Prevalence and Correlates of Renal Disease in Older Lithium Users: A Population-Based Study

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Objective: *Lithium is an important treatment for mood disorders, but concern about its association with renal disease has contributed to its limited use, particularly in older adults. Because high-quality evidence examining renal disease in this population is lacking, this study aims to quantify the prevalence and identify clinical correlates of renal disease in geriatric lithium users.* **Methods:** *In a population-based cross-sectional study on 2,480 lithium users aged 70 or more years, the authors searched the provincial administrative health data from Ontario, Canada between April 1, 2005 and March 31, 2011. Prevalence of chronic kidney disease (CKD), acute kidney injury (AKI), and nephrogenic diabetes insipidus (NDI) was measured using* International Classification of Diseases, Tenth Revision *codes. Logistic regression analyses were used to identify independent correlates of renal disease.* **Results:** *The 6-year prevalence rates of CKD, AKI, and NDI were 13.9%, 1.3%, and 3.0%, respectively. Hypertension (odds ratio [OR]: 2.05; 95% confidence interval [CI]: 1.50−2.79), diabetes mellitus (OR: 1.86; 95% CI: 1.45−2.38), ischemic heart disease (OR: 1.65; 95% CI: 1.24−2.20), NDI (OR: 2.54; 95% CI: 1.47−4.40), AKI (OR: 11.7; 95% CI: 5.26−26.1), lithium use for more than 2 years (OR: 1.71; 95% CI: 1.05−2.81), loop diuretic use (OR: 1.74; 95% CI: 1.26−2.41), hydrochlorothiazide use (OR: 1.48; 95% CI: 1.07−2.05), and atypical antipsychotic use (OR: 1.49; 95% CI: 1.17−1.89) were all independently associated with CKD.* **Conclusion:** *Older lithium users have high rates of CKD. Lithium use duration was independently associated with CKD. Longitudinal studies including individuals without lithium exposure will be necessary to confirm whether lithium is indeed a risk factor for CKD in older adults.* (Am J Geriatr Psychiatry 2014; ■:■−■)

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INTRODUCTION

Lithium remains an essential treatment in bipolar disorder and unipolar depression.[1] It is less expensive and is likely more effective than other treatments[2,3] in preventing mood disorder relapse, suicide,[4] and subsequent use of acute psychiatric services.[3] Moreover, all consensus guidelines and treatment algorithms for mood disorders include lithium as a first-line mood stabilizer. Despite this, lithium prescriptions have markedly decreased for older mood disorder patients,[5,6] in large part due to its perceived association with adverse renal events, including chronic kidney disease (CKD, previously chronic renal failure), acute kidney injury (AKI, previously acute renal failure), and nephrogenic diabetes insipidus (NDI).[7] Elderly users of lithium have a high burden of comorbid conditions,[8] including hypertension, diabetes, and cardiovascular disease, which increases their susceptibility to AKI and CKD. Both AKI and CKD have been associated with an increased risk of hospitalization, need for dialysis, and death.[7]

In spite of these potentially serious renal consequences and concomitant clinical concerns affecting practice, very little high-quality evidence addresses the relationship between lithium and renal disease in the elderly. Previous studies have been largely cross-sectional, have included small sample sizes ($N < 100$) of almost exclusively nongeriatric lithium users treated at tertiary care centers, and have failed to demonstrate a clear association between lithium use and chronic renal disease.[7,9] In the available literature, renal disease prevalence estimates have varied widely, from 1.2% to 85%. Clinicians are thus faced with the dilemma of balancing the potential for renal injury associated with the use of lithium and the risks of mood episode relapse,[3,10] impaired functioning, and suicide risk,[2,3] which may occur with its discontinuation. As a result, in older lithium users there is a pressing need to better characterize the burden of renal disease and identify high-risk groups using large population-based studies.[11]

The objective of this study was to estimate the prevalence of and describe the clinical correlates of renal disease in a cohort of lithium-using older adults. We expected CKD prevalence in older lithium users to be higher than the 1.2% rate cited in the *Lancet*.[9,12] We also hypothesized that CKD would be independently associated with some or all factors previously described in the literature: lithium variables[7] (duration, dose, and long-acting formulation), increased age,[13] medical comorbidity[7] (diabetes, hypertension, cardiovascular disease), and concurrent medication use (diuretics, angiotensin-converting enzyme [ACE] inhibitors,[14] nonsteroidal anti-inflammatory drugs [NSAIDs], antipsychotics,[15] and other psychotropic medications[16]). We also examined whether CKD was associated with exploratory variables (prescribing by a family physician versus a psychiatrist, being a long-term care resident).

METHODS

Design, Setting, and Participants

This was a population-based cross-sectional analysis of multiple linked healthcare databases in Ontario, Canada, using data from April 1, 2005 to March 31, 2011. Ontario is Canada's largest province, with a population of 13 million, of whom 1.3 million are aged 70 years and older. Ontarians have access to provincially subsidized hospital care and physician services as well as outpatient prescription drug coverage for individuals over age 65 years. Ethics approval was obtained from Sunnybrook Health Sciences Centre's Research Ethics Board for this study. Data sets were held securely in a linkable, de-identified form and analyzed at the Institute for Clinical and Evaluative Sciences.

Data Sources and Study Cohort

Drug use data were obtained from the Ontario Drug Benefit database, which records all outpatient prescription drugs dispensed through the provincial health insurance program. The Ontario Health Insurance Plan database contains information from all outpatient and inpatient physician billing claims, including primary diagnoses given during health appointments. The Canadian Institute for Health Information Discharge Abstract Database contains discharge information on all acute care hospitalizations, including diagnoses and length of stay. The National Ambulatory Care Reporting System records data from all emergency department visits in