Letter to the Editor

Diabetes Insipidus Secondary to Combination Atypical Antipsychotic and Lithium Use in a Bipolar Disorder Patient: A Case Report

To the Editor: We describe the case of 27-year-old woman with bipolar disorder who developed symptomatic and laboratory evidence of diabetes insipidus only when lithium was used in combination with risperidone or quetiapine, but not when lithium was used alone. We speculate a mechanism involving renal modulation of the antidiuretic hormone (ADH)–desensitizing effect of lithium by the antipsychotics used. This case highlights the importance of regular renal monitoring and patient inquiry for diabetes insipidus symptoms, especially in the context of combined use of lithium and antipsychotics.

Case report. Ms A, a 27-year-old woman with *DSM-IV* bipolar disorder, type I, had been on lithium treatment for 1 month when first hospitalized and diagnosed in 2007. This was followed by risperidone 3 mg/d for 2 months and paliperidone 6 mg/d intermittently for 8 months. The medications were never taken concurrently. Polydipsia, polyuria, and nocturia had not occurred previously. Her medical history was negative for diabetes mellitus, intracranial pathology, or other potential causes of diabetes insipidus.

In December 2009, after 5 months without medications, she suffered a manic episode; lithium was restarted at 1,050 mg/d and was maintained at serum levels between 0.45 and 0.90 mEq/L. Long-acting injectable risperidone 25 mg every 2 weeks was also initiated. Ten weeks after starting lithium plus long-acting injectable risperidone, she developed polydipsia and nocturia 5–6 times per night (baseline was once per night). Fasting serum glucose level was 3.2 mmol/L, serum sodium level was 143 mmol/L, and urine specific gravity was 1.010. Four weeks following onset of symptoms, long-acting injectable risperidone was discontinued, and Ms A was asked to record her liquid intake and urinary frequency. Three weeks after discontinuation of long-acting injectable risperidone, the nocturia resolved, liquid intake decreased from 3.5 to 1.5 L/d, 12-hour fasting urine osmolality was 750 mOsm/kg, urine specific gravity was 1.020, and serum lithium level was 0.88 mEq/L. Serum sodium level was 137 mmol/L; serum creatinine level was 57 µmol/L; serum prolactin, glucose, thyroid-stimulating hormone, calcium, and phosphate levels were within normal limits; and head computed tomography revealed no abnormalities.

The patient agreed to a rechallenge with risperidone 0.25 mg/d. Five days later, nocturia 4–6 times per night recurred. After 4 nights of symptoms, urine osmolality was 550 mOsm/kg (< 600 mOsm/kg), urine specific gravity was 1.015, lithium level was 0.75 mEq/L, and serum osmolality was 297 mOsm/kg. Symptoms resolved within 2 days of risperidone discontinuation. A few weeks later, quetiapine 25 mg each night was started for insomnia. Within 1 week, nocturia 3 times per night recurred, but resolved with discontinuation. Three weeks after quetiapine was discontinued, urine osmolality was 845 mOsm/kg, urine specific gravity was 1.025, serum lithium level was 0.92 mEq/L, and serum sodium level was 139 mmol/L. Throughout, Ms A's bipolar I disorder remained in remission. A fine tremor was consistently observed, but there was no evidence of lithium toxicity or hypernatremia.

Lithium-induced diabetes insipidus is characterized by decreased urinary concentrating ability and polyuria. Polydipsia or nocturia can also be present. In patients taking lithium long-term, the prevalences of polyuria (> 3 L/24 h), urine osmolalities less than 300 mOsm/L, and reduced renal concentrating ability (urine osmolality < 500–800 mOsm/L) are 19%, 12%, and 50%,[1] respectively. Antipsychotic use has not been shown to be an independent risk factor for lithium-associated diabetes insipidus,[2] despite the common coprescription of lithium and antipsychotics.

In our patient, the onset of polydipsia/nocturia with lithium plus antipsychotic use, resolution of symptoms/laboratory findings outside normal limits with antipsychotic discontinuation, and recurrence with antipsychotic rechallenge are highly suggestive of diabetes insipidus induced by the combination of lithium and an antipsychotic. Serum lithium levels were lower during polyuria, so renal elimination was most likely not reduced by the antipsychotics. We speculate that the mechanism of polyuria involved modulation of the ADH-desensitizing effect of lithium by risperidone/quetiapine renally.

In summary, this case emphasizes the importance of regular renal monitoring and patient inquiry for diabetes insipidus symptoms, especially in the common clinical setting when lithium and antipsychotics are coprescribed. Vigilance for potential long-term renal compromise needs to be balanced with clinically sound bipolar disorder management.

References

1. Boton R, Gaviria M, Batlle DC. Prevalence, pathogenesis, and treatment of renal dysfunction associated with chronic lithium therapy. *Am J Kidney Dis*. 1987;10(5):329–345.
2. Movig KL, Baumgarten R, Leufkens HG, et al. Risk factors for the development of lithium-induced polyuria. *Br J Psychiatry*. 2003;182(4):319–323.

Soham Rej, MD
soham.rej@mail.mcgill.ca
Howard C. Margolese, MD, MSc, FRCPC
Nancy C. P. Low, MD, MSc

Author affiliations: Department of Psychiatry, McGill University, Montreal, Quebec, Canada.

Potential conflicts of interest: **Dr Margolese** has received grant/research support from Pfizer, Bristol-Myers Squibb, and Janssen; has received honoraria from Pfizer, Bristol-Myers Squibb, and Novartis; and has been on speakers or advisory boards for Novartis and Janssen. **Drs Rej** and **Low** report no potential conflicts of interest relevant to the subject of this letter.
Funding/support: **Dr Low** holds a Clinical Research Scholar Salary Award from the Health Research Foundation of Quebec (Fonds de la recherche en santé du Quebec) and the T. H. P. Molson Fellowship from the Research Institute of the McGill University Health Centre.
Published online: July 21, 2011 (doi:10.4088/PCC.11l01138).
Prim Care Companion CNS Disord 2011;13(4):doi:10.4088/PCC.11l01138