

Lithium monitoring in clinical practice

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BACKGROUND

Lithium is widely used for the treatment of bipolar disorder. Owing to its narrow therapeutic index and side-effect profile, regular monitoring is recommended by all major guidelines on lithium use.

AIMS

The aim of this study was to determine whether routine lithium monitoring practice at the local mental hospital in Malta reaches the standard set by the NICE guidelines in 2014.

METHOD

All patients on lithium maintenance treatment for bipolar disorder at the local Mental Hospital were included. Blood tests within the last one year were collected using iSOFT clinical manager (iCM). After the first audit cycle, a lithium monitoring sheet was created in accordance with the NICE guideline and after 6 months of implementation, the second audit cycle was conducted.

RESULTS

In the first cycle, 28 patients met the NICE criteria for increased risk of toxicity and have a recommended testing frequency for lithium levels of every 3 months. However, only 1 patient (3.7%) was observed to meet this criteria. When assessing the last lithium level only 35.7% were within 0.4-0.8 mmol/L. In the second audit cycle, 28 patients met the NICE criteria for increased risk of toxicity and have a recommended testing frequency for lithium levels of every 3 months. Almost half of the patients (12 patients, 42.8%) were observed to meet this criteria. When assessing the last lithium level, 50.0% were within 0.4-0.8 mmol/L.

CONCLUSIONS

The introduction of the lithium monitoring sheet helped significantly in increasing the monitoring of lithium levels in patients which are at a higher risk of lithium toxicity. Moreover, the monitoring sheet helped the clinicians in maintaining lithium levels within the normal therapeutic range, hence prevent unwanted side effects related to lithium toxicity.

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INTRODUCTION

Lithium is treatment used for bipolar mood disorder, both in the acute and maintenance phase.¹ Mood stabilizers effectively treat the symptoms of bipolar disorder however, they are potential linked with adverse drug events (ADEs).² Nederlof in 2015,³ mentioned that apart from lithium serum levels, monitoring of should include other laboratory tests and physical parameters. Lithium use has been associated with a gradual decline in renal function, however, this decline can become irreversible and may also lead to renal failure.⁴ Moreover, the decline in renal function can lead to an increased risk of lithium toxicity.⁵ In view of possible hypothyroidism and hyperparathyroidism, monitoring of thyroid function and calcium levels is recommended.⁶ Physical parameters such as weight and blood pressure may also be influenced with lithium use so regular monitoring of such parameters are crucial.⁴

OBJECTIVES

The aim of this study was to determine whether routine lithium monitoring practice during maintenance phase treatment of bipolar mood disorder, at the local Mental Hospital in Malta reaches the standard set by the National Institute for Health and Care Excellence (NICE) guideline "Bipolar disorder: assessment and management" published in 2014.⁷

METHODOLOGY

Approval was sought from the Clinical Chairman of Psychiatry and Data Protection officer. Retrospective data were extracted from patient's clinical file and iSOFT clinical manager (iCM). All patients on lithium maintenance phase treatment for bipolar disorder at the local Mental Hospital were included in the study. Blood test monitoring

and physical parameters within the last 1 year were collected for each patient.

After the first audit cycle, a lithium monitoring sheet was created in accordance with the NICE guideline "Bipolar disorder: assessment and management" published in 2014. After getting the necessary approval, this monitoring sheet was disseminated in every ward at the local hospital. Training on how to use the sheet was provided all the foundation doctors and psychiatric trainees to facilitate usage. After 6 months of implementation, the second audit cycle will commence.

RESULTS

Audit Cycle 1

A sample of 42 patients were collected. 25 were males and 17 were females. Of these 42 participants, 23.8% were aged 65 and above, 35.7% had interacting medications (NSAID, COX II inhibitor, thiazide or loop diuretic, ACE inhibitor or angiotensin II receptor antagonist), 64.3% had co-morbid disease (hypertension, diabetes and/or any thyroid disorder) and 21.4% had kidney impairment (EGFR less than 60).

When assessing the last lithium level, 35.7% were within 0.4-0.8 mmol/L, 35.7% were within 0.8-1.0 mmol/L, 19% were below 0.4 mmol/l and 9.5% were above 1.0 mmol/L. (Figure 1).

For those patients who had >1 test result in the database, the recommendation of at least one blood test every 6 months was met 76.1% of cases for lithium level, 88.0 % of cases for EGFR and renal function and 71.4% of cases for thyroid function. However, only 38.0% had a serum calcium level within the last 6 months. BMI or weight monitoring are recommended at least yearly, but only 14.2% met this recommendation within the last year. (Figure 2).

Figure 1 Serum lithium levels

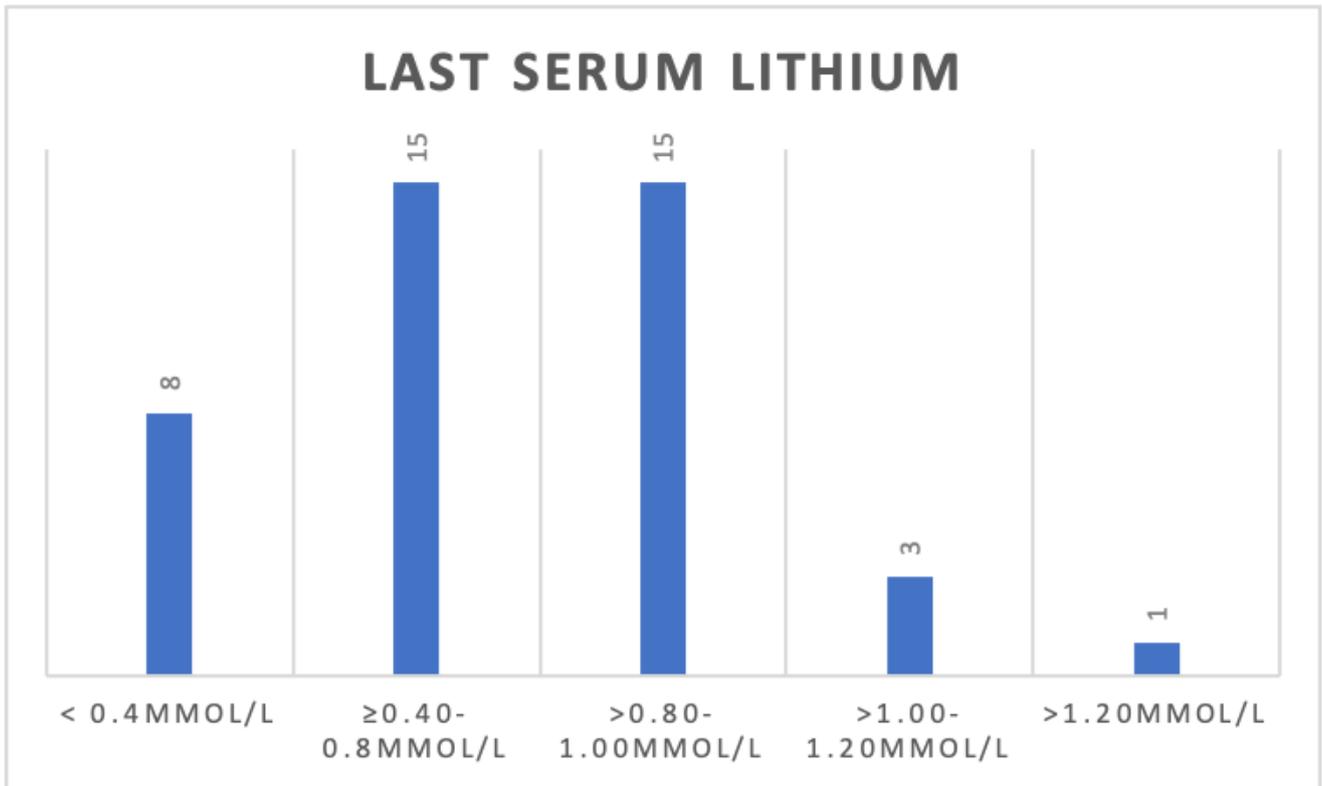
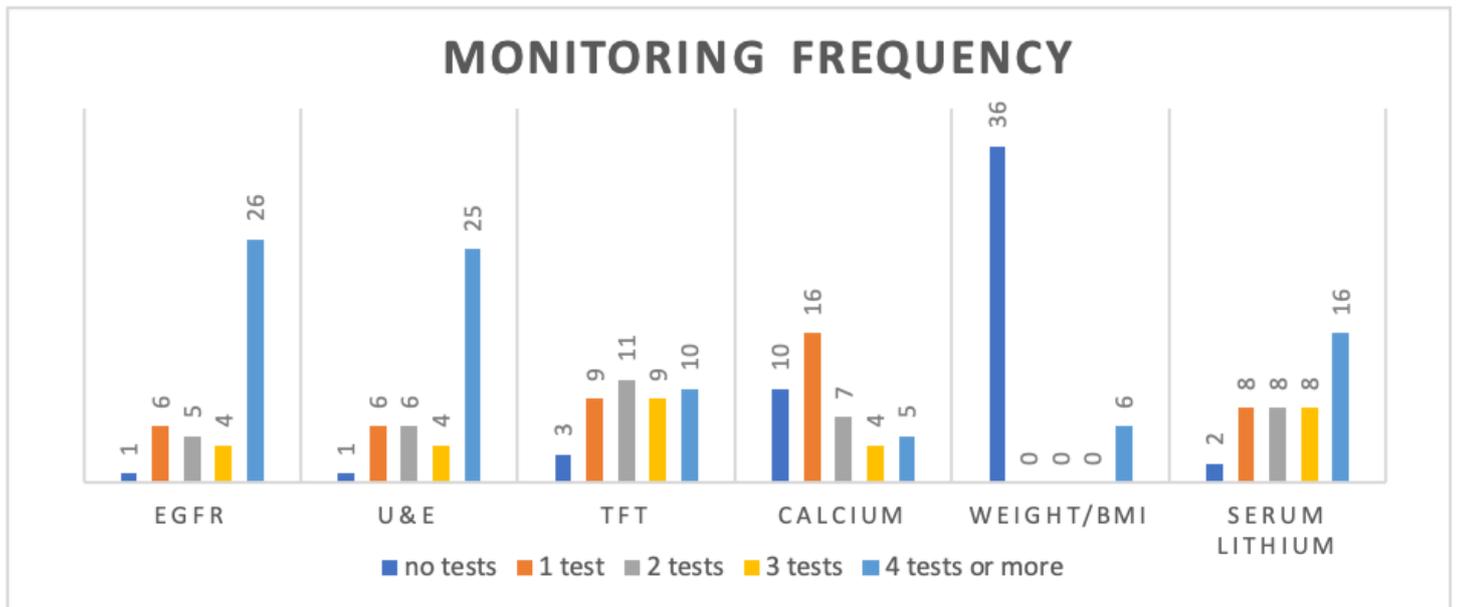


Figure 2 Frequency of monitoring



Twenty-eight out of the 42 patients, had met the NICE 2014 criteria for increased risk of toxicity (i.e. elderly, chronic co-morbidity and/or were co-prescribed at least one medication with a BNF specified interaction with lithium). In such cases, serum lithium monitoring frequency is recommended to be least once every 3 months. However, only 1 patient (3.6%) was observed to meet the criteria. 12 patients were observed to be monitored on a period of between 5-7 months, whilst 15 patients were observed on a period of greater than 7 months.

Audit Cycle 2

A sample of 44 patients were collected. 23 were males and 21 were females. Out of the 44 patients, 9.0% were aged 65 and above, 50.0% had interacting medications (NSAID, COX II inhibitor, thiazide or loop diuretic, ACE inhibitor or angiotensin II receptor antagonist) and 39.0% had chronic co morbidity (hypertension, diabetes, any thyroid disorder).

When assessing the last lithium level, 50.0% were within 0.4-0.8 mmol/L, 16.0% were within 0.8-1.0 mmol/L, 25.0% were below 0.4 mmol/l, 5.0% were

above 1.0 mmol/L and 5.0% had no bloods recorded. (Figure 3).

For those patients who had >1 test result in the database, the recommendation of at least one blood test every 6 months was met 80.0% of cases for lithium level, 52.0% of cases for EGFR and renal function and 71.4% of cases for thyroid function. However, only 25.0% had a serum calcium level within the last 6 months. BMI or weight monitoring are recommended at least yearly, but none of the patients met this recommendation within the last year (Figure 4).

28 out of 44, had met the NICE 2014 criteria for increased risk of toxicity (i.e. elderly, chronic co-morbidity and/or were co-prescribed at least one medication with a BNF-specified interaction with lithium) and have a recommended testing frequency for lithium levels of every 3 months. Almost half of the patients (12 patients, 42.0%) were to observed to meet these criteria. 12 patients were observed to be monitored on a period of between 5-7 months, whilst 4 patients were observed on a period of greater than 7 months. (Figure 5).

Figure 3 Serum lithium levels

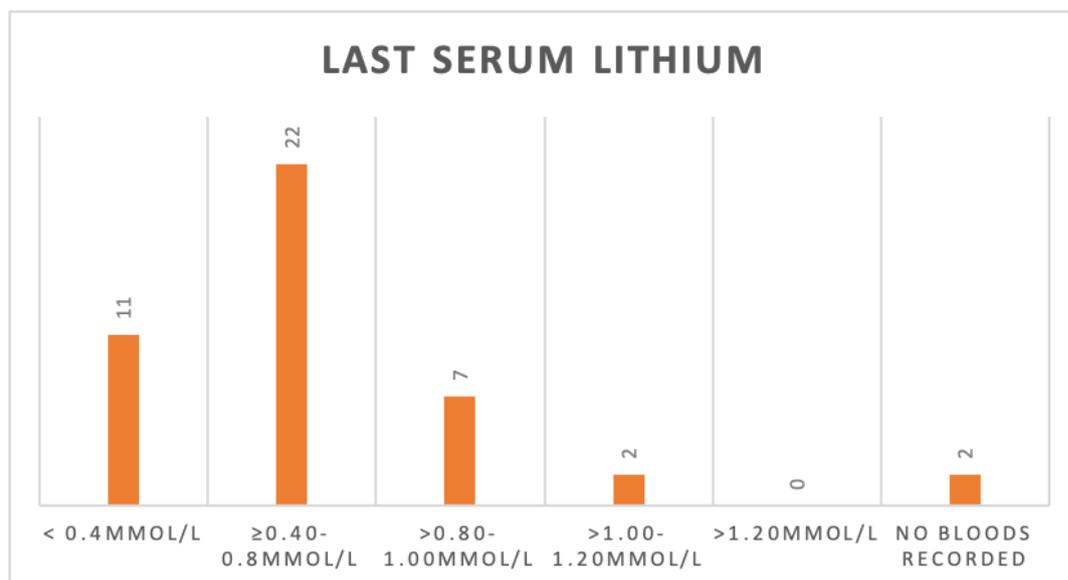


Figure 4 Frequency of monitoring

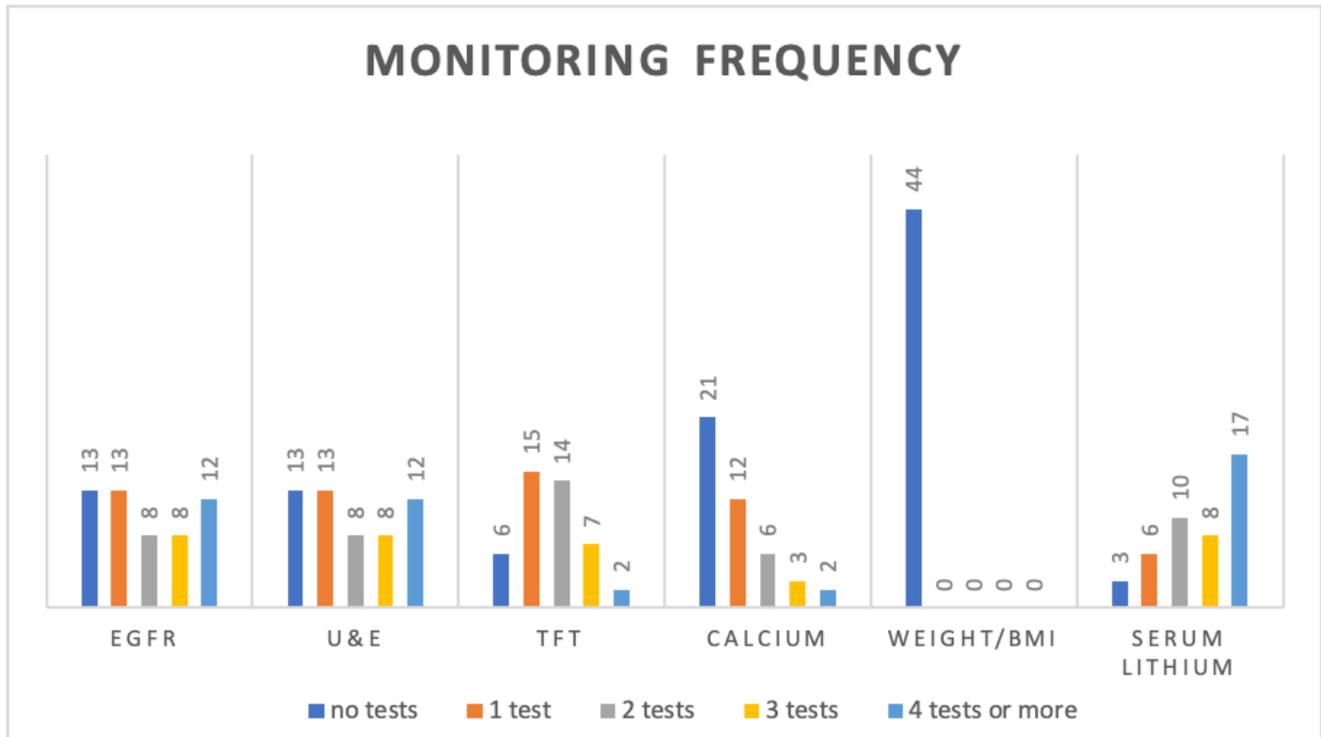
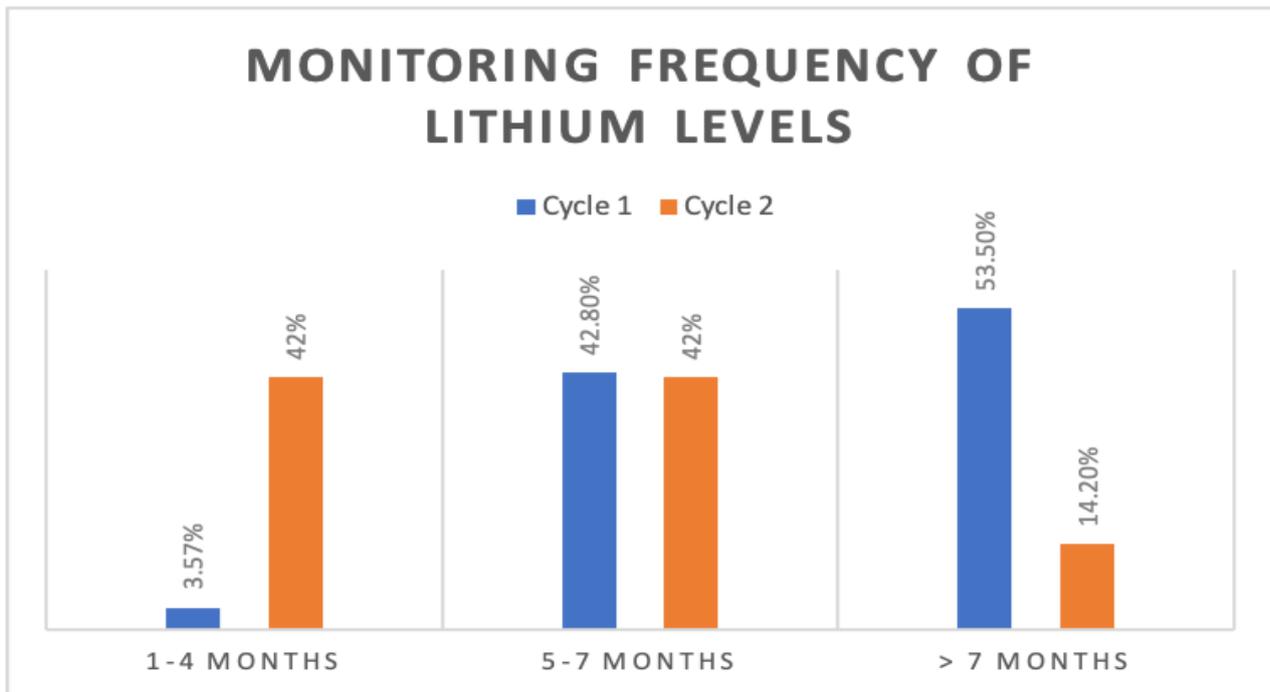


Figure 5 Comparing the monitoring frequency of lithium levels in cycle 1 and cycle 2



CONCLUSION

The introduction of the lithium monitoring sheet helped significantly in increasing the monitoring of lithium levels in patients which are at a higher risk of lithium toxicity. Moreover, the monitoring sheet helped the clinician in maintaining lithium levels within the normal therapeutic range, hence prevent unwanted side effects related to lithium toxicity.

RECOMMENDATIONS

Introducing the lithium monitoring sheet in the Community Mental Health Clinics and disseminating amongst general practitioners may help in increasing safety practices amongst all mental health services and primary care.

REFERENCES

1. Licht, R. (2011). Lithium: Still a Major Option in the Management of Bipolar Disorder. *CNS Neuroscience & Therapeutics*, 18(3), 219-226. doi: 10.1111/j.1755-5949.2011.00260.x
2. Rothschild, J., Mann, K., Keohane, C., Williams, D., Foskett, C., & Rosen, S. et al. (2007). Medication safety in a psychiatric hospital. *General Hospital Psychiatry*, 29(2), 156-162. doi: 10.1016/j.genhosppsy.2006.12.002
3. Nederlof M, Stoker LJ, Egberts TCG, Heerdink ER. Instructions for clinical and biomarker monitoring in the summary of product characteristics (SmPC) for psychotropic drugs: overview and applicability in clinical practice. *J Psychopharmacol Oxf Engl*. 2015;29(12):1248–54. *Disorders*, 6(1). doi: 10.1186/s40345-018-0120-1
4. Gitlin, M. (2016). Lithium side effects and toxicity: prevalence and management strategies. *International Journal Of Bipolar Disorders*, 4(1). doi: 10.1186/s40345-016-0068-y
5. Lepkifker E, Sverdlik A, Iancu I, Ziv R, Segev S, Kotler M. Renal insufficiency in long-term lithium treatment. *J Clin Psychiatry*. 2004;65(6):850–6.
6. Nederlof, M., Heerdink, E., Egberts, A., Wilting, I., Stoker, L., Hoekstra, R., & Kupka, R. (2018). Monitoring of patients treated with lithium for bipolar disorder: an international survey. *International Journal Of Bipolar*
7. *Bipolar disorder: assessment and management*. (2014). Retrieved 24 January 2021, from <https://www.nice.org.uk/guidance/cg185/resources/bipolar-disorder-assessment-and-management-35109814379461>