anywhere from 1 week to several months. He had no history of suicide attempts, (hypo)manic episodes, delusions or hallucinations. He denied using any drugs. He did not smoke, and he drank alcohol occasionally. Some obsessive–compulsive traits were identified.

Family history revealed that his brother committed suicide at the age of 27. His mother, 2 maternal uncles, and his paternal grandfather all may have suffered from depression.

The patient was admitted full-time to the psychiatric ward for 1 month, followed by day hospitalization for 2 months. He was then treated with up to 40 mg of escitalopram, a recommended first-line antidepressant,[1] and 50 mg of trazodone for sleep. Partial remission was observed for several weeks. Bupropion was then added to improve efficacy, but was soon stopped owing to increased urinary retention. When entering our outpatient program, the patient's self-report Quick Inventory of Depressive Symptomatology (QIDS) scores[2] reached 20 out of 42. Trazodone was replaced by 15 mg and then 30 mg of mirtazapine for its effect on anxiety and sleep, but mirtazapine was then stopped owing to intolerance. Because of lack of improvement after 12 weeks, escitalopram was replaced by venlafaxine XR, another efficient first-line antidepressant,[3] and the dose was gradually increased over 2 months to 375 mg/d. The patient reached a partial remission state (QIDS = 11) but still felt functionally impaired, as confirmed by the Quality of Life Enjoyment and Satisfaction Questionnaire.[4] Of note, the patient was particularly compliant and active in his treatment, which included individual cognitive behavioural therapy and physical activity.

Lithium was then introduced in an augmentation strategy, with a dose of up to 900 mg/d and a plasmatic level of 0.6 mmol/L within 1 month. Lithium, rather than antipsychotics, was used as an add-on agent primarily owing to family history of depression and number of depressive episodes, which have previously been associated with lithium augmentation response.[5] Side effects, including shaking and postural instability, were observed. Depression and quality of life scores started to improve quickly within the following month. Two months after introduction of lithium, full remission was reported. This state was maintained for 12 months and enabled the patient to return to work. Lithium was then discontinued over 3 months, followed by venlafaxine being discontinued over 6 months, with no relapse reported to date.

This patient's case illustrates the potential benefits of lithium in the acute treatment of unipolar depression. Side effects, narrow therapeutic margin and regular blood and urinary screening[6] explain some clinicians' reluctance to prescribe lithium. However, it remains an effective and fast-acting augmentation medication, as revealed by a meta-analysis.[7] The STAR*D study showed that up to 16% of nonresponders at stage 3 could benefit from lithium adjunction.[8] It was recommended as a first-line add-on treatment for unipolar depression by the CANMAT 2009 guidelines,[1] although some reviews have been less supportive.[9] Moreover, augmentation with lithium may also be more cost-effective than augmentation with atypical antipsychotics.[10] Lithium was also confirmed as a potent antisuicidal drug in a recent meta-analysis[11] — a finding that is particularly relevant here given our patient's family history. Lithium should be used at blood levels between 0.5 and 0.8 mmol/L, and sparse data suggest that if efficient, it should be maintained for a period of at least 1 year to avoid recurrence.[12] Finally, although antidepressant mechanisms are largely unknown, support for neuroprotective effects has been convincing.[13] While lithium is not a panacea, the literature supports a broader use of this drug.

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