BRITISH JOURNAL OF HOSPITAL MEDICINE

REVIEW

Lithium-associated hyperparathyroidism

Simon Mifsud[1]

Kyle Cilia[2]

Emma L Mifsud[2]

Mark Gruppetta[1]

Author details can be found at the end of this article

Correspondence to:
Simon Mifsud;
mifsudsimon@hotmail.com

Abstract

Lithium is a mood stabiliser widely used in the treatment and prophylaxis of mania, bipolar disorders and recurrent depression. Treatment with lithium can give rise to various endocrine and metabolic abnormalities, including thyroid dysfunction, nephrogenic diabetes insipidus and hypercalcaemia. Lithium may induce hypercalcaemia through both acute and chronic effects. The initial acute effects are potentially reversible and occur as a result of lithium's action on the calcium-sensing receptor pathway and glycogen synthase kinase 3, giving rise to a biochemical picture similar to that seen in familial hypocalciuric hypercalcaemia. In the long term, chronic lithium therapy leads to permanent changes within the parathyroid glands by either unmasking hyperparathyroidism in patients with a subclinical parathyroid adenoma or possibly by initiating multiglandular hyperparathyroidism. The latter biochemical picture is identical to that of primary hyperparathyroidism. Lithium-associated hyperparathyroidism, especially in patients on chronic lithium therapy, is associated with increased morbidity. Hence, regular monitoring of calcium levels in patients on lithium therapy is of paramount importance as early recognition of lithium-associated hyperparathyroidism can improve outcomes. This review focuses on the definition, pathophysiology, presentation, investigations and management of lithium-associated hyperparathyroidism.

Key words: Adenoma; Cinacalcet; Hypercalcaemia; Hyperparathyroidism; Hyperplasia; Lithium

Submitted: 28 July 2020; accepted following double-blind peer review: 30 July 2020

Introduction

Lithium-induced hypercalcaemia is characterised by elevated calcium levels that occur chronically or intermittently. This hypercalcaemia arises as a result of lithium-associated hyperparathyroidism – an ill-defined endocrinopathy that consists of a spectrum of biochemical abnormalities. These range from overt hyperparathyroidism to hypercalcaemia with inappropriately normal parathyroid hormone levels and normocalcaemia with raised parathyroid hormone levels in patients on concomitant lithium therapy. The common feature within this spectrum is the presence of a raised or an inappropriately normal parathyroid hormone level (Szalat et al, 2009; Dorflinger and Fuller, 2019).

Lithium-associated hyperparathyroidism cannot be diagnosed based on symptoms and signs alone, as the underlying psychiatric illness may mask or make such presenting complaints difficult to interpret. Hence, regular monitoring of corrected serum calcium levels is needed for earlier detection of these cases.

This review is based upon literature found in MEDLINE (PubMed) from 1973 to June 2020. The keywords used for the search were: 'lithium', 'hypercalcaemia' and 'hyperparathyroidism'. Additional literature was obtained from reference lists. This review explores and outlines the definition and management of lithium-associated hyperparathyroidism.

Pathophysiology

Lithium induces alterations to parathyroid hormone dynamics. Lithium exerts these initial effects by interacting with the calcium-sensing receptor (CaSR) and its intracellular signal transduction system at the level of the parathyroid glands and the kidneys (Szalat et al, 2009).

The CaSR is a G-protein coupled receptor that is primarily expressed in the parathyroid glands and the kidneys. When the CaSR and its intracellular signal transduction system is activated, it inhibits further parathyroid hormone secretion by the parathyroid chief cells and reduces further renal tubular calcium reabsorption in the renal thick ascending limb of the loop of Henle.

How to cite this article:
Mifsud S, Cilia K, Mifsud EL, Gruppetta M. Lithium-associated hyperparathyroidism. Br J Hosp Med. 2020. https://doi.org/10.12968/hmed.2020.0457

Lithium is a monovalent cation that acts as a weak activator of the CaSR (Szalat et al, 2009). However, patients with lithium-associated hyperparathyroidism tend to exhibit elevated levels of parathyroid hormone and hypocalciuria – biochemical findings that are not in keeping with CaSR activation. Several studies have also identified that lithium interferes with the intracellular cascade of reactions brought on by activation of G-protein coupled receptors, including CaSR. Lithium is a potent and uncompetitive inhibitor of inositol monophosphatase which converts inositol monophosphate to inositol (Lenox and Wang, 2003). In addition, it also inhibits inositol polyphosphatase, which converts inositol biphosphate to inositol monophosphate (Lenox and Wang, 2003). By inhibiting these intracellular enzymes, lithium blocks the intracellular cascade of reactions brought about by CaSR activation. Hence, the end result is that lithium inhibits the CaSR, as the strong and uncompetitive inhibitory effect of lithium on inositol monophosphatase outweighs its weaker activation of the CaSR (Szalat et al, 2009).

By inhibiting the CaSR, lithium increases the set point at which the parathyroid cells slow and stop secreting parathyroid hormone. Thus, the parathyroid cells in lithium-treated patients have a reduced sensitivity to serum calcium levels (Haden et al, 1997).

In addition, by inhibiting the CaSR at the level of the kidney, lithium leads to increased renal tubular calcium reabsorption irrespective of the parathyroid hormone and serum calcium levels, leading to hypercalcaemia and hypocalciuria. This scenario is very similar to that found in patients with familial hypocalciuric hypercalcaemia. However, many patients with lithium-associated hyperparathyroidism also exhibit hypercalciuria and in some instances even renal calculi, thus challenging the concept that lithium inhibits the CaSR (Szalat et al, 2009). Nonetheless, hypercalciuria may be encountered in some families with familial hypocalciuric hypercalcaemia (Carling et al, 2000). In addition, hypercalciuria may also signify that permanent parathyroid gland pathology may have been present or may have occurred in patients taking chronic lithium therapy (Szalat et al, 2009).

Furthermore, lithium inhibits glycogen synthase kinase 3 (Meehan et al, 2018), which is responsible for inhibition of parathyroid hormone gene transcription. Hence, by inhibiting glycogen synthase kinase 3, lithium allows overproduction of parathyroid hormone (Ballehaninna et al, 2011).

Apart from the above acute effects of lithium therapy on the parathyroid chief cells and thick ascending limb of the loop of Henle, chronic lithium therapy may lead to increased parathyroid mass (Mallette et al, 1989). This may result from hyperplastic or adenomatous change caused by chronic lithium exposure. This leads to chronic and persistent effects that are identical to primary hyperparathyroidism, which become independent of the presence or absence of lithium (McHenry and Lee, 1996). The latter effects can lead to serious end-organ damage just like that seen in primary hyperparathyroidism (McHenry and Lee, 1996).

The type and extent of glandular pathology as a result of lithium therapy is a subject of debate – is it a uniglandular disease or a multiple gland disease? Uniglandular disease is defined by the presence of abnormal growth in only one parathyroid gland, with the three remaining glands uninvolved. Multiple gland disease refers to cases where abnormal growth occurs in more than one parathyroid gland. Most commonly this involves parathyroid hyperplasia, and to a lesser extent multiple adenomas. The concept of multiple adenomas is also controversial as some studies suggest that multiple parathyroid adenomas are a distinct entity, while others propose that they represent a form of asynchronous four-gland hyperplasia (Ghandur-Mnaymneh and Kimura, 1984; Barczyński et al, 2015).

Lithium may unmask frank hyperparathyroidism in a subset of patients with an underlying subclinical parathyroid adenoma (Blackburn and Diamond, 2007). A study by Saxe and Gibson (1991) revealed that lithium in therapeutic doses increased tritiated thymidine incorporation into adenoma cells. The tritiated thymidine incorporation serves as a measure of DNA synthesis, implying that lithium serves as a mitogen for human parathyroid adenoma formation and could promote or accelerate hyperparathyroidism.

However, lithium-associated hyperparathyroidism may also be associated with double adenomas and parathyroid hyperplasia (Awad et al, 2003; Aksakal et al, 2015). Most studies suggest that there is a higher prevalence of multiple gland disease in patients with lithium-associated hyperparathyroidism than in those with idiopathic sporadic hyperparathyroidism (Dwight et al, 2002; Hundley et al, 2005; Marti et al, 2012). Furthermore, Dwight et al

Table 1. Parathyroid gland pathology in patients on lithium therapy

Findings	References
Single parathyroid adenoma	Garfinkel et al (1973), Ananth and Dubin (1983), Abdullah et al (1999), Awad et al (2003), Shen et al (2007), Carchman et al (2008), Pamathy et al (2018)
Multiple gland disease	Nordenström et al (1992), Wolf et al (1997), Dieserud et al (2001), Dwight et al (2002), Hundley et al (2005), Rizwan and Perrier (2009), Szalat et al (2009), Järhult et al (2010), Marti et al (2012), Norlén et al (2014)

(2002) support the hypothesis that lithium may initiate multiglandular hyperparathyroidism. Moreover, Skandarajah et al (2011) also suggest that lithium-associated hyperparathyroidism is predominantly a multiglandular disease, characterised by asymmetrical hyperplasia. Table 1 summarises the findings of published literature on parathyroid gland pathology in patients on lithium therapy.

Interestingly, a study by Nordenström et al (1992) revealed that the median duration of lithium therapy for patients with hyperparathyroidism secondary to a parathyroid adenoma was 3 years. On the other hand, patients with hyperparathyroidism secondary to parathyroid hyperplasia had a median duration of 13 years of lithium therapy. These results indicate that parathyroid hyperplasia or multiple gland disease may be induced by chronic exposure to lithium therapy (Nordenström et al, 1992). Hence, this observation highlights the fact that lithium-treated patients with an underlying parathyroid adenoma may present with hyperparathyroidism earlier than those with multiple gland disease.

Symptoms and signs

Most patients with lithium-associated hyperparathyroidism tend to have mild hypercalcaemia and are usually asymptomatic (Khandwala and Van Uum, 2006).

Another study by Nordenström et al (1994) concluded that most of the patients treated with chronic lithium therapy who had biochemical hyperparathyroidism did not exhibit clinical signs of primary hyperparathyroidism and had no evidence of reduced bone mineral density. A 2-year study on the effect of lithium therapy on bone mineral density also revealed that despite elevated levels of parathyroid hormone, the study population exhibited reduced bone resorption (Mak et al, 1998).

It is interesting to note that patients with normocalcaemic primary hyperparathyroidism appear to have increased bone resorption with osteopenia and osteoporosis and increased fracture risk (Díaz-Soto et al, 2012). Hence, the latter finding is the opposite to the former two studies with lithium-associated normocalcaemic hyperparathyroidism. This suggests that lithium therapy might actually preserve bone mass. In fact, a study by Zamani et al (2009) found that there is a lower bone turnover state in patients receiving lithium therapy.

Other studies suggest that lithium-associated hyperparathyroidism is associated with reduced bone mineral density and increased fracture risk (Albert et al, 2015; Hanna et al, 2019). Thus there is conflicting evidence on the matter and further studies are required.

Thus the presence of symptoms is not typical in patients with lithium-associated hyperparathyroidism. Symptoms may highlight the presence of serious end-organ damage from hyperparathyroidism, either from underlying subclinical parathyroid gland pathology unmasked by lithium or as a result of parathyroid gland pathology secondary to chronic lithium stimulation (McHenry and Lee, 1996). Physicians should have a low threshold for serum calcium level assessment in patients who complain of loin to groin pain, haematuria, generalised aches and pains, constipation, polyuria and polydipsia or worsening neuropsychiatric symptoms.

Investigations and diagnosis

Patients on lithium therapy who present with hypercalcaemia should first have their hypercalcaemia confirmed by repeating serum calcium and albumin measurements.

Hypercalcaemia is confirmed when corrected serum calcium levels are repeatedly and persistently elevated. These patients should be assessed for any symptoms and signs of hypercalcaemia and have their previous and current drug history thoroughly evaluated. The following investigations should also be performed to establish the aetiology of the hypercalcaemia:

- Parathyroid hormone
- Parathyroid hormone-related protein
- Serum creatinine
- 1,25-dihydroxyvitamin D
- 25-hydroxyvitamin D
- 24-hour urine creatinine and calcium
- Serum magnesium
- Serum phosphate.

Lithium-associated hyperparathyroidism consists of a spectrum of biochemical abnormalities ranging from overt hyperparathyroidism, hypercalcaemia with inappropriately normal parathyroid hormone levels and normocalcaemia with raised parathyroid hormone levels in patients on concomitant lithium therapy. Hence, it is characterised by the presence of a raised or inappropriately normal parathyroid hormone level. Additional findings include a low parathyroid hormone-related protein level, normo- or hypermagnesaemia, normophosphataemia and hypocalciuria in the absence of any other cause. The differential diagnosis for the above mentioned findings include hypovitaminosis D, familial hypocalciuric hypercalcaemia, thiazide-associated hypercalcaemia and primary hyperparathyroidism with concomitant hypovitaminosis D (Griebeler et al, 2016).

However, as mentioned, there are instances where there is hypercalciuria in lithium-associated hyperparathyroidism (especially in patients on chronic lithium therapy with underlying or induced parathyroid gland pathology). In this case, the differential diagnoses include sporadic primary hyperparathyroidism (Afzal and Kathuria, 2020).

Management

Achieving normocalcaemia in patients with lithium-associated hyperparathyroidism may be challenging. There is a lack of clear guidance with regards to the management of lithium-associated hyperparathyroidism, and medical and surgical approaches have been used to manage it. In most reported cases, surgery is the mainstay of treatment for lithium-associated hyperparathyroidism (Nordenström et al, 1994; Awad et al, 2003; Hundley et al, 2005; Carchman et al, 2008; Szalat et al, 2009; Järhult et al, 2010).

Demographic trends in cases of lithium-associated hyperparathyroidism are similar to those seen in cases of primary hyperparathyroidism. Thus, the guidelines for managing primary hyperparathyroidism provide a framework for the management of lithium-associated hyperparathyroidism (Shapiro and Davis, 2015). Nonetheless, lithium-associated hyperparathyroidism remains a separate entity with additional management considerations such as discontinuation of lithium therapy. Hence, management decisions should be based on the patient's symptoms, medical and psychiatric history, and corrected serum calcium levels.

Patients who are asymptomatic and have a corrected serum calcium level of <2.85 mmol/litre should ideally have their lithium therapy discontinued and undergo vigilant surveillance. The decision to withdraw lithium therapy should be made after discussion with the patient's psychiatrist (Albert et al, 2014). In some patients the discontinuation of lithium may be enough to achieve normocalcaemia (McHenry and Lee, 1996; Khandwala and Van Uum, 2006). The likelihood of such success depends on the duration of lithium therapy and severity of hypercalcaemia. Discontinuation of lithium therapy has a higher rate of success in patients who have been on lithium for a short period of time (less than 10 years) (Saunders et al, 2009). A short duration of lithium therapy has a lower chance of inducing permanent parathyroid gland pathology, explaining the reversible hypercalcaemia sometimes seen on cessation of lithium (Shapiro and Davis, 2015). Keeping this concept in mind, hypocalciuria may be a useful marker of reversible hypercalcaemia in patients with lithium-associated hyperparathyroidism.

In cases where discontinuation of lithium therapy is not feasible, because of a higher rate of relapse of the underlying psychiatric condition (Smith et al, 2007), or was not successful

or refused (Smith et al, 2007), the use of calcimimetic therapy such as cinacalcet, may be considered. Cinacalcet may also be an alternative to surgery, especially in patients with mild disease or contraindications to surgery (Sloand and Shelly, 2006; Szalat et al, 2009). Gregoor and de Jong (2007) reported a good response with cinacalcet, despite continuation of lithium therapy. In another report, normocalcaemia was achieved in two patients with cinacalcet with modest reduction of serum parathyroid hormone levels, with one patient remaining on lithium (Sloand and Shelly, 2006). The use of cinacalcet was also reported to be successful in normalising serum calcium concentrations, but with persistently high parathyroid hormone levels, in a patient with postoperative recurrence of lithium-associated hyperparathyroidism (Szalat et al, 2009). This is similar to another case reported by Dixon et al (2018), where the use of cinacalcet managed to achieve normocalcaemia in a patient with recurrence of lithium-associated hyperparathyroidism following parathyroidectomy.

Furthermore, those patients undergoing surveillance with gradually increasing serum calcium levels or those who failed medical therapy with calcimimetic therapy should have localisation studies performed if they are candidates for surgery.

Patients who are symptomatic or have corrected serum calcium levels >2.85 mmol/litre should ideally have their lithium therapy stopped and undergo surgical intervention. Other indications for surgical intervention include those of the 2014 4th International Workshop in Asymptomatic Primary Hyperparathyroidism guidelines (summarised in Table 2) (Bilezikian et al, 2014).

Given the high prevalence of multiple gland disease, bilateral neck exploration is advised rather than focal neck exploration, unless there is clear evidence of a solitary parathyroid adenoma on imaging (Nordenström et al, 1994; Szalat et al, 2009; Järhult et al, 2010; Ballehaninna et al, 2011). This is in contrast with the surgical management of patients with primary hyperparathyroidism, where focal neck exploration is the most commonly used surgical approach. Intraoperative parathyroid hormone monitoring also limited the extent of surgery in some reported cases (Ballehaninna et al, 2011). Failure of intraoperative parathyroid hormone normalisation or a decrease of less than 50% during operation leads to more extensive surgery.

In the majority of cases (67–100%), parathyroidectomy managed to achieve normocalcaemia (Ballehaninna et al, 2011). However, surveillance is still required to identify recurrence. Järhult et al (2010) reported that among 71 surgically treated patients, 30 patients had failure or recurrence of hyperparathyroidism. The management of lithium-associated hyperparathyroidism is summarised in Figure 1.

Conclusions

Lithium therapy leads to alterations in calcium and parathyroid hormone dynamics. Lithium-associated hyperparathyroidism is classically biochemically characterised by hypercalcaemia, an inappropriately normal or elevated parathyroid hormone level, normophosphataemia, normo- or hypermagnesaemia and hypocalciuria. This closely resembles the biochemical

Table 2. Indications for surgical intervention as per the 2014 4th International Workshop in Asymptomatic Primary Hyperparathyroidism guidelines

Indications for surgical intervention	Details
Hypercalcaemia	>2.85 mmol/litre
Hypercalciuria, renal function and the presence of renal calculi	24-hour urinary calcium of >400 mg or >10 mmol/24 hours
	Estimated glomerular filtration rate <60 ml/min or a reduction of creatinine clearance by >30%
	Presence of renal calculi on ultrasonography, computed tomography or on magnetic resonance imaging
Osteoporosis	A T-score of ≤2.5 at lumbar spine, total hip, femoral neck or distal radius
	Presence of vertebral fractures on imaging modalities
Age	<50 years of age

From Bilezikian et al (2014)

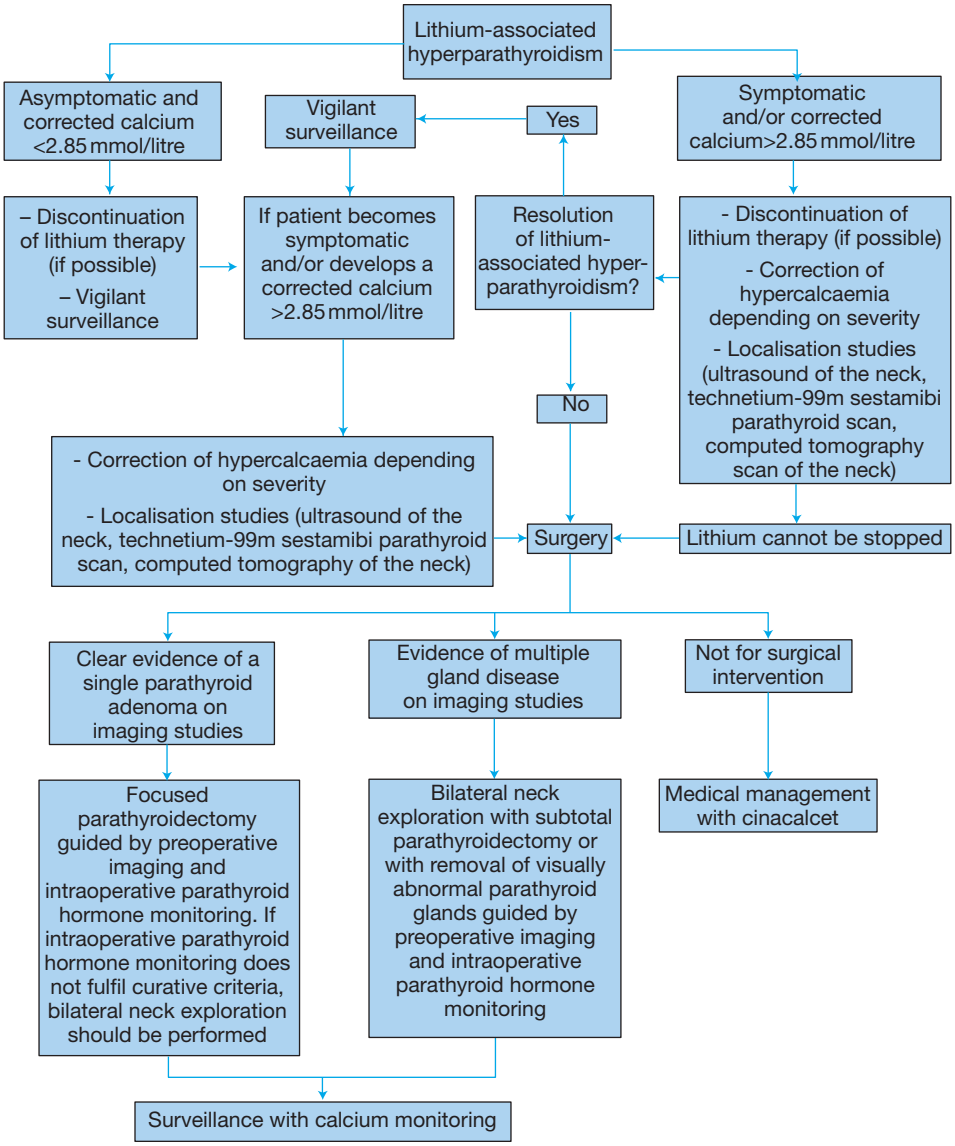

Figure 1. Management of lithium-associated hyperparathyroidism.

picture seen in patients with familial hypocalciuric hypercalcaemia. In patients with a short duration of lithium therapy, the hypercalcaemia usually reverses on discontinuing lithium. However, the hypercalcaemia may not always resolve when lithium is discontinued, especially in patients on chronic lithium therapy. This suggests that chronic lithium therapy leads to permanent changes in the parathyroid glands by either unmasking hyperparathyroidism in patients with an underlying subclinical parathyroid adenoma or possibly by inducing hyperplastic or adenomatous changes within the parathyroid glands. In the latter, patients may exhibit hypercalciuria, nephrolithiasis and/or reduced bone mineral density, suggesting end-organ damage as a result of the 'primary' hyperparathyroidism. These patients should be managed as patients with primary hyperparathyroidism. Patients who are symptomatic or fulfil any of the criteria of the 2014 4th International Workshop in Asymptomatic Primary Hyperparathyroidism guidelines should be referred for surgery. Poor surgical candidates or patients who are asymptomatic and do not fulfil the criteria, should have their calcium levels monitored and be considered for calcimimetic therapy with cinacalcet.

Author details

[1]Department of Diabetes and Endocrinology, Mater Dei Hospital, Msida, Malta

[2]Department of Medicine, Mater Dei Hospital, Msida, Malta

Key points

- Lithium-associated hyperparathyroidism is an ill-defined endocrinopathy which consists of a spectrum of biochemical abnormalities ranging from overt hyperparathyroidism, hypercalcaemia with inappropriately normal parathyroid hormone levels and normocalcaemia with raised parathyroid hormone levels in patients on concomitant lithium therapy.
- Lithium may induce hypercalcaemia through both acute and chronic effects.
- Lithium-associated hyperparathyroidism is classically characterised by the presence of a raised or an inappropriately normal parathyroid hormone level, a low parathyroid hormone-related protein level, normo- or hypermagnesaemia, normophosphataemia and hypocalciuria in the absence of any other cause in patients on concomitant lithium therapy.
- Chronic lithium therapy leads to permanent changes in the parathyroid glands and in such cases patients may exhibit hypercalciuria, nephrolithiasis and/or reduced bone mineral density, suggesting end-organ damage as a result of the 'primary' hyperparathyroidism.
- There is a higher prevalence of multiple gland disease in lithium-associated hyperparathyroidism compared to idiopathic sporadic hyperparathyoidism.
- Since the demographic trends in lithium-associated hyperparathyroidism cases are similar to those seen in cases of primary hyperparathyroidism, the guidelines for managing primary hyperparathyroidism provide a framework for the management of lithium-associated hyperparathyroidism.

Conflicts of interest
The authors declare that they have no conflicts of interest.

References

Abdullah H, Bliss R, Guinea AI et al. Pathology and outcome of surgical treatment for lithium-associated hyperparathyroidism. Br J Surg. 1999;86(1):91–93. https://doi.org/10.1046/j.1365-2168.1999.00977.x

Afzal M, Kathuria P. Familial hypocalciuric hypercalcemia (FHH). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020

Aksakal N, Erçetin C, Özçınar B et al. Lithium-associated primary hyperparathyroidism complicated by nephrogenic diabetes insipidus. Ulus Cerrahi Derg. 2015;31(3):166–169. https://doi.org/10.5152/UCD.2014.2859

Albert U, De Cori D, Blengino G et al. Trattamento con litio e potenziali effetti collaterali a lungo termine: una revisione sistematica della letteratura Albert U, De Cori D, Blengino G, [Lithium treatment and potential long-term side effects: a systematic review of the literature]. Riv Psichiatr. 2014;49(1):12–21. https://doi.org/10.1708/1407.15620

Albert U, De Cori D, Aguglia A et al. Effects of maintenance lithium treatment on serum parathyroid hormone and calcium levels: a retrospective longitudinal naturalistic study. Neuropsychiatr Dis Treat. 2015;11:1785–1791. https://doi.org/10.2147/NDT.S86103

Ananth J, Dubin SE. Lithium and symptomatic hyperparathyroidism. J R Soc Med. 1983;76(12):1026–1029. https://doi.org/10.1177/014107688307601210

Awad SS, Miskulin J, Thompson N. Parathyroid adenomas versus four-gland hyperplasia as the cause of primary hyperparathyroidism in patients with prolonged lithium therapy. World J Surg. 2003;27(4):486–488. https://doi.org/10.1007/s00268-002-6824-4

Ballehaninna U, Nguyen S, Chamberlain R. Lithium associated hyperparathyroidism: an evidence based surgical approach. Surg Sci. 2011;02(10):468–475. https://doi.org/10.4236/ss.2011.210103

Barczyński M, Bränström R, Dionigi G et al. Sporadic multiple parathyroid gland disease: a consensus report of the European Society of Endocrine Surgeons (ESES). Langenbecks Arch Surg. 2015;400(8):887–905. https://doi.org/10.1007/s00423-015-1348-1

Bilezikian JP, Brandi ML, Eastell R et al. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. J Clin Endocrinol Metab. 2014;99(10):3561–3569. https://doi.org/10.1210/jc.2014-1413

Blackburn M, Diamond T. Primary hyperparathyroidism and familial hyperparathyroid syndromes. Aust Fam Physician. 2007;36(12):1029–1033

Carchman E, Ogilvie J, Holst J et al. Appropriate surgical treatment of lithium-associated hyperparathyroidism. World J Surg. 2008;32(10):2195–2199. https://doi.org/10.1007/s00268-008-9616-7

Carling T, Szabo E, Bai M et al. Familial hypercalcemia and hypercalciuria caused by a novel mutation in the cytoplasmic tail of the calcium receptor. J Clin Endocrinol Metab. 2000;85(5):2042–2047. https://doi.org/10.1210/jcem.85.5.6477

Díaz-Soto G, Julián MT, Puig-Domingo M. Normocalcemic primary hyperparathyroidism: a newly emerging disease needing therapeutic intervention. Hormones (Athens). 2012;11(4):390–396. https://doi.org/10.14310/horm.2002.1370

Dieserud F, Brun AC, Låhne PE, Normann E. Litiumbehandling og hyperparatyreoidisme [Lithium treatment and hyperparathyroidism]. Tidsskr nor Laegeforen. 2001;121(22):2602–2603

Dixon M, Luthra V, Todd C. Use of cinacalcet in lithium-induced hyperparathyroidism. BMJ Case Rep. 2018;2018:bcr2018225154. https://doi.org/10.1136/bcr-2018-225154

Dorflinger C, Fuller M. Lithium-induced hypercalcemia with normal parathyroid hormone: a case report. Ment Health Clin. 2019;9(5):318–321. https://doi.org/10.9740/mhc.2019.09.318

Dwight T, Kytölä S, Teh BT et al. Genetic analysis of lithium-associated parathyroid tumors. Eur J Endocrinol. 2002;146(5):619–627. https://doi.org/10.1530/eje.0.1460619

Garfinkel PE, Ezrin C, Stancer HC. Hypothyroidism and hyperparathyroidism associated with lithium. Lancet. 1973;302(7824):331–332. https://doi.org/10.1016/s0140-6736(73)90846-5

Ghandur-Mnaymneh L, Kimura N. The parathyroid adenoma. A histopathologic definition with a study of 172 cases of primary hyperparathyroidism. Am J Pathol. 1984;115(1):70–83

Gregoor PS, de Jong GM. Lithium hypercalcemia, hyperparathyroidism, and cinacalcet. Kidney Int. 2007;71(5):470. https://doi.org/10.1038/sj.ki.5002065

Griebeler ML, Kearns AE, Ryu E et al. Thiazide-associated hypercalcemia: incidence and association with primary hyperparathyroidism over two decades. J Clin Endocrinol Metab. 2016;101(3):1166–1173. https://doi.org/10.1210/jc.2015-3964

Haden ST, Stoll AL, McCormick S, Scott J, El-Hajj Fuleihan G. Alterations in parathyroid dynamics in lithium-treated subjects. J Clin Endocrinol Metab. 1997;82(9):2844–2848. https://doi.org/10.1210/jcem.82.9.4218

Hanna RM, Hasnain H, Sangalang MD et al. Three patients with lithium-associated hyperparathyroidism: literature review regarding medical and surgical management. Case Rep Nephrol Dial. 2019;9(2):108–118. https://doi.org/10.1159/000502399

Hundley JC, Woodrum DT, Saunders BD et al. Revisiting lithium-associated hyperparathyroidism in the era of intraoperative parathyroid hormone monitoring. Surgery. 2005;138(6):1027–1032. https://doi.org/10.1016/j.surg.2005.09.028

Järhult J, Ander S, Asking B et al. Long-term results of surgery for lithium-associated hyperparathyroidism. Br J Surg. 2010;97(11):1680–1685. https://doi.org/10.1002/bjs.7199

Khandwala HM, Van Uum S. Reversible hypercalcemia and hyperparathyroidism associated with lithium therapy: case report and review of literature. Endocr Pract. 2006;12(1):54–58. https://doi.org/10.4158/ep.12.1.54

Lenox R, Wang L. Molecular basis of lithium action: integration of lithium-responsive signaling and gene expression networks. Mol Psychiatry. 2003;8(2):135–144. https://doi.org/10.1038/sj.mp.4001306

Mak TW, Shek CC, Chow CC, Wing YK, Lee S. Effects of lithium therapy on bone mineral metabolism: a two-year prospective longitudinal study. J Clin Endocrinol Metab. 1998;83(11):3857–3859. https://doi.org/10.1210/jcem.83.11.5269

Mallette LE, Khouri K, Zengotita H, Hollis BW, Malini S. Lithium treatment increases intact and midregion parathyroid hormone and parathyroid volume. J Clin Endocrinol Metab. 1989;68(3):654–660. https://doi.org/10.1210/jcem-68-3-654

Marti JL, Yang CS, Carling T et al. Surgical approach and outcomes in patients with lithium-associated hyperparathyroidism. Ann Surg Oncol. 2012;19(11):3465–3471. https://doi.org/10.1245/s10434-012-2367-6

McHenry CR, Lee K. Lithium therapy and disorders of the parathyroid glands. Endocr Pract. 1996;2(2):103–109. https://doi.org/10.4158/EP.2.2.103

Meehan AD, Udumyan R, Kardell M et al. Lithium-associated hypercalcemia: pathophysiology, prevalence. World J Surg. 2018;42(2):415–424. https://doi.org/10.1007/s00268-017-4328-5

Nordenström J, Strigård K, Perbeck L et al. Hyperparathyroidism associated with treatment of manic-depressive disorders by lithium. Eur J Surg. 1992;158(4):207–211

Nordenström J, Elvius M, Bågedahl-Strindlund M, Zhao B, Törring O. Biochemical hyperparathyroidism and bone mineral status in patients treated long-term with lithium. Metabolism. 1994;43(12):1563–1567. https://doi.org/10.1016/0026-0495(94)90017-5

Norlén O, Sidhu S, Sywak M et al. Long-term outcome after parathyroidectomy for lithium-induced hyperparathyroidism. Br J Surg. 2014;101(10):1252–1256. https://doi.org/10.1002/bjs.9589

Pamathy G, Jayarajah U, Wangmo T, Banagala ASK. Lithium-induced symptomatic hypercalcemia and hyperparathyroidism in a patient with bipolar affective disorder: a case report and review of literature. Indian J Psychol Med. 2018;40(4):378–380. https://doi.org/10.4103/IJPSYM.IJPSYM_305_17

Rizwan MM, Perrier ND. Long-term lithium therapy leading to hyperparathyroidism: a case report. Perspect Psychiatr Care. 2009;45(1):62–65. https://doi.org/10.1111/j.1744-6163.2009.00201.x

Sauer-Schulz A, Schnauder G, Dittmann H, Müssig K. Seltene Differenzialdiagnose des primären Hyperparathyreoidismus - Fall 12/2011 [A rare differential diagnosis of primary hyperparathyreoidism - case 12/2011]. Dtsch Med Wochenschr. 2011;136(50):2621–2621. https://doi.org/10.1055/s-0031-1292848

Saunders BD, Saunders EF, Gauger PG. Lithium therapy and hyperparathyroidism: an evidence-based assessment. World J Surg. 2009;33(11):2314–2323. https://doi.org/10.1007/s00268-009-9942-4

Saxe AW, Gibson G. Lithium increases tritiated thymidine uptake by abnormal human parathyroid tissue. Surgery. 1991;110(6):1067–1077

Shapiro HI, Davis KA. Hypercalcemia and "primary" hyperparathyroidism during lithium therapy. Am J Psychiatry. 2015;172(1):12–15. https://doi.org/10.1176/appi.ajp.2013.13081057

Shen HC, Li JY, Lo YK. Lithium intoxication-induced acute parkinsonism complicated with hyperparathyroidism and nephrogenic diabetes insipidus: report of a case. Acta Neurol Taiwan. 2007;16(4):231–233

Skandarajah AR, Palazzo FF, Henry JF. Lithium-associated hyperparathyroidism: surgical strategies in the era of minimally invasive parathyroidectomy. World J Surg. 2011;35(11):2432–2439. https://doi.org/10.1007/s00268-011-1220-6

Sloand JA, Shelly MA. Normalization of lithium-induced hypercalcemia and hyperparathyroidism with cinacalcet hydrochloride. Am J Kidney Dis. 2006;48(5):832–837. https://doi.org/10.1053/j.ajkd.2006.07.019

Smith LA, Cornelius V, Warnock A, Bell A, Young AH. Effectiveness of mood stabilizers and antipsychotics in the maintenance phase of bipolar disorder: a systematic review of randomized controlled trials. Bipolar Disord. 2007;9(4):394–412. https://doi.org/10.1111/j.1399-5618.2007.00490.x

Szalat A, Mazeh H, Freund HR. Lithium-associated hyperparathyroidism: report of four cases and review of the literature. Eur J Endocrinol. 2009;160(2):317–323. https://doi.org/10.1530/EJE-08-0620

Wolf ME, Moffat M, Mosnaim J et al. Lithium therapy, hypercalcemia, and hyperparathyroidism. Am J Ther. 1997;4(9-10):323–325. https://doi.org/10.1097/00045391-199709000-00007

Zamani A, Omrani GR, Nasab MM. Lithium's effect on bone mineral density. Bone. 2009;44(2):331–334. https://doi.org/10.1016/j.bone.2008.10.001