CASE REPORT

POLYPHARMACY MAY BE THE CAUSE OF ACUTE LITHIUM INTOXICATION AT THE SECOND DAY OF TREATMENT

Irfan Tursun*, Gokhan Tazegul, Ogur Karhan, Neslihan Gunes, Ece Ulukal, Muge Arpali Atcakarlar, Tolgahan Akca, Erkan Coban

Department of Internal Medicine, Faculty of Medicine, Akdeniz University, Antalya, Turkey

ПОЛИФАРМАЦИЯ МОЖЕТ БЫТЬ ПРИЧИНОЙ ОСТРОЙ ЛИТИЕВОЙ ИНТОКСИКАЦИИ ЕЩЁ НА ВТОРОЙ ДЕНЬ ЛЕЧЕНИЯ

Ирфан Турсун*, Гокхан Тазегул, Огур Кархан, Неслихан Гюнес, Еце Уликал, Муге Арпали Ацакарлар, Толгхан Акча, Еркин Чобан

Кафедра внутренних болезней, Факультет медицины, Университет Акдениз, Анталия, Турция

ABSTRACT

Lithium is frequently used as a mood stabilizer in patients with mood disorders. Lithium has a narrow therapeutic index and high toxicity. Predisposing factors for intoxication are advanced age, diet disturbances, comorbid medical conditions affecting heart, kidneys or central nervous system and polypharmacy. **CASE REPORT:** Here we present a case of a 74-year-old woman with a history of Parkinson's disease, hypertension and bipolar disorder. She was using quetiapine, valsartan with hydrochlorothiazide and levodopa with carbidopa. She presented with altered mental status and muscle rigidity. The patient was admitted with acute lithium intoxication after her second dose of treatment. Blood lithium level increased to 3.58 mEq/L. The woman was hospitalized in the Internal Medicine Intensive Care Unit. With hydration, her symptoms resolved and her lithium level returned to normal after 118 hours. **CONCLUSIONS:** Prescribing physicians and emergency room physicians should be aware of conditions which may cause a decreased threshold for intoxication.

Key words: *lithium, polypharmacy, drug overdose*

Folia Medica 2015;57(3&4):261-263

Copyright © 2015 Medical University, Plovdiv

РЕЗЮМЕ

Литиум является лекарственным средством, которое применяется часто для выведения из депрессивного эпизода пациентов с депрессивными расстройствами. Он является лекарственным продуктом с ограниченным терапевтическим индексом и высокой токсичностью. Усугубляющими факторами для интоксикации являются пожилой возраст, пищевые расстройства, коморбидные состояния с воздействием на сердце, почки или на центральную нервную систему, а также полифармация (полипрагмазия). **Представление клинического случая:** Сообщаем о женщине 74 лет, страдающей паркинсоном, высоким давлением и с биполярным расстройством. При лечении применялись кветиапин, валсартан с гидрохлоротиазидом и леводопа с карбидопой. При приёме пациентки был установлен изменённый психический статус и мышечная ригидность. При приёме в отделение скорой помощи был поставлен диагноз: острая интоксикация литием после двух приёмов лекарства. Концентрация литиума в крови составляла 3.58 mEq/L. Пациентка была принята в отделение интенсивной терапии внутренних заболеваний. После гидратации симптомы исчезают, а концентрация литиума нормализуется по истечении 118 часов. **Выводы:** Общепрактикующим врачам и специалистам отделений скорой помощи должны быть известны состояния, которые могут вызвать понижение порога интоксикации.

Ключевые слова: *литий, полифармация, передозировка лекарств*

Folia Medica 2015;57(3&4):261-263

© 2015 Все права защищены. Медицинский университет, Пловдив

INTRODUCTION

Lithium is often used as mood stabilizing medication in patients with mood disorders. A serum level between 0.8 miliequivalent/liter (mEq/l) and 1.2 mEq/l

is normal, and a daily oral dose is approximately between 900 to 1200 mg.¹ The maximum effective blood lithium concentration is 1.4 mEq/l, higher

Article's history: Received: 17 July 2015; Received in a revised form: 27 Jan 2016; Accepted: 17 Feb 2016

*Correspondence and reprint request to: *I. Tursun, Department of Internal Medicine, Faculty of Medicine, Akdeniz University, Antalya;* E-mail: *itursun@hotmail.com;* Tel: *+90 532 511 00 55 Akdeniz University, Dumlupınar Boulevard, Antalya, Turkey*

concentrations show that intoxication is likely.²

Lithium has a narrow therapeutic index and high toxicity. Clinical status of patients should be closely monitored for early symptoms of intoxication even when blood levels are normal.² Acute intoxication may be accidental or suicidal and is characterized by gastrointestinal and cardiotoxic side effects. Neurotoxic side effects are more common in chronic toxicity.³

We present a case of a 74-year-old woman with a history of Parkinson's disease, hypertension and bipolar disorder. Her medication included quetiapine, valsartan with hydrochlorothiazide and levodopa with carbidopa. The patient was admitted with predominant gastrointestinal and neurological symptoms of acute lithium intoxication after her second dose of treatment.

CASE REPORT

A 74-year-old female patient with a history of Parkinson's disease, hypertension and bipolar disorder was admitted to the emergency room. She was taken there by her son and presented with altered mental status and muscle rigidity. She had had nausea and vomiting for 4 hours before admission and was unresponsive to her son for 15 minutes. She was disoriented, confused and was in a stupor. The patient could only respond to questions with incomprehensible slurred sounds (Glasgow Coma Scale: eye: 2, verbal: 2, motor: 4, 8/15). Her blood pressure was elevated to 145/90 mm Hg; the heart rate, respiratory rate and temperature were within normal limits. Both lower and upper extremity muscles were rigid and fasciculations were seen, however symptoms were present predominantly on the lower extremities.

Her past medical history was positive for Parkinson's disease (5 years), hypertension (18 years) and bipolar disorder (10 months). She received 400 mg/day quetiapine, a combined preparation of 160 mg valsartan with 25 mg hydrochlorothiazide once daily and another combined preparation of 250 mg levodopa with 25 mg carbidopa twice daily. A daily dose of 900 mg lithium (300 mg/tablet) was added to her therapy regimen two days before her admission. Her son stated that she only ingested 6 tablets and the last oral reception was 12 hours before admission. It was later confirmed by checking her drug box that only 6 tablets were missing.

An electrocardiogram was done and revealed sinus rhythm. Blood chemistry and complete blood count were within normal limits, acute renal insufficiency was not present. Thyroid stimulating hormone and free thyroid hormones were within normal limits. Brain MRI conducted to differentiate any central nervous system related pathology was consistent with age without any abnormalities. Chest and abdominal x-rays were normal. Blood lithium level increased to 3.58 mEq/L.

The patient was hospitalized in the Internal Medicine Intensive Care Unit. A psychiatric consultation was made, all drugs were discontinued and she received intravenous hydration. Lithium levels were followed up at 12-hour intervals (Fig. 1). Patient's confusion resolved at 36 hours. Eye opening was spontaneous, person and place orientation was intact, however, time orientation was not. She could move her extremities on command, but fasciculations were still seen (eye: 4, verbal: 4-5, motor: 6, Glasgow Coma Scale 14-15). Remnant symptoms resolved and her lithium level returned to the normal range after 118 hours. She

Figure 1. Patient's lithium level plotted against time.

was transferred to Internal Medicine ward for a follow-up. At discharge she was prescribed her previous medications apart from lithium and was recommended to have a psychiatric follow up.

DISCUSSION

Lithium is frequently used to manage bipolar disorder. It has a narrow therapeutic index; intoxication is still an important issue in lithium treatment. Symptoms of lithium intoxication include gastrointestinal (vomiting, diarrhea), renal (renal insufficiency, polyuria, polydipsia), cardiovascular (arrhythmias, syncope, myocarditis) and neurological (fatigue, apathy, delirium, stupor, coma, hyperreflexia, coarse tremors and fasciculations) manifestations. Most frequent symptoms of lithium intoxication are neurological manifestations which may be non-specific such as weakness, slurred speech and lethargy at early phase.⁴

Lithium levels peak between 1 to 4 hours after oral intake. Lithium is not protein bound and slowly equilibrates in days between tissues and plasma: some patients may have lithium intoxication with normal serum lithium levels, therefore a normal lithium level does not exclude intoxication. Serum lithium levels do not always correlate with patient's symptoms, treatment choices should be decided on patient's symptomatology rather than serum lithium levels.⁵

Our patient experienced intoxication symptoms after her second dose of lithium. Known predisposing factors for lithium intoxication are advanced age, diet disturbances (anorexia, diarrhea, vomiting), comorbid medical conditions affecting heart, kidneys or central nervous system. Our patient was complicated with advanced age, hypertension and Parkinson's disease which may lower the threshold for toxicity.⁴

Drugs such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, non-steroidal anti-inflammatory drugs, diuretics, calcium antagonists and neuroleptics may increase the odds of lithium intoxication.⁶ Kidneys are the major route of lithium elimination.⁴ Angiotensin converting enzyme inhibitors may cause lithium intoxication by decreasing angiotensin II and aldosterone, which results in natriuresis and facilitates retention of lithium.⁷ Angiotensin receptor blockers may contribute to toxicity as well, cases of lithium intoxication with various angiotensin receptor blockers (candesartan, irbesartan, valsartan and losartan) have been reported.⁷⁻⁹ Our patient was

using an angiotensin-receptor blocker (valsartan), a diuretic (hydrochlorothiazide) and an antipsychotic (quetiapine). As mentioned earlier, combined use of these three interacting drugs may cause a decreased threshold to intoxication.

Lithium intoxication, due to narrow therapeutic index and frequent use is a common clinical picture. Both prescribing physicians and emergency room physicians should be aware of conditions which may cause a decreased threshold for intoxication. Lithium intoxications may occur even after the first dose of treatment but it is not common. This patient was evaluated as prone to intoxication (a) due to her old age, (b) due to using valsartan, hydrochlorothiazide and quetiapine and (c) due to her comorbidities affecting her heart and central nervous system: hypertension and Parkinson's disease. Physicians should be aware that patients with multiple comorbidities and interfering drug usage may suffer from acute lithium intoxication even early in their treatment.

REFERENCES

1. Canan F, Kaya A, Bulur S, Albayrak ES, Ordu S, Ataoglu A. Lithium intoxication related multiple temporary ECG changes: A case report. *Cases J* 2008;1(1):156. doi: 10.1186/1757-1626-1-156.
2. Peng J. Case report on lithium intoxication with normal lithium levels. *Shanghai Arch Psychiatry* 2014;26(2):103-4.
3. Haussmann R, Bauer M, von Bonin S, Lewitzka U. Non-fatal Lithium Intoxication with 5.5 mmol/L Serum Level. *Pharmacopsychiatry* 2015;48(3):121-2.
4. Delva NJ, Hawken ER. Preventing lithium intoxication. Guide for physicians. *Can Fam Physician* 2001;47:1595-600.
5. Sadosty AT, Groleau GA, Atcherson MM. The use of lithium levels in the emergency department. *J Emerg Med* 1999;17(5):887-91.
6. Krenová M, Pelclová D. A 4-year study of lithium intoxication reported to the Czech Toxicological Information Centre. *Pharm World Sci* 2006;28(5):274-7.
7. Su YP, Chang CJ, Hwang TJ. Lithium intoxication after valsartan treatment. *Psychiatry Clin Neurosci* 2007;61(2):204.
8. Spinewine A, Schoevaerdt D, Mwenge GB, Swine C, Dive A. Drug-induced lithium intoxication: a case report. *J Am Geriatr Soc* 2005;53(2):360-1.
9. Ma CC, Shiah IS, Chang SW, Kao YC, Lee WK. Telmisartan-induced lithium intoxication in a patient with schizoaffective disorder. *Psychiatry Clin Neurosci* 2012;66(2):165-6. .