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Minimizing negative outcomes associated with potentially harmful lithium levels by means of pharmacist-led educational interventions in an inpatient psychiatric facility

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Abstract

Introduction: Studies examining educational interventions led by pharmacists to minimize negative outcomes associated with elevated and potentially harmful lithium levels in inpatient psychiatric facilities are lacking. Other studies indicate a need for improvement of therapeutic drug monitoring for lithium. The aim of this article is to identify potential improvements in negative outcomes associated with harmful lithium blood levels after educational interventions are delivered by a clinical pharmacist to providers of an inpatient psychiatric facility.

Methods: Medication reports were queried from the pharmacy database to identify all patients who were taking lithium within 1 year. Laboratory results, physician progress notes, nursing progress notes, and treatment plans were studied to detect any adverse events associated with lithium levels. Educational interventions created by pharmacy services were tailored toward medical staff and delivered over a 3 month period. Learning was assessed at pre-educational and posteducational interventions.

Results: One hundred fifteen patients received lithium between March 2012 and March 2013. The most-frequent adverse effects reported associated with lithium included tremor, dizziness, slurred speech, and lethargy. Two patients were sent to the local emergency department for lithium toxicity and required dialysis. Fifty-two patients received lithium after educational interventions, and no adverse events were reported. A lithium drug-monitoring spreadsheet was created for pharmacy use, and drug-monitoring guidelines were revised and disseminated throughout the facility.

Discussion: A reduction in negative outcomes associated with lithium was noted after educational interventions to medical staff occurred. The impact of pharmacist-led educational interventions demonstrated a high potential for success.

Keywords: lithium, toxicity, educational interventions, pharmacist, education, adverse effects, drug interactions, lithium levels

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Introduction

Lithium is a mood-stabilizing drug approved in the 1970s for the treatment of mania by the US Food and Drug Administration (FDA). Lithium is used in the treatment of acute episodes and for maintenance in bipolar disorder and may be beneficial for major depressive disorder, reducing suicide risk, vascular headache, and neutropenia. The exact mechanism of lithium is not completely understood, but it is known that lithium blocks potassium

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channels and disrupts monoamine neurotransmitter action in the brain and increases serotonin (5-HT) synthesis and release from the central nervous system.[1] The efficacy of lithium is dose dependent and may be directly related to serum concentrations.[2] Guidelines suggest a lithium serum level between 0.5 or 0.6 and 1.1 or 1.2 mmol/L for both the management of acute mania and the prophylaxis of mania. Maintenance therapy for elderly patients should target levels on the lower end of the range.[3]

Lithium is a narrow therapeutic index drug and is associated with a high number of reported adverse effects in the general population.[4] Many patients in acute inpatient psychiatric facilities receive concomitant medications, such as diuretics, angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, and antipsychotics, which may increase their risk of developing lithium toxicity.[5] Adverse events associated with lithium toxicity may include nausea, vomiting, diarrhea, confusion, renal failure, ataxia, tremor, delirium, seizures, coma, and death.[1,2] There is concern with lithium use during pregnancy because of reports of teratogenicity, and lithium monitoring is especially important during pregnancy to avoid lithium toxicity in both the mother and fetus.[6]

According to Oakley and colleagues,[7] severe lithium neurotoxicity occurs at levels greater than 1.5 mmol/L, and toxicity is more likely to result from chronic therapeutic administration when compared with acute poisoning. Adityanjee and colleagues[8] found lithium-associated neurotoxicity occurred in 25% of cases at serum lithium levels of 1.2 mmol/L or less. In addition to serum lithium-level monitoring, other patient factors to monitor should include body weight, body mass index or waist circumference, thyroid function, and renal function.[9,10] Another important consideration includes the patient's clinical response to long-term lithium treatment. Patients who do not respond to lithium treatment develop side effects more frequently than do those who respond, even when serum lithium levels are comparable.[11] Patients experiencing side effects may be admitted on a lithium dose that has not been changed in many years, and laboratory results may indicate their lithium levels are much higher than 1.0 mmol/L. Education for hospital staff on appropriateness of lithium sample collection, interpretation, and proper use of serum drug levels is encouraged.[12]

Pharmacists, who serve as the medication experts, are ideal for educating other health care professionals on lithium adverse effects, drug interactions, signs and symptoms of toxicity, drug-level monitoring, and treatment options for patients with adverse events from lithium. Lithium monitoring standards may be improved through the involvement of a multidisciplinary team and a comprehensive education system.[13]

Methods

Adult patients, ages 18 years or older, admitted to an inpatient psychiatric facility within the past year who received lithium were sorted through an electronic pharmacy database. Data recorded included date lithium initiated or changed, dose, frequency, and lithium levels with monitoring frequency. The active and discharged patient charts were reviewed to further assess laboratory values, physician progress notes, nursing progress notes, and treatment plans to determine whether any adverse events associated with lithium levels occurred. Additionally, toxic serum levels were defined from the lithium package insert as any concentration greater than 1.5 mmol/L with signs and symptoms of lithium intoxication or any level where signs and symptoms of lithium toxicity were present. Admission data to emergency departments or other acute care hospitals associated with toxicity was recorded. The estimated renal function of each patient was calculated via the Cockcroft-Gault equation.

A list of negative outcomes was recorded, and educational interventions were created to emphasize the results of the chart reviews. The pharmacy team created an interactive PowerPoint® (Microsoft, Redmond, WA) presentation that highlighted lithium pharmacology, pharmacokinetics, and pharmacodynamics and included case discussions based on patient scenarios encountered during the manual chart audits. A clinical pharmacist delivered the in-service workshop in a conference room on 3 separate occasions over a 3 month period until all providers completed the training. Medical staff was required by the department's medical director to attend one presentation.

An institutional review board informed-consent document for research was disseminated to all in-service attendees. Thirteen providers (ie, psychiatrists and nurse practitioners) completed the educational interventions, with most (69%) attending the first presentation. Knowledge of key concepts was assessed at preintervention (immediately before the presentation) and posteducational intervention (immediately after the presentation) through a 7-question exam (Figure 1) with case scenarios throughout (Figure 2). Verbal and written feedback was provided to practitioners and a peer review data collection form specific to lithium was created.

Once educational interventions ceased in August 2013, a list of adult patients who had received lithium therapy for the past 3 months (August-October) was sorted in an electronic pharmacy database. Active and discharged patient charts were once again reviewed to assess laboratory values, physician progress notes, nursing progress notes, and treatment plans to determine whether any adverse events associated with lithium levels occurred. Toxic serum levels were recorded along with

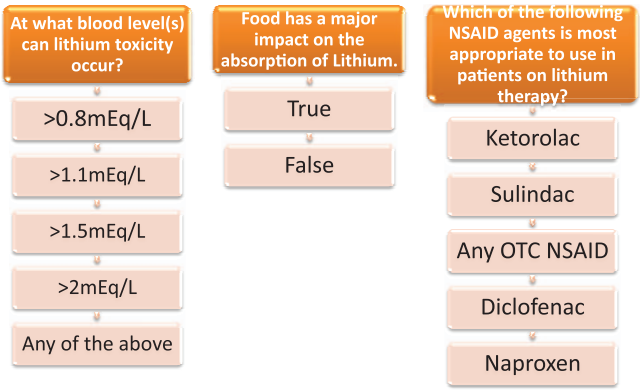


FIGURE 1: Assessment questions used pre-educational and posteducational interventions

NSAID = nonsteroidal anti-inflammatory drug; OTC = over-the-counter

signs and symptoms of lithium intoxication. The estimated renal function of each patient was calculated via the Cockcroft-Gault equation. The results of the lithium peer review data collection form were disseminated to the facility's medical director.

Results

Before educational interventions, 115 charts of patients taking lithium and admitted to a state psychiatric hospital between March 2012 and March 2013 were reviewed. The primary adverse drug reactions observed included tremor, dizziness, slurred speech, and lethargy. Two patients were sent to the nearest academic medical center for treatment of lithium toxicity, and dialysis was used. A negative outcomes list was compiled, and educational interventions were tailored to include those events. Pharmacology, pharmacokinetics, drug interactions, and drug level monitoring of lithium were incorporated into the in-services and assessments provided to medical staff (n = 13) over 3 months. The average score on preassessment questions was a 71%, whereas the average score on postassessment questions was 100%.

Once educational interventions were completed, 52 charts were reviewed of patients taking lithium between August 2013 and October 2013. There were no adverse events reported, and all lithium levels were ≤ 1.5 mmol/L. Therefore, a reduction in negative outcomes associated with lithium was noted after the educational interventions

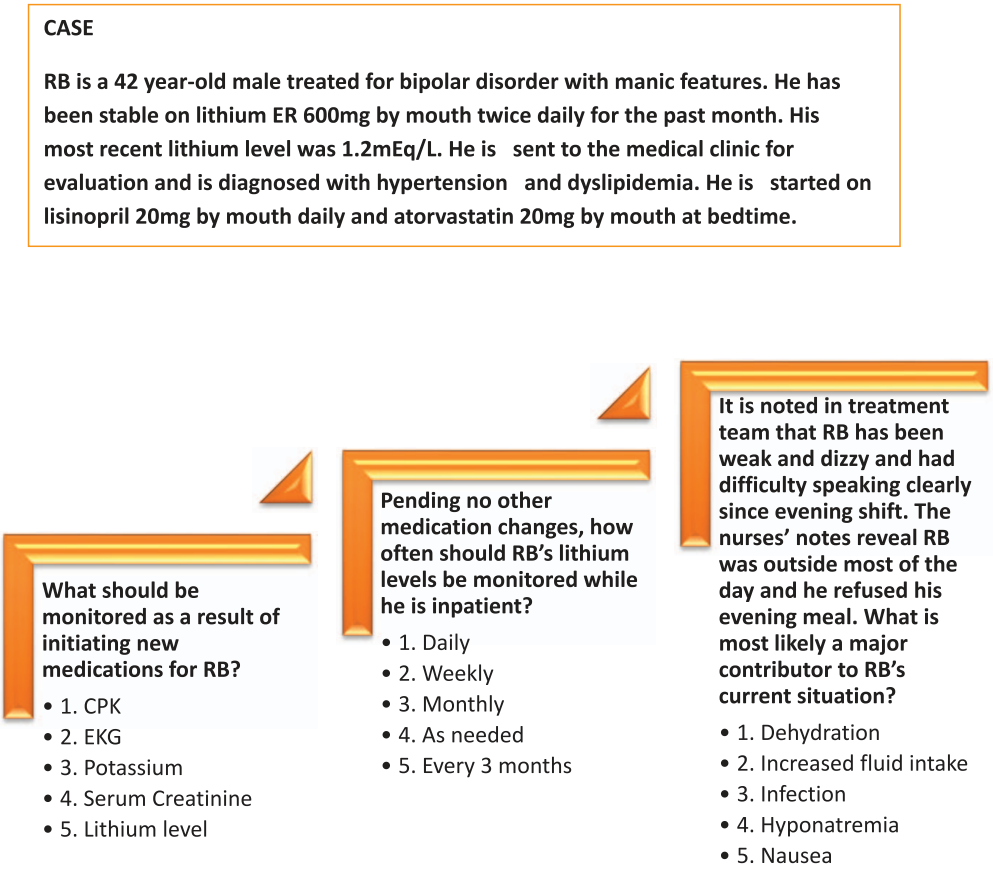


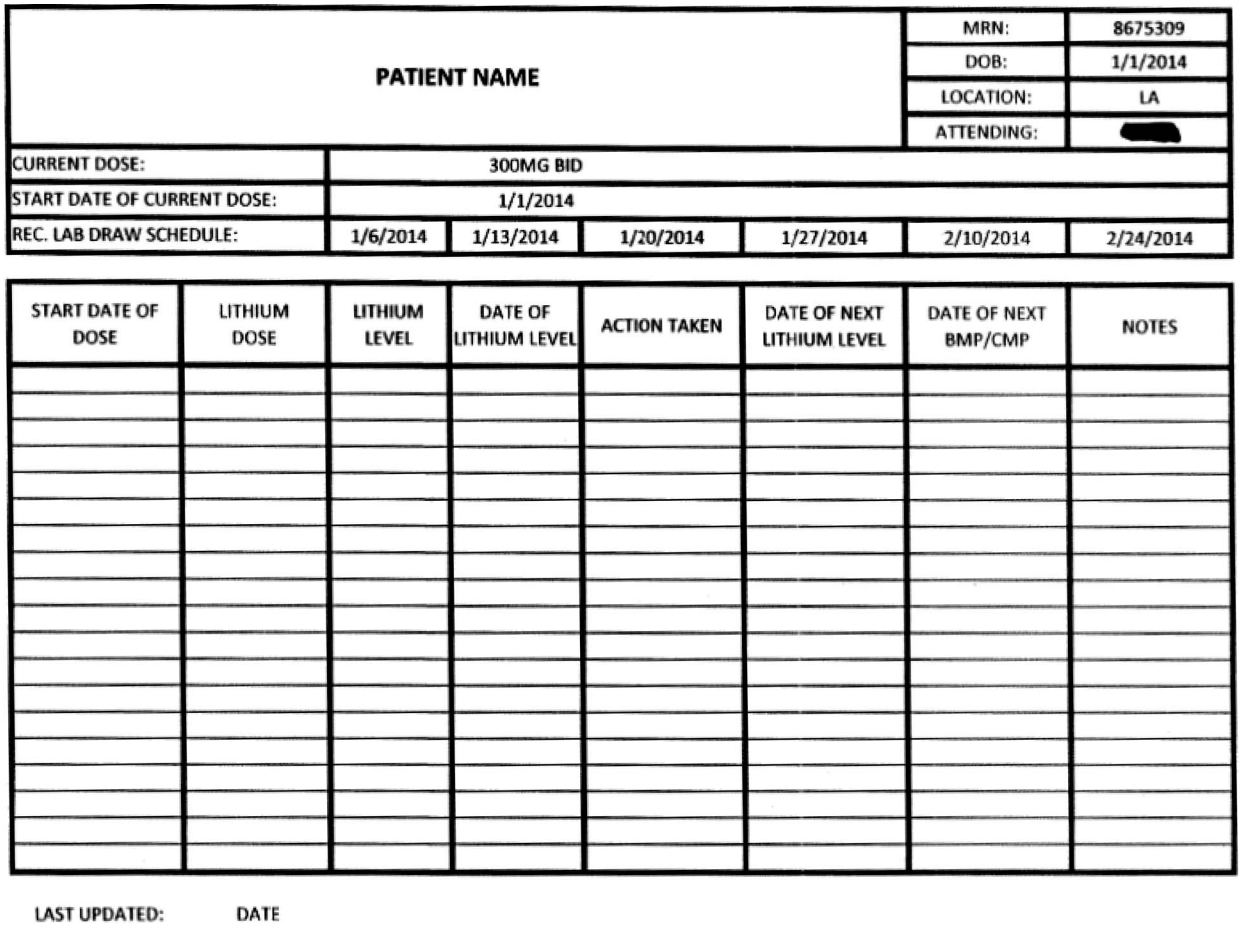
FIGURE 2: Case scenario and assessment questions used pre-educational and posteducational interventions

CPK = creatine phosphokinase; EKG = electrocardiogram

TABLE: Division of inpatient services, lithium monitoring, and laboratory protocol

At Time of Admission	Initial Monitoring Schedule	Maintenance Monitoring Schedule
• CBC with differential/platelets, CMP, TSH in am	• Lithium level, in AM, after 5 d from initiation/change of lithium; then weekly × 4 wk; then every 2 wk × 4 wk; then monthly.	• Lithium level monthly or whenever clinical status changes
• Date of last menstrual period/pregnancy test (if applicable)	→ Range 0.5-1.5 mEq/L (mmol/L)	• After a dosage change, return to initial monitoring schedule
• Lithium blood level (if applicable)	→ Preferred 0.8-1.0 mEq/L (mmol/L)	• Documentation advised for levels monitored less frequently than monthly (ie, chronic, stable patients with no therapy changes)
• EKG (for patients ≥ 40 y or history of cardiac disease)	• Weekly BMP/CMP • Weekly weight • Fluid intake* (goal: 2000 to 3000 mL fluid/d) *Whenever fluid intake is compromised (ie, patient refusal, nausea, vomiting, diarrhea, dehydration, sweating, or other condition that decreases fluid volume) notify provider	• For patients on HCTZ, ACEI/ARB, or any medication that may increase lithium levels, then more frequent lithium level checks are recommended • BMP/CMP, TSH every 3 mo

ACEI = angiotensin-converting enzyme inhibitor; AM = morning; ARB = angiotensin receptor blocker; BMP = basic metabolic panel; CBC = complete blood count; CMP = comprehensive metabolic panel; EKG = electrocardiogram; HCTZ = hydrochlorothiazide; TSH = thyroid stimulating hormone



PATIENT NAME					MRN:	8675309
					DOB:	1/1/2014
					LOCATION:	LA
					ATTENDING:	[redacted]
CURRENT DOSE:	300MG BID					
START DATE OF CURRENT DOSE:	1/1/2014					
REC. LAB DRAW SCHEDULE:	1/6/2014	1/13/2014	1/20/2014	1/27/2014	2/10/2014	2/24/2014

START DATE OF DOSE	LITHIUM DOSE	LITHIUM LEVEL	DATE OF LITHIUM LEVEL	ACTION TAKEN	DATE OF NEXT LITHIUM LEVEL	DATE OF NEXT BMP/CMP	NOTES

LAST UPDATED: DATE

FIGURE 3: Patient-specific lithium monitoring form

BMP = basic metabolic panel; CMP = comprehensive metabolic panel

to medical staff occurred. Additional actions included revising the inpatient lithium drug-monitoring guidelines (Table), which were shared with all practitioners. A drug-monitoring worksheet was generated for all patients on lithium and maintained in the pharmacy (Figure 3). After the conclusion of this study, further lithium in-service sessions were created and delivered to nursing staff at the request of the nursing director. The impact of pharmacist-led educational interventions demonstrated a high potential for success.

Discussion

The narrow therapeutic index of lithium dictates drug-level monitoring. Previous studies indicate the need to improve the use of therapeutic drug monitoring for lithium, and education for practitioners involved in direct patient care is warranted. The development of a lithium-monitoring form maintained by a pharmacist containing essential data for individualized patients, such as lithium level, date of next lithium level, lithium dose, and date of next laboratory test providing renal function (eg, basic metabolic panel, comprehensive metabolic panel) would be ideal and may optimize medication therapy and decrease potential negative outcomes to patients. Additional data, such as concomitant medications/drug interactions, signs/symptoms of lithium toxicity, and the hydration status of the patient, would be beneficially included to assist the provider with serum-level monitoring and dosage adjustment when indicated.

A study by Collins and colleagues[9] determined lithium monitoring was superior when overseen by a psychiatrist or a pharmacist. Pharmacists are valued members of the health care team with unique knowledge and skills that may be used to provide education to other health care professionals in an inpatient psychiatric setting. Although educational material alone is unlikely to give rise to changes in clinical practice, lithium-monitoring standards may be improved through the involvement of a multidisciplinary team and a more detailed provider education system.[14]

Although the implementation of pharmacist-led in-services as well as the lithium-monitoring form containing essential data for individualized patients (Figure 3) may have optimized therapy and decreased negative outcomes, there were several limitations in this study. Although providers attended the first educational session, several attended the later session in August. The second portion of the study reviewed charts in August and may have included patients of providers who had not yet attended the in-services. The learning from the educational interventions was assessed immediately after the conclusion of the presentation for each provider and resulted in perfect scores. If assessments of posteducational intervention learning were observed later, then scores may have decreased. Practitioner recall was recorded immediately following educational interventions with practitioner retention based on the results of the second set of chart reviews.

Another limitation includes the timeline of the data collection. The initial data collection involved 12 months of chart reviews; however, after the completion of educational interventions only 3 months of chart reviews were performed. Although 3 months of data demonstrated a positive trend, emphasizing that pharmacists can serve as educators to other health care professionals in an inpatient psychiatric setting, the outcomes would have been strengthened if 12 months of charts had been reviewed. A medication-use evaluation by pharmacy staff for lithium is scheduled at the end of 2014, approximately 1 year after the conclusion of this study to further assess provider adherence to lithium monitoring and to reporting adverse events associated with lithium.

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References

1. Stahl S. Lithium. In: The prescriber's guide—Stahl's essential psychopharmacology online [Internet]. New York: Cambridge University Press; 2014. [cited 2014 Jul 14]. Available from: http://stahlonline.cambridge.org.
2. Grandjean EM, Aubry JM. Lithium: updated human knowledge using an evidence-based approach, part 1: clinical efficacy in bipolar disorder. CNS Drugs. 2009;23(3):225-40. DOI: 10.2165/00023210-200923030-00004.
3. National Institute for Health and Clinical Excellence. Bipolar disorder: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care—clinical guideline 38. Leicester (UK): British Psychological Society; 2006. Available from: http://www.nice.org.uk.
4. McKnight RF, Adida M, Budge K, Stockton S, Goodwin GM, Geddes JR. Lithium toxicity profile: a systematic review and meta-analysis. Lancet. 2012;379(9817):721-8. DOI: 10.1016/S0140-6736(11)61516-X. PubMed PMID: 22265699.
5. Wijeratne C, Draper B. Reformulation of current recommendations for target serum lithium concentration according to clinical indication, age and physical comorbidity. Aust N Z J Psychiatry. 2011;45(12):1026-32. DOI: 10.3109/00048674.2011.610296. PubMed PMID: 21961481.
6. Tillery EE, Tonet RL, Trahan CA. Oh baby! a review of mood stabilizers for bipolar disorder in the child-bearing woman. Ment Health Clin. 2013;3(2):100. DOI: 10.9740/mhc.n163522.

7. Oakley PW, Whyte IM, Carter GL. Lithium toxicity: an iatrogenic problem in susceptible individuals. Aust N Z J Psychiatry. 2001; 35(6):833-40. PubMed PMID: 11990895.
8. Adityanjee, Mushi KR, Thampy A. The syndrome of irreversible lithium-effectuated neurotoxicity. Clin Neuropharmacol. 2005; 28(1):38-49.
9. Collins N, Barnes TRE, Shingleton-Smith A, Gerrett D, Paton C. Standards of lithium monitoring in mental health trusts in the UK. BMC Psychiatry. 2010;10(1):80. DOI: 10.1186/1471-244X-10-80.
10. Calkin C, Alda M. Beyond the guidelines for bipolar disorder: practical issues in long-term treatment with lithium. Can J Psychiatry. 2012;57(7):437-45. PubMed PMID: 22762299.
11. Müller-Oerlinghausen B, Bauer M, Grof P. Commentary on a recent review of lithium toxicity: what are its implications for clinical practice? BMC Med. 2012;10:132. DOI: 10.1186/1741-7015-10-132. PubMed PMID: 23121772.
12. Ratanajamit C, Soorapan S, Doang-ngern T, Waenwaisart W, Suwanchavalit L, Suwansiri S, Jantasaro S, Yanate I. Appropriateness of therapeutic drug monitoring for lithium. J Med Assoc Thai. 2006;89(11):1954-60. PubMed PMID: 17205880.
13. Udumaga E, Mannion L. An audit in general adult psychiatry service. Ir Med J. 2010;103(4):123-4. PubMed PMID: 20486321.
14. Gupta N. Guidelines for lithium monitoring: are they ideal [comment]? Acta Psychiatr Scand. 2001;104(1):76-8.