

Is it NICE to monitor lithium routinely?

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Abstract

Introduction Lithium has a narrow and well described therapeutic range.

Aim The aim of this study was to evaluate lithium blood concentration monitoring in Canterbury District Health Board (CDHB) and consider whether it meets the UK National Institute for Health and Clinical Excellence (NICE) standard (in lieu of more local standards).

Methods Lithium dispensing data for patients within the CDHB boundaries was combined with lithium blood concentrations for the period of 1 July 2009 to 30 June 2010 and the results analysed.

Results Lithium was prescribed for 1416 patients with a mean daily dose of 507 mg per day. 92% of patients in CDHB had had a lithium blood concentration performed at least once during the year. Twenty percent had had four or more lithium blood concentrations analysed. The mean ($\pm 95\%$ CI) lithium blood concentration was 0.63 (0.62 to 0.64) mmol/L; the median (interquartile range) was 0.6 (0.43 to 0.80) mmol/L and the range was 0 to 2.8 mmol/L. The median (interquartile range) sampling interval was 35 (13–93) days. Sampling was performed approximately every 3 months (80 to 100 days) in 11 patients (<1%). Of those 56 patients that had a lithium blood concentrations >1.2 mmol/L only 7 patients had this repeated within 3 weeks.

Discussion In conclusion, lithium blood monitoring at CDHB did not achieve the NICE standard. This is in keeping with a number of other audits conducted of lithium blood monitoring.

Lithium is commonly used for the prophylaxis of bipolar affective disorder (BPAD) and in the treatment of moderate to severe mania. It has been used for more than sixty years since its role in BPAD was first described in 1949.¹

Lithium has a narrow and well described therapeutic range. It is not metabolised, is excreted unchanged by the kidneys (fraction excreted unchanged \approx 1) and has a half life of 21 hours. Lithium blood concentrations (LBC) are ideally taken just before the next dose. If this is not possible, samples should be taken at least 8 to 12 hours after a dose. Samples should ideally be performed at steady state. This is reached at 5 days on a maintenance dose. For maintenance therapy and acute mania lithium blood concentrations should be within the range of 0.4 to 0.8 mmol/L and 0.8 to 1.2 mmol/L respectively.²

Dose related adverse reactions to lithium usually occur at blood concentrations greater than 1.5 mmol/L. These include increasing anorexia, nausea, diarrhoea, muscle weakness, drowsiness, ataxia and tremor. At concentrations above 2 mmol/L increasing disorientation and seizures often occur which can progress to coma and death.³

Lithium is also subject to drug interactions. Drugs that impair the kidney's ability to excrete sodium will also have a similar effect on lithium. Angiotensin converting enzyme (ACE) inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs) and diuretics can all lead to elevated LBCs.³

Different formulations of lithium are not considered to be bioequivalent and inadvertent changing of formulations may lead to changes in LBCs.³

The UK National Institute for Health and Clinical Excellence (NICE) recently published standards for lithium monitoring. These state that patients should have a LBC performed at least once every 3 months and renal tests and thyroid function tests every 6 months.⁴

To encourage safe practice the NHS National Patient Safety Agency issued an alert in December 2009 requiring all health organisations in the United Kingdom to have a reliable system in place to ensure that these standards are being met.⁵

In this study we aim to examine lithium blood concentration monitoring in Canterbury District Health Board (CDHB) and consider whether it meets the UK National Institute for Health and Clinical Excellence (NICE) Standard (in lieu of local standards).

Methods

Lithium dispensing data for patients within the CDHB boundaries were retrieved from the national database (NZ Health Information Service) via CDHB Planning and Funding for the period of 1st July 2009 to 30 June 2010. LBCs were retrieved for the same period from all three of the laboratories in CDHB (Canterbury Health Labs; MedLab South; Southern Community). The results were combined and analysed on Microsoft Excel™ software.

Results

Lithium was prescribed for 1416 patients during the period of 1 July 2009 to 30 June 2010 with a mean daily dose of 507 mg per day.

1342 patients had at least one sample taken. 39 of these patients were excluded from the analysis as the patient identification had not been completed correctly leaving 1303 patients. As 1416 patients were prescribed lithium and 1303 patients had at least one sample, 92 % of patients in CDHB had had a LBC performed at least once during the year. Twenty percent had had four or more LBCs analysed.

The median (interquartile range) LBC was 0.6 (0.43 to 0.80) mmol/L (mean (95% CI) = 0.63 (0.62 to 0.64) mmol/L; range = 0 to 2.8 mmol/L). A total of 136 samples (from 56 patients) were above the upper end of the therapeutic range of 1.2 mmol/L. 690 samples were between 0.8 and 1.2 mmol/L (the range for acute mania); 2687 samples were between 0.4 and 0.8 mmol/L (the range for maintenance therapy); 610 samples (from 378 patients) were below 0.4 mmol/L (subtherapeutic) and 19 results were incomplete.

In those patients with LBCs > 1.2 mmol/L, 7 out of the 56 patients were retested within 3 weeks.

The median (interquartile range) sampling interval was 35 (13–93) days. The median (interquartile range) number of samples per patient was 2 (1 to 3). The range was 1 to 23 samples per patient.

The median (interquartile range) LBC was from 0.57 (0.4 to 0.7) mmol/L for those patients who had one sample and 0.75 (0.58 to 0.92) mmol/L for the patient who had 23 samples taken.

Likewise the median (interquartile range) interval between samples was 149 (78 to 196) days for those sampled twice to 6 (4 to 8) days for the patient who had 23 samples taken.

Sampling was performed approximately every 3 months (80 to 100 days) in 11 patients (<1%). When the interval was widened to 60 to 130 days this increased to 42 patients (3%). 85 patients (6%) had 1 or 2 dosing intervals that were approximately 3 months (80 to 100 days) apart.

Discussion

A recent retrospective UK audit of 2976 patients taking lithium found that 30% of patients had had 4 or more LBCs analysed during a 1-year period. 9% of patients had not had a LBC analysed.⁶

In comparison, 20% of Canterbury patients had had 4 or more LBCs analysed, 8% had not had a LBC analysed at all during the one year period and LBCs were taken on a regular basis (at least every 60 to 130 days) in only 3% of patients. There could be a number of reasons why the monitoring of LBCs was less than ideal. This includes lack of knowledge of lithium therapeutics, patients failing to attend laboratory appointments, differences between psychiatrist and primary care.

Other audits found that monitoring of LBCs did not meet the relevant standards.⁷⁻¹³ Although we could not find evidence to show a reduction in mortality with regular monitoring of LBCs, it appears to be prudent to do so, given the predictable toxicity with elevated LBCs.

Eagles et al noted that monitoring of LBCs improved in the year after the distribution of guidelines in northeast Scotland.¹⁴ Fielding et al found that a dedicated lithium monitoring service in Southampton, UK led to higher compliance with the relevant guidelines.¹⁵ A lithium monitoring database run by a hospital pharmacy service in Norfolk, UK led to a substantial improvement in compliance with NICE standards.¹⁶

Although this audit did not look at whether the monitoring of renal and thyroid function occurred every 6 months as the complete dataset was not available, other studies did. They found that these monitoring targets were achieved in between 50% and 66% of patients^{6-8,12} although other audits found much lower rates had been achieved.^{9,10}

Eagles et al. found that this monitoring improved significantly after the introduction of guidelines.¹⁴ A dedicated lithium monitoring service achieved annual monitoring of thyroid and renal function test in 83.7% of patients.¹⁵

The mean LBC in our cohort was 0.63 mmol/L. Other studies found similar mean LBCs of 0.69 mmol/L;¹³ 0.64 mmol/L¹⁷ and 0.63 mmol/L.¹⁸ It is reassuring that the Canterbury population has a similar mean LBC to other published mean values.

When high LBCs (>1.2 mmol/L) were examined, 12.5% (7/56) of patients were retested within 3 weeks. This is concerning as lithium has predictable toxicity when the blood concentrations are elevated. When patients present with an elevated LBC, it

should be standard practice to promptly repeat the LBC and reduce the dose if appropriate.

Other centres have improved their monitoring by either publishing and distributing guidelines or introducing a lithium patient database and monitoring service. We suggest that these improvements should be implemented in Canterbury. Patient information should be updated and a comment on pathology reports indicating how frequent LBC should occur is also desirable. We would intend to audit the monitoring of LBC after the above has been implemented.

There were a number of limitations of this audit. It was conducted retrospectively. Lithium usage was based on subsidised pharmacy dispensing data and does not reflect patient compliance with treatment. There were no patient-identifying details with the dispensing data, thus we did not have a complete record of the patients on lithium in Canterbury. Patient records were not reviewed.

In conclusion, LBC monitoring at CDHB did not achieve the targets of the NHS National Patient Safety Agency patient safety alert. This is in keeping with a number of other international audits of LBC monitoring. Given lithium's predictable dose related adverse effects and propensity for drug interactions, it would be desirable to achieve these targets.

Competing interests: None declared.

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