



Lithium therapy and parathyroid gland interaction

Ramin Tolouian¹ , Azar Baradaran^{2*}

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 as 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

Please cite this paper as: Tolouian R, Baradaran A. Lithium therapy and parathyroid gland interaction. *J Parathyroid Dis.* 2022;10:e11178. doi: 10.34172/jpd.2022.11178.

Copyright © 2022 The Author(s); Published by Nickan Research Institute. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

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 as 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 micro-cyst 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.

Authors' contribution

Conceptualization and validation: AB; Research, data curation, writing—original draft preparation, writing—reviewing and editing, visualization, supervision: AB & RT.

Conflicts of interest

AB is a researcher at Nickan Research Institute. However, the process of peer-review was not affected by her job.

Received: 24 September 2022, Accepted: 29 October 2022, ePublished: 1 November 2022

¹Division of Nephrology, Southern Arizona VA Health Care System and University of Arizona College of Medicine, Tucson, Arizona, USA.

²Nickan Research Institute, Isfahan, Iran.

*Corresponding author: Prof. Azar Baradaran, Email: azarbaradaran@yahoo.com, azarbaradaran@med.mui.ac.ir

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Terao T. Is lithium potentially a trace element? *World J Psychiatry*. 2015;5:1-3. doi: 10.5498/wjp.v5.i1.1.
2. Gong R, Wang P, Dworkin L. What we need to know about the effect of lithium on the kidney. *Am J Physiol Renal Physiol*. 2016;311:F1168-F1171. doi: 10.1152/ajprenal.00145.2016.
3. Mifsud S, Cilia K, Mifsud EL, Gruppeta M. Lithium-associated hyperparathyroidism. *Br J Hosp Med (Lond)*. 2020;81:1-9. doi: 10.12968/hmed.2020.0457.
4. Hoekstra R, Lekkerkerker MN, Kuijper TM, Bosch TM, van Alphen AM. Renal function after withdrawal of lithium. *Bipolar Disord*. 2022;24:667-670. doi: 10.1111/bdi.13178.
5. Zarse K, Terao T, Tian J, Iwata N, Ishii N, Ristow M. Low-dose lithium uptake promotes longevity in humans and metazoans. *Eur J Nutr*. 2011;50:387-9.
6. McCann SM, Daly J, Kelly CB. The impact of long-term lithium treatment on renal function in an outpatient population. *Ulster Med J*. 2008;77:102-5.
7. Tredget J, Kirov A, Kirov G. Effects of chronic lithium treatment on renal function. *J Affect Disord*. 2010;126:436-40.
8. Graziani R, Monti M, Sejdiu B, Gozzetti F, Martelli D, Tampieri E, et al. Minimal change disease during lithium therapy: case report. *G Ital Nefrol*. 2019;36:2019-vol4. [Italian].
9. Łukawska E, Frankiewicz D, Izak M, Woźniak A, Dworacki G, Niemir ZI. Lithium toxicity and the kidney with special focus on nephrotic syndrome associated with the acute kidney injury: A case-based systematic analysis. *J Appl Toxicol*. 2021;41:1896-1909. doi: 10.1002/jat.4167.