

# Psychopharmacology for the Clinician

*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.*

## Will lithium damage my kidneys?

A 37-year-old male patient had been feeling predominantly depressed and anxious over the past 15 years. About twice a year, he experienced a self-limited hypomanic episode. He never sought treatment for the hypomanic episodes, and for the past 5 years, he has been maintained on low-dose antidepressant treatment, which he credited for “taking the edge” off his symptoms of depression and anxiety.

The patient was recently admitted to hospital for a severe manic episode with psychotic features. This episode lasted several weeks and caused major disruptions in his life. While in hospital, the patient agreed to pharmacologic treatment of his manic episode. Consistent with the CANMAT guidelines for the treatment of acute bipolar mania, the patient was started on divalproex and an antipsychotic in the emergency room.<sup>1</sup>

A first-degree relative of the patient also had bipolar disorder and was successfully treated with lithium (Li) for more than 15 years. This relative was recently taken off Li owing to concerns about worsening kidney function. Given his relative’s excellent response to Li, the patient wondered if it would be a good option for him. At the same time, he worried about being at increased risk for renal side effects.

Lithium has been used for more than 50 years as an effective pharmacologic agent for the treatment of acute mania and for bipolar disorder.<sup>2–4</sup> Long-term treatment with Li also results in markedly reduced suicidal behaviour and death from all causes in patients with bipolar disorder.<sup>5</sup> Despite recent advances in pharmacotherapy for bipolar disorder, Li is still considered a first-line agent to

manage the condition.<sup>2,6</sup> Concerns about somatic side effects, including effects of Li on the thyroid and kidneys, have contributed to less frequent use of Li in the past few years.

Nephrogenic diabetes insipidus (NDI) is characterized by polydipsia, polyuria and an inability to concentrate the urine. Nephrogenic diabetes insipidus results from unresponsiveness of the kidneys to the effects of antidiuretic hormone (ADH). Polyuria, polydipsia and NDI are frequent complications of treatment with Li that may be present shortly after starting treatment.<sup>7</sup>

Long-term treatment with Li can have a harmful effect on renal function. After more than 10 years of treatment with Li, 15%–20% of patients show signs of renal insufficiency.<sup>8,9</sup> A smaller number go on to experience potentially irreversible renal insufficiency.<sup>10,11</sup> Renal insufficiency can be irreversible even after discontinuation of Li and can ultimately result in the need for hemodialysis.

A variety of histopathologic renal changes, including tubular atrophy, interstitial fibrosis, cysts and glomerular changes, have been described after long-term treatment with Li.<sup>12</sup> These nephrotoxic effects are caused by a Li-induced dysregulation of aquaporin 2 (a membrane protein of the apical cells of the collecting duct that facilitates the reabsorption of water) and the accumulation of cytotoxic concentrations of Li in the collecting ducts of the kidneys.<sup>13</sup>

So far, no tools exist to identify patients at risk for Li-induced nephropathies early.<sup>14</sup> Serial measurements of serum creatinine have traditionally been used as a marker of renal function in patients treated with Li. More recently, serum creatinine has been replaced by estimated glomerular filtration rate (eGFR), which offers a correc-

tion of creatinine levels for age, sex and race. Based on the eGFR, Kripalani and colleagues<sup>15</sup> offer guidelines on monitoring kidney function before and during treatment with Li. They recommend a referral to a nephrologist if the eGFR is moderately or severely decreased. However, the eGFR is an insensitive marker of renal function. Over the next few years, additional markers may help to reliably identify patients at risk for significant renal side effects from Li.

Recent studies suggest that a beneficial therapeutic response to Li runs in families and that children with bipolar disorder respond to the same mood stabilizer as their bipolar parent.<sup>16</sup> Based on his relative’s excellent response to Li, our patient is likely to be a lithium responder. However, little is known about genetic aspects of Li-induced nephropathies.

Given his concerns about his risk for Li-induced nephropathy, the patient decided against a trial on Li. He was willing to consider Li as a treatment option should he fail to achieve ongoing stabilization with his current pharmacologic treatment.

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*Psychopharmacology for the Clinician* columns are usually based on a case report that illustrates a point of interest in clinical psychopharmacology. They are about 650 words long. Columns can include a bibliography which will be available only at the journal website.

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