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Letter to the Editor

Lithium Nephrotoxicity: When Is the Time for Nephrology Consultation?

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Dear Editor-in-chief

End-stage renal disease (ESRD) is one possible consequence of chronic kidney disease (CKD) that causes costly renal replacement therapy in the context of dialysis or kidney transplantation. Improved awareness of CKD risk factors has led to decrease the incidence of ESRD in developed countries, whereas no tangible change is being observed in developing countries (1).

A rising body of evidence advocates that the lack of adequate care exist among people with mental illnesses. The average life span of patients with severe mental disorder is 25 years less than that of the general population, and 60% of premature deaths arises from preventable reasons. Patients with mental illness have fewer regular preventive facilities, poorer diabetic control, lower number of cardiovascular procedures performed, and less compliance with renal replacement therapy (2).

Considering that lithium therapy could be a hidden risk factor contributing to renal dysfunction in bipolar affective disorder, investigating and heightened awareness of lithium renal abnormalities are warranted (3).

This study was performed in the Iran Psychiatry Hospital in Tehran, Iran. This cross sectional study was approved by Ethics Committee of Iran University of Medical Sciences. All cases provided written informed consent before study registration.

Patients with a diagnosis of bipolar disorder (ICD, 10th edition), over the age of 18 yr who underwent lithium therapy for at least 3 months were included. Patients were excluded if they had diabetic nephropathy, hypertension, renal failure, and history of NSAID, ACEIs or ARB and diuretic use.

Data on duration of lithium therapy, urine osmolarity, serum calcium concentration, serum creatinine and BUN were collected. Polyuria was defined as urine volume above 3 L /24 h. Hypercalcemia was defined as a serum calcium concentration ≥ 10.4 mg/dL. Urine osmolarity ≤350 mosm/L was considered abnormal. Estimated Glomerular Filtration Rate (eGFR) was applied to classify kidney disease staging which was calculated using the Cockcroft and Gault formula (4). Stages of CKD were defined according to the National Kidney Foundation criteria (K/DOQI Clinical Practice Guidelines).

Fifty-five patients were enrolled in the study. No statistically significant differences were observed

between the two groups in terms of demographic data and clinical characteristics. The estimated mean dose of lithium carbonate was 954 ± 522 mg. Mean lithium therapy duration was 83.38 ± 11.00 months.

Polyuria was observed in 10/55 of patients. Hypercalcemia was observed in 9/55 of patients. Abnormal urine osmolarity was detected in 46/55 of patients. Stage 2 and 3 of CKD were identified in 14/ 55 and 1/55 of patients, respectively.

Patients who received lithium for a longer time had significantly lower eGFR. Furthermore, relation between duration of lithium therapy and reduced urine osmolarity was significant. Patients who treated by higher daily dose of lithium had significantly lower eGFR and diminished urine osmolarity, respectively. Higher stages of CKD were directly correlated with the duration of lithium therapy.

In this study, patients who underwent lithium therapy were at risk for various types of renal abnormalities including CKD. About 84% of our patients had polyuria and diminished urine osmolarity which might be due to lithium induced nephrogenic diabetes insipidus or in the course of CKD progression. Stage 2 and 3 of CKD were observed in 25% and about 2% of patients, respectively. In a recent study, the prevalence of stage 1-2 and 3-4 CKD were 10.63% and 8.89% in northeast Iran, respectively (5). According to this data, the prevalence of lithium induced CKD seems to be high. It appears that one the important aspects of this problem stems from inadequate provision of medical care.

Suboptimal renal support and lower access to nephrologists in patients with mood disorder were associated with their higher risk for hospital admission and mortality. In fact, profound health problems of mental disorder patients can usually be related to overlooked physical condition (6).

Lithium has long been recognized as a cornerstone in the treatment of bipolar affective disorder. The nephrotoxic effects of lithium include decreased urinary concentrating ability that could occur about eight weeks after lithium therapy and CKD detected after long-term administration (3). These findings reveal the need for paying more attention to patients.

In patients receiving lithium therapy, regular measurements of serum creatinine, calcium concentration, urine analysis and close monitoring of serum lithium level should be considered to detect alterations in renal function. Psychiatrists and nephrologists should be aware that the patients with bipolar affective disorder treated by lithium have low access to health screening, and insufficient renal support. Close multidisciplinary collaboration to improve health care access and the quality of renal care are mandatory.

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