Irish Journal of Medical Science (1971 -) (2019) 188:1103–1109
https://doi.org/10.1007/s11845-018-01963-9

ORIGINAL ARTICLE

The clinical characteristics and correlates of lithium toxicity in a tertiary referral centre

Niamh M. Ganter[1] · Kezanne Tong[2] · Colm McDonald[1,2] · Anne M. Doherty[2]

Received: 10 October 2018 / Accepted: 31 December 2018 / Published online: 10 January 2019

Abstract

Introduction Lithium is a medication indicated for the treatment of bipolar disorder and treatment-resistant depression, with a narrow therapeutic index. Overdose, either acute or chronic can result in neurological symptoms, requiring dialysis and admission to intensive care in some cases. Lithium toxicity is avoidable with careful monitoring. However, we have noted several recent cases of lithium toxicity in our local service and thus sought to investigate this issue in a more systematic manner.

Aim We aimed to quantify the incidence of lithium toxicity in our local population over a single year and identify the patients most at risk. We also aimed to generate clinical recommendations on the prevention of lithium toxicity to improve patient safety.

Method We identified the incidence of lithium toxicity in our local population, by searching the hospital pathology database for patients with serum lithium levels greater than 1.0 mmol/L. We examined the available clinical notes for these patients.

Results We identified 74 serum lithium readings above 1.0 mmol/L measured in 44 individual patients. The highest recorded level was 3.2 mmol/L. Of these, 11 patients were aged 65 years or older. Hospital admission was required in 14 cases. There were missing data of note: 29.5% had no renal function/eGFR measurement at time of toxicity and 52.3% without a baseline eGFR.

Conclusion Lithium toxicity is common in our population. Given the narrow therapeutic index, this demonstrates the need for careful monitoring and prescribing, especially patients aged 65 and over.

Keywords Clinical · Galway · Lithium · Monitoring · Overdose · Tertiary · Toxicity · Toxicology

Introduction

Cade initially described the use of lithium in 1949 [1]. Lithium is a medication with a strong evidence base for the prophylaxis of bipolar affective disorder, treatment of mania/hypomania and augmentation in treatment-resistant depressive disorder. It is clinically effective at plasma concentrations of 0.4–0.8 mmol/L. Lithium has a narrow therapeutic index of 0.4–0.8 mmol/L, with 0.6–0.8 mmol/L preferred for optimal clinical efficacy. Above 1.5 mmol/L, it produces a wide range of toxic effects [2], although clinical lithium toxicity has been reported at 'normal serum' levels [3].

Lithium toxicity is rare, but may occur for several reasons, including its use in a cohort already at risk of overdose, inadequate monitoring of lithium use, and rapid onset of any factors which reduce renal excretion of lithium. Lithium is excreted unchanged through the kidneys; hence, its serum level depends on renal function and is affected by polypharmacy. Lithium excretion is a function of renal sufficiency [4, 5]. Salt depletion, dehydration or diuretics all increase serum lithium levels as well as some common medications such as angiotensin converting enzyme (ACE) inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs) and diuretics.

Lithium toxicity may be either acute or chronic and could potentially lead to serious adverse effects, affecting the central nervous system, cardiovascular system, gastrointestinal system and renal system [6]. Intentional overdose with lithium is another reason for presentation to the hospital with acute lithium toxicity. Symptoms range from nausea, vomiting and diarrhoea to life-threatening features like coma, convulsions and potentially death at dangerously high lithium plasma levels.

The risk of developing lithium toxicity can be reduced by guideline-based monitoring of plasma lithium levels, and

✉ Niamh M. Ganter
niamhmganter@gmail.com

[1] School of Medicine, National University of Ireland, Galway, Ireland

[2] Department of Psychiatry, University Hospital Galway, Galway, Ireland

psycho-education about lithium therapy. Current guidelines recommend that lithium levels be checked 1 week following initiation or dose change. Once therapeutic level is achieved, levels can be repeated 3-monthly for the first year and 6-monthly thereafter (or 3-monthly for people who are at high risk of developing toxicity). Renal and thyroid function tests need to be tested at baseline and repeated every 6 months [7, 8]. These tests allow for early detection of declining function. Where renal function is moderately impaired (stage 3 a or 3b: eGFR = 30–59), renal function should be monitored every 3 months, and a referral to nephrology is indicated in stage 3b if heavy proteinuria (or proteinuria and haematuria) is present, or if there has been a rapid decline in eGFR (NICE 2008). In severe renal failure (stages 4 and 5; eGFR < 29) lithium is usually contraindicated, and a nephrology opinion is required [2]. Discontinuation of lithium may not halt the decline in renal function [8, 9].

Despite clear guidelines, a UK-based study found that only 30% of mental health trusts met targets for lithium monitoring [10]. A local audit found that less than 20% of patients had monitoring in line with best practice guidelines (Dunne A, personal correspondence 12th December 2017).

The incidence of lithium toxicity was found to be approximately 5.4 cases per 100,000 per year in Cork, Ireland [11]. A retrospective, observational study of cases of lithium toxicity reported to the California Poisons Control System from 2003 to 2007, reported 502 hospitalised cases due to lithium toxicity in the 5-year period [12]. Inadequate monitoring and management of lithium therapy could potentially lead to life-threatening risks as well as undesired economic consequences on the health service. In the UK, between 2003 and 2008, there were 567 incident reports received concerning lithium therapy with two cases indicating severe harm. Between 1995 and 2004, the NHS Litigation Authority acted on two fatal incidents as well as 12 cases of severe harm incidents relating to the use of lithium [13]. Locally, over a period of 6 years between 2004 and 2010, the Clinical Indemnity Scheme under the State Claims Agency in Ireland recorded 1106 reports relating to medication incidents in mental health, of which 7.7% related to treatment with lithium [14]. These incidents could be mitigated with proper education and monitoring in patients receiving lithium therapy.

There is little data regarding the incidence of lithium toxicity in our local population. The aim of this study is to investigate the incidence and clinical associations of lithium toxicity in the Galway and Mayo population in 2016.

Method

This was a retrospective study, which analysed clinical and laboratory data, which was collected as part of routine clinical care. In collaboration with the hospital laboratory services at GUH, we identified patients through the hospital laboratory information system, which includes lithium levels for patients residing in the West Galway and Mayo region and who presented for medical attention in hospitals or community primary care centres.

Patients with serum lithium level greater than 1.0 mmol/L over the 12-month period of 1 January to 31 December 2016 were included in this study: we chose this level, lower than the traditional cut off for toxicity of 1.5 mmol/L, to reflect newer guidelines for the management of patients on lithium at a trough serum level of 0.6 to 0.8 mmol/L [7]. NICE guidelines recommend a brief trial of levels between 0.8 and 1.0 mmol/L only where the person has had a relapse while taking lithium in the past or has sub-threshold symptoms with functional impairment despite lithium at levels of 0.6 to 0.8 mmol/L [7].

Demographic and clinical characteristics of these patients were obtained from their respective psychiatry clinical notes and electronic discharge summaries: age, gender, diagnosis (in accordance with ICD-10 criteria), frequency of serum lithium level sampling, thyroid and renal function monitoring were obtained. Where available, we also recorded the cause of overdose in this subset of patients. We also identified patients who required hospital admission as well as those who required input during their admission from the liaison psychiatry team.

Data were entered into SPSS. Basic statistical data on demographic and clinical variables were calculated, and bivariate data were analysed. Chi-squared and *t*-test analyses were used where data were separated by age. The findings were then interpreted and presented in the form of summary tables.

This study was granted ethical approval by the Clinical Research Ethics Committee of the Saolta Hospital Group.

Results

We identified 74 serum lithium levels above 1.0 mmol/L from 44 individual patients (26 patients had one elevated lithium only: the remainder had multiple levels above 1.0 mmol/L some within the same day). Table 1 summarises the demographic and clinical characteristics of patients included in this study. Of 44 patients, 32 (72.7%) were aged less than 65 years while the remaining patients were ≥ 65 years of age. There were similar number of female ($n = 21$) and male ($n = 23$) patients. Of the 26 whose diagnoses were recorded, 17 had bipolar affective disorder, three had schizoaffective disorder and six were diagnosed with recurrent depressive disorder. Diagnosis and indication for lithium therapy could not be obtained for 18 patients, who did not have a medical or psychiatric file available for review at the hospital. When we compared the demographic and clinical characteristics of those patients for whom we had complete data with those with

Table 1 Demographic and clinical characteristics

		$N = 44$
Age, mean (SD)		52.9 (17.7)
Age, *n* (%)	≤ 64	32 (72.7)
	≥ 65	12 (27.3)
Gender, *n* (%)	Female	21 (47.7)
	Male	23 (52.3)
Diagnosis, *n* (%)	Bipolar affective disorder	17 (38.6)
	Schizoaffective disorder	3 (6.8)
	Recurrent depressive disorder	6 (13.6)
	Unknown	18 (40.9)
Serum lithium level, mean (SD)		1.43 (0.48)
Renal function test performed, *n* (%)		39 (88.6)
Baseline eGFR mL/min, mean (SD)		70.6 (15.3)
Toxicity eGFR mL/min, mean (SD)		62.9 (18.8)
KDOQI renal failure stage (baseline)	Stage 1	12 (30.8)
	Stage 2	16 (41)
	Stage 3	11 (28.2)
	Stage 4	0 (0)
KDOQI renal failure stage (toxicity)	Stage 1	6 (15.4)
	Stage 2	18 (46.2)
	Stage 3	14 (35.9)
	Stage 4	1 (2.6)
Thyroid function test performed, *n* (%)		39 (88.6)
Requiring hospital admission, *n* (%)		14 (31.8)
Liaison psychiatry consult, *n* (% of adm)		6 (42.9)
Source, *n* (%)	Primary care	20 (45.5)
	OPD	14 (31.8)
	Inpatient	10 (22.7)

partial data only (missing diagnosis), there were no significant differences between the two groups in terms of age, serum lithium or eGFR.

The highest recorded lithium level was 3.2 mmol/L with mean level of 1.4 (SD 0.5) mmol/L. The majority of patients had renal function tests performed, with mean baseline eGFR of 70.6 mL/min. The mean eGFR in patients with lithium toxicity was 62.9 mL/min. Of the studied patients, 39 (88.6%) had some degree of renal impairment prior to onset of episode of toxicity. Almost 90% of the patients had thyroid function tests done. Thirty patients were treated for their lithium toxicity as outpatients, while 14 required hospital admission. Of these, six patients (43%) received input from liaison psychiatry team during their admission.

Table 2 demonstrates the difference in demographic and clinical characteristics of patients aged ≤ 64 and ≥ 65 years. Despite the lower baseline eGFR in the over-65 group, 25% of the patients did not have renal function tests performed when they developed toxicity. At toxicity, the older patient group developed a significantly lower eGFR level of 52.7 mL/min compared to the younger age group (66.5 mL/min; $p = 0.045$).

Table 3 demonstrates clinical and demographic characteristics of patients with serum lithium levels above and below 1.5 mmol/L. Patients with serum lithium levels above 1.5 mmol/L were more likely to be hospitalised (61.5%) than those with lower lithium levels (19.4%; $p = 0.009$). Patients with higher serum lithium levels were more likely to be referred to the liaison psychiatry team ($p = 0.006$). We noted that 40% of patients with levels greater than 1.5 mmol/L have no record of attending hospital. There were no significant differences between groups when we excluded patients who presented with intentional self-poisoning. There were no deaths directly attributable to lithium toxicity.

Discussion

In this study, we identified in the incidence of lithium toxicity over 1 year and examined the demographics and clinical characteristics of those 44 patients with recorded lithium levels over 1.0 mmol/L. The highest recorded lithium level was 3.2 mmol/L with mean level of 1.4 (SD 0.5) mmol/L. The

majority of patients studied were aged less than 65 years. This may reflect clinicians' higher threshold for commencing lithium in the elderly population, or perhaps medically necessary discontinuation of lithium in later life due to the development of the sequelae of long-term lithium use such as nephrotoxicity. Moreover, as elderly patients tend to seek medical attention more frequently than younger patients, rising lithium levels may have been detected sooner, and interventions put in place before they develop toxicity. There were similar proportion of males and females in our cohort, which is not consistent with most studies [15]. This may be due to our small patient number included in this study.

We were unable to identify the clinical diagnosis for 18 of 44 patients. These patients were generally out of area, and we had no access to their mental health records; however, we have no reason to suspect that their clinical characteristics would differ from those whom we had more detailed information. Four of the 12 patients were managed by their GPs in the community. One patient, for whom a chart was available, did not have an Axis I mental health diagnosis. Patients with borderline personality disorder may be prescribed lithium to manage emotional lability [16].

Lithium levels above 2.5 mmol/L are potentially fatal [4]. We identified four patients with levels equal to or greater than this. This is a significant number in the space of 1 year for our catchment area, considering that frequent serum lithium level monitoring should prevent these events. However, two of these high levels were attributed to self-poisoning. Our highest recorded lithium level in the database was 3.2 mmol/L. The toxic level was attributed to the addition of a thiazide diuretic to the patient's medication regime, an agent known to reduce renal clearance of lithium, thereby increasing plasma lithium levels [17]. Co-prescription of medications known to interact with lithium is frequently reported in patients who presented with lithium toxicity as reported by Dennison. Their study found that 49% of patients were co-prescribed drugs that interact with lithium: 21.3% were prescribed diuretics [10]. A Canadian study similarly reported an elevated increased risk of lithium toxicity among patients concomitantly prescribed loop diuretics or ACE inhibitors [158]. A 7-year prospective study of lithium levels among hospitalised patients found an incidence of lithium toxicity (defined as ≥1.5 mmol/L) of 6.8% in 2210 hospital admissions where lithium was administered. Less than 30% of patients with toxic levels showed signs of toxicity, and excess levels were more commonly seen in female and elderly patients [18]. A Californian study published in 2010 described a large cohort of lithium-overdose hospitalised patients and found 629 cases of lithium toxicity per 5 years, with 80% requiring hospitalisation. The majority were the consequence of chronic overdose, and many required haemodialysis [10].

Table 2 Clinical and demographic characteristics of patients aged below and over 65 years

		≤64	≥65	*p*
Gender, *n* (%)	Female	13 (40.6)	8 (66.7)	0.124[a]
	Male	19 (59.4)	4 (52.3)	
Diagnosis, *n* (%)	Bipolar affective disorder	14 (43.8)	3 (25.0)	0.085[a]
	Schizoaffective disorder	3 (9.4)	0 (0.0)	
	Recurrent depressive disorder	2 (6.3)	4 (33.3)	
	Unknown	13 (40.6)	5 (41.7)	
Serum lithium level, mean (SD)		1.5 (0.55)	1.25 (0.12)	0.123[b]
Renal function test performed, *n* (%)		22 (69)	9 (75)	0.286[c]
Baseline eGFR mL/min, mean (SD)		75.2 (14.7)	59 (9.8)	< 0.001[b]
Toxicity eGFR mL/min, mean (SD)		66.5 (19.1)	52.7 (14.3)	0.045[b]
KDOQI renal failure stage at baseline	Stage 1	12 (42.9)	0 (0)	< 0.001[a]
	Stage 2	13 (46.4)	3 (27.3)	
	Stage 3	3 (10.7)	8 (72.7)	
	Stage 4	0 (0.0)	0 (0.0)	
KDOQI renal failure stage at time of toxicity	Stage 1	6 (20.1)	0 (0)	0.057[a]
	Stage 2	15 (51.7)	3 (30)	
	Stage 3	7 (24.1)	7 (70)	
	Stage 4	1 (3.4)	0 (0.0)	
Thyroid function test performed, *n* (%)		28 (87.5)	11 (91.7)	0.583[c]
Requiring hospital admission, *n* (%)		11 (34.4)	3 (25.0)	0.417[c]
Liaison psychiatry consult, *n* (% of adm)		4 (36.4)	2 (67)	0.529[c]

[a] Chi-squared [b] independent sample *t*-test [c] Fisher's test

Table 3 Clinical and demographic characteristics of patients with serum lithium levels above and below 1.5 mmol/L

		Serum lithium ≤ 1.4 mmol/L $n = 31$	Serum lithium ≥ 1.5mmol/L $n = 13$	p
Gender, *n* (%)	Female	16 (51.6)	5 (38.5)	0.426[a]
	Male	15 (48.4)	8 (61.5)	
Diagnosis, *n* (%)	Bipolar affective disorder	12 (38.7)	5 (38.5)	0.477[c]
	Schizoaffective disorder	1 (3.2)	2 (15.4)	
	Recurrent depressive disorder	5 (16.1)	1 (7.7)	
	Unknown	13 (41.9)	5 (38.5)	
Age, mean (SD)		55.2 (18.9)	47.5 (13.6)	0.192[b]
Renal function test performed within 6 months, *n* (%)		23 (74.2)	9 (62.9)	0.736[a]
Baseline eGFR mL/min, mean (SD)		68.6 (14.5)	66 (15.9)	0.734[b]
Toxicity eGFR mL/min, mean (SD)		64.0 (19.0)	60.9 (27.8)	0.725[b]
KDOQI renal failure stage at baseline	Stage 1	4 (25)	1 (20)	0.974[c]
	Stage 2	6 (37.5)	2 (40)	
	Stage 3	6 (37.5)	2 (40)	
	Stage 4	0 (0)	0 (0)	
KDOQI renal failure stage at time of toxicity	Stage 1	5 (22.7)	3 (33.3)	0.365[c]
	Stage 2	6 (27.3)	2 (22.2)	
	Stage 3	11 (50)	3 (33.3)	
	Stage 4	0 (0)	1 (11.1)	
Thyroid function test performed within 6 months, *n* (%)		28 (90.3)	8 (61.5)	0.024[a]
Requiring hospital admission, *n* (%)		6 (19.4)	8 (61.5)	0.006[a]
Liaison psychiatry consult, *n* (% of adm)		1 (3.2)	5 (38.5)	0.002[a]

[a] Chi-squared[b] independent sample *t*-test[c] Fisher's test

While there is evidence that lithium reduces suicidal risk in patients with mood disorders [19], its narrow therapeutic index means it may be fatal in self-poisoning or intentional overdose. A study by Dyson et al. of 68 admissions for lithium toxicity over a 16-year period found that the majority (63%) were due to self-poisoning [20]. Psychiatrists who prescribe lithium should ultimately weigh the therapeutic benefits against the risks before prescribing lithium in view of the drug's potential dangers. In order to avoid lithium toxicity, NICE suggests that patients who are prescribed lithium are measured for plasma lithium level every 3 months for the first year and 6-monthly thereafter, unless a patient is at high risk of developing adverse effects from lithium in which they may need 3-monthly monitoring [7]. It is important to consider the risk factors for developing renal failure, thyroid dysfunction and cardiovascular disease before making decisions regarding maintenance treatment with lithium. A 2016 systematic review investigated the adherence to lithium monitoring guidelines in the UK and Ireland [10]. Their findings showed that no study in the review showed total adherence to every guideline. This is consistent with our study that suggests that lithium monitoring is not conducted in accordance with established guidelines.

Lithium is primarily excreted unchanged by the kidneys. Elderly patients may be more vulnerable to lithium toxicity as they were more likely to have some form of renal impairment at baseline as suggested by our findings, i.e. 11 out of 12 patients over age 65 had stage 2 and 3 chronic kidney disease at baseline. Elderly patients may have a longer duration of lithium treatment, resulting in an increased risk of renal impairment in their later years, compounded by age-related decline in their renal function [21]. Studies in Scotland, Asia and the Czech Republic found high rates of renal failure following lithium toxicity [18, 19, 22]. The course of renal impairment following the discontinuation of lithium is unpredictable, and cessation may not halt the decline in renal function [9].

Recognising the vulnerability to lithium toxicity in this age group, NICE recommends that older people have plasma lithium level monitoring every 3 months. As elderly patients tend to attend their GPs more frequently for routine medical check-ups, high lithium levels are more likely to be detected and treated before complications develop. In addition, elderly patients tend to be maintained on lower lithium dose [7]. Another study discussed the differences in the incidence of adverse lithium therapy effects in patients younger than and

Table 4 Initial workup and monitoring of lithium

Baseline	Information (verbal and written) on lithium, including side-effects and symptoms of toxicity, pregnancy if applicable. Risk of manic relapse on sudden discontinuation.	
	Height, weight, BMI	
	Renal function incl eGFR, thyroid function. Full blood count if indicated	
	ECG	
	Lithium levels weekly until stable in range 0.6–0.8 mmol/L	
Monitoring once stable	Renal function	6-monthly
		More frequently if declining renal function
	Thyroid function	6-monthly
	Weight/BMI	Annually
	Blood pressure, glucose	Annually
	Lipid profile	Annually for patients aged > 40 years

older than 65 years of age. Their study, similarly to ours, was retrospective. They found a significant difference in severity of side effects; more moderate to severe effects were seen in those older than 65 [23].

In a prospective study, Webb et al. observed a decline in lithium toxicity over 7-year period as a result of education by a drug guidelines and education committee [22]. Measures such as the provision of a lithium alert card along with verbal and written information about lithium may reduce similar incidents in the future [13]. All prescribing clinicians should be aware of the guidelines in the area: this is particularly the case when patients are under the shared care of psychiatry and general practice. The guidelines for monitoring are all broadly similar—the main difference is that NICE and the Maudsley Guidelines suggest 6-monthly monitoring of lithium (3-monthly in the elderly) and the IMSN guidelines suggest 3-monthly monitoring of lithium levels for all (2, 15, 29): the IMSN guidelines are summarised in Table 4. In addition, it may be helpful to have renal function as an automated electronic accompaniment to the laboratory report on serum lithium levels.

A small proportion of the patients admitted medically were referred for liaison psychiatry review during their admission. There are no guidelines in this area, beyond the National Clinical Programme in Self-Harm [24] which would suggest review for all patients presenting with self-poisoning—as was the case in our sample. We do not see it as necessary for all patients with levels > 1.0 mmol/L to be seen, but those presenting with self-poisoning, extreme toxicity or a dramatic change in levels should be seen, and all cases should be discussed with the liaison psychiatry registrar.

The limitations of this project include its design as a retrospective study, and its small sample size due to lithium toxicity being a rare occurrence. A further limitation of this study was the partial accessibility of clinical information of patients not seen within the Galway Mental Health Service. However, unlike a chart-based study, our use of the laboratory system used by the hospitals allowed easy identification of patients meeting our inclusion criteria. Other limitations are that we did not have access to a denominator for the total number of patients prescribed lithium and so could not calculate an incidence rate, for comparison with previous years or other areas/health services, and we only collected data for 1 year so could not test whether the incidence of lithium toxicity as identified in the hospital is changing over time.

Conclusion

Lithium is a commonly prescribed drug in psychiatry for the treatment of severe mental illness. However, it is associated with many adverse effects ranging from mild and self-limiting side effects to life-threatening adverse events. Given the narrow therapeutic index, this demonstrates the need for careful guideline-based prescribing and monitoring, especially in patients who are at high risk of developing lithium toxicity. Lithium toxicity outside of intentional overdose continues to occur regularly and may be related to inadequate implementation of safe guidelines around monitoring and unawareness of safe prescribing such as the co-prescription of ACE inhibitors. Clinicians therefore need to be vigilant and to closely follow available clinical guidelines in the area. Further prospective research is required in this area.

Funding information Grant supplied by Undergraduate Research Committee, School of Medicine, National University of Ireland, Galway.

Compliance with ethical standards

Ethical disclosure statement For this project, we sought quality and integrity. We were in contact with no patients for the duration of the study. No identifiable patient data was used. Data was obtained via an electronic hospital laboratory system and was anonymised to ensure patient confidentiality. Data was stored on a fire-walled computer with coded access. Funding was obtained from the undergraduate research program at NUI Galway.

Conflict of interest No conflicts of interest existed in relation to this.

References

1. Cade J (1999) Lithium salts in the treatment of psychotic excitement. Aust N Z J Psychiatry 33:349–352. https://doi.org/10.1080/j.1440-1614.1999.06241.x
2. NICE: National Institute for Health and Clinical Excellence (2008) Early identification and management of chronic kidney disease in adults in primary and secondary care. (Clinical guideline 73)
3. Fouser P, Abbasi Y, Mathilakath A (2017) Nilforooshan R. Case report: Do not treat the numbers: lithium toxicity. BMJ Case Rep. https://doi.org/10.1136/bcr-2017-220079
4. Birch N, Greenfield A, Hullin R (1980) Pharmacodynamic aspects of long-term prophylactic lithium. Int Pharmacopsychiatry 15:91–98. https://doi.org/10.1159/000468418
5. Freeman M, Freeman S (2006) Lithium: clinical considerations in internal medicine. Am J Med 119:478–481. https://doi.org/10.1016/j.amjmed.2005.11.003
6. Oruch R, Elderbi M, Khattab H et al (2014) Lithium: a review of pharmacology, clinical uses, and toxicity. Eur J Pharmacol 740:464–473. https://doi.org/10.1016/j.ejphar.2014.06.042
7. (2018) Bipolar disorder: assessment and management | Guidance and guidelines | NICE. In: Nice.org.uk. https://www.nice.org.uk/guidance/cg185. Accessed 13 May 2018
8. Taylor DM, Barnes TRE, Young AH (2018) The Maudsley prescribing guidelines in psychiatry, 13th edn. Wiley-Blackwell, London
9. Markowitz GS, Radhakrishnan J, Kambham N, Valeri AM, Hines WH, D'Agati VD (2000) Lithium nephrotoxicity: a progressive combined glomerular and tubulointerstitial nephropathy. J Am Soc Nephrol 11:1439
10. Aubry R, Scott L, Cassidy E (2017) Lithium monitoring patterns in the United Kingdom and Ireland: can shared care agreements play a role in improving monitoring quality? A systematic review. Ir J Psychol Med 34:127–140. https://doi.org/10.1017/ipm.2017.2
11. Dennison U, Clarkson M, O'Mullane J, Cassidy EM (2011) The incidence and clinical correlates of lithium toxicity: a retrospective review. Ir J Med Sci 180:661–665. https://doi.org/10.1007/s11845-011-0712-6
12. Offerman S, Alsop J, Lee J et al (2010) Hospitalized lithium overdose cases reported to the California poison control system. Clin Toxicol 48:443–448. https://doi.org/10.3109/15563650.2010.482533
13. (2009) Safer lithium therapy. In: Nrls.npsa.nhs.uk. http://www.nrls.npsa.nhs.uk/alerts/?entryid45=65426. Accessed 13 May 2018
14. Davis A (2012) Best practice guidelines for prescribing and monitoring if lithium therapy. 1–10. http://www.imsn.ie/images/guidelines/imsn-lithium-guidelines-may-2012.pdf. Accessed 3 Jan 2019
15. Ott M, Stegmayr B, Salander Renberg E, Werneke U (2016) Lithium intoxication: incidence, clinical course and renal function – a population-based retrospective cohort study. J Psychopharmacol 30:1008–1019. https://doi.org/10.1177/0269881116652577
16. Mercer D, Douglass A, Links P (2009) Meta-analyses of mood stabilizers, antidepressants and antipsychotics in the treatment of borderline personality disorder: effectiveness for depression and anger symptoms. J Personal Disord 23:156–174. https://doi.org/10.1521/pedi.2009.23.2.156
17. Finley P, Warner M, Peabody C (1995) Clinical relevance of drug interactions with lithium. Clin Pharmacokinet 29:172–191. https://doi.org/10.2165/00003088-199529030-00004
18. Juurlink D, Mamdani M, Kopp A et al (2004) Drug-induced lithium toxicity in the elderly: a population-based study. J Am Geriatr Soc 52:794–798. https://doi.org/10.1111/j.1532-5415.2004.52221.x
19. Cipriani A, Hawton K, Stockton S, Geddes JR (2013) Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. BMJ 346:f3646–f3646. https://doi.org/10.1136/bmj.f3646
20. Dyson E, Simpson D, Prescott L et al (1987) Self-poisoning and therapeutic intoxication with lithium. Hum Toxicol 6:325–329. https://doi.org/10.1177/096032718700600410
21. Shine B, McKnight R, Leaver L et al (2015) Long-term effects of lithium on renal, thyroid, and parathyroid function: a retrospective analysis of laboratory data. Lancet 386:461–468. https://doi.org/10.1016/s0140-6736(14)61842-0
22. Webb A, Solomon D, Ryan C (2001) Lithium levels and toxicity among hospitalized patients. Psychiatr Serv 52:229–231. https://doi.org/10.1176/appi.ps.52.2.229
23. Smith R, Helms P (1982) Adverse effects of lithium therapy in the acutely ill elderly patient. J Clin Psychiatry
24. HSE & NSRF. Saving lives and reducing harmful outcomes: care systems for self harm and suicidal behaviour. National guidelines for the assessment and management of patients presenting to Irish emergency departments following self-harm. 2016