Lithium is a trace element that has been commonly used in treating bipolar affective disorder for years (1). Lithium therapy causes renal failure, several endocrine and metabolic abnormalities, such nephrogenic diabetes insipidus, thyroid abnormalities, and hypercalcemia (2-4). Despite the renal and endocrine disturbances, it has been demonstrated that a micro-dose of lithium may have anti-aging and anti-dementia effects in addition to its anti-suicidal efficacy (5). A micro-dose of lithium could also have an ameliorative impact on preventing cognitive loss (5). Hypercalcemia could be a side effect of acute or chronic Lithium therapy. In the short term, lithium effects on calcium-sensing receptors and glycogen synthase kinase 3 cause hypercalcemia, however this condition is potentially reversible (5). In contrast, after chronic long-term lithium therapy, hypercalcemia is due to permanent alteration of parathyroid glands, which leads to hyperparathyroidism through a parathyroid adenoma or a four glands parathyroid hyperplasia (3). Chronic reduction of glomerular filtration rate, acute kidney injury (AKI), proteinuria/nephrotic syndrome, polyuria, nephrogenic diabetes insipidus, and distal renal tubular acidosis are common renal side effects of lithium therapy. Renal histologically of chronic lithium nephrotoxicity is perceived by the presence of microcyst formation and interstitial nephritis, which can be accompanied by focal segmental glomerulosclerosis (2,4). Although polyuria can be due to hypercalcemia, this drug can directly stimulate polyuria with the exact mechanism (6,7). Graziani et al reported a case of AKI and nephrotic syndrome following Li therapy, in which renal histology was compatible with minimal change disease. Both AKI and nephrotic syndrome improved with the withholding of lithium (8). Łukawska et al also presented a 49-year-old woman who developed nephrotic syndrome following lithium administration and spontaneously resolved following the drug discontinuation (9). The hypercalcemia right after lithium therapy has biochemical features like familial hypocalciuric hypercalcemia, while hypercalcemia of chronic Li therapy has the characteristics of primary hyperparathyroidism (3). Hyperparathyroidism, particularly in chronic lithium therapy cases, is accompanied by higher morbidity. In summary clinical administration of lithium could be problematic according to its limited therapeutic index and lithium toxicity in different organs. Early detection of lithium-related hypercalcemia and primary hyperparathyroidism will ameliorate patients’ situations. Besides, regular serum calcium and PTH assessment in individuals on lithium therapy is strongly recommended.

Implication for health policy/practice/research/medical education
Lithium is a trace element that has been commonly used in treating bipolar affective disorder for years. Lithium therapy causes renal failure, several endocrine and metabolic abnormalities, such nephrogenic diabetes insipidus, thyroid abnormalities, and hypercalcemia. Early detection of lithium-related hypercalcemia and primary hyperparathyroidism will ameliorate patients’ situations. Besides, regular serum calcium and parathormone assessment in individuals on lithium therapy is strongly recommended.

Keywords: Lithium toxicity, Bipolar affective disorders, Parathyroid glands, Focal segmental glomerulosclerosis, Interstitial nephritis, Acute kidney injury


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