

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Lithium-induced hypercalcaemia

Lithium carbonate, a commonly prescribed mood stabilizer, has significant metabolic and endocrine adverse effects. Although thyroid dysfunction is the most widely recognised endocrine side effect, hypercalcaemia with laboratory evidence and symptoms of hyperparathyroidism occurs in approximately 10-15% of lithium-treated patients.

Parathyroid dysfunction can present with fatigue, delirium, abdominal pain, constipation, renal calculi and osteoporosis. The biochemical changes occurring in lithium-induced hyperparathyroidism are similar but not identical to those that occur in sporadic primary hyperparathyroidism. The serum calcium concentration is mildly elevated and parathyroid hormone (PTH) is usually elevated or inappropriately normal for the concomitant serum calcium level. Other findings are also suggestive of hyperparathyroidism that is lithium-induced (uncommon in primary hyperparathyroidism) include a normal serum phosphate level and an elevated magnesium concentration. Hyperparathyroidism associated with lithium therapy seems to be unrelated to lithium concentration, duration of treatment or cumulative dose.

The exact mechanism causing hypercalcaemia and hyperparathyroidism in patients receiving lithium treatment is not known but several hypotheses have been proposed. Lithium blocks the entry of calcium into various cells by competitively inhibiting calcium transport across cell membranes. Thus, hypercalcaemia may result from the inhibition of calcium influx.

A second possibility is that lithium raises the threshold of the calcium sensing receptor within the parathyroid gland, thus increasing the plasma concentration of calcium required to suppress PTH secretion. Consequently, PTH secretion continues despite elevated calcium levels. Lithium also inhibits the production of inositol monophosphate (IMP), a cellular messenger which regulates calcium exposure to the calcium sensing receptor in parathyroid cells. Depletion of IMP reduces the amount of calcium reaching the calcium sensing receptor, thus altering the set-point for PTH gene transcription and causing more PTH to be produced.

Lastly, it is postulated lithium may induce morphological changes in the parathyroid gland, leading to hyperplasia or adenoma formation, which can cause persistent hyperparathyroidism despite lithium cessation.

Current guidelines do not specifically mention the monitoring of calcium levels with lithium therapy. However, periodic monitoring of serum calcium is warranted in patients taking lithium and hypercalcaemia should be considered in any patient who develops any of the aforementioned symptoms. Patients who are known to have hypercalcaemia or hyperparathyroidism prior to the initiation of a mood stabilizer should probably not be treated with lithium.

In most cases, lithium induced hypercalcaemia and hyperparathyroidism resolves once lithium is ceased, but in some cases parathyroidectomy may be required.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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