

An Investigation into the Frequency and Clinical Symptoms of Lithium Poisoning in patients Admitted to Razi Hospital, Ahvaz in 2015 -2018

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Abstract

Background: Bipolar disorder (BD) is considered as a severe mental disease. Lithium, which is widely used to treat BD, has a limited therapeutic index, and its toxicity is common in people who use it. Lithium poisoning can occur intentionally or accidentally.

Methods: In this cross-sectional study, we assembled data from 21 profiles of patients with lithium poisoning that referred to Razi Hospital in Ahvaz from 2015 to 2018. After studying the records of lithium poisoning patients, the checklist was adjusted based on demographic characteristics (age, gender, and cause of poisoning) and clinical information (need for dialysis, duration of hospitalization, clinical signs, and ...). The data were analyzed using the SPSS software.

Results: Finding shows that among 21 subjects, 10 patients (47.6%) were men and 11 (52.4%) were women. In addition, most of the patients poisoned with lithium (47.6%) were in the age range of 20-29 years. Among all patients younger than 50 years, poisoning was caused by suicide. Also, decreased consciousness (47.6%) was the most common symptom of poisoning, and 16 patients (76.2%) were hospitalized in the ICU. 71.4% of lithium poisoning patients were associated with concomitant use of other drugs, and one person died in this study.

Conclusion: Considering the use of lithium with the intention of suicide in 90.5% of cases with lithium poisoning and also the significant simultaneous use of lithium with antidepressants and hypnotic drugs, further research should be seemingly performed in the psychological and social fields for preventive measures, as well as planning to reduce committing suicide and poisoning.

Keywords: Lithium, Poisoning, Patient, Suicide, Iran

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INTRODUCTION

Bipolar Disorder (BD) is regarded as a severe, cyclical mental disease characterized by recurrent manic or depressed mood states (1). Since 1970, lithium salts, notably lithium carbonate, have been widely used to treat acute and maintenance treatment of BD (2, 3).

Lithium, as a metal, is not metabolized, and when taken orally, full absorption through the gastrointestinal system usually takes 8 hours, with blood levels peaking after one to six hours. It is almost entirely (95%) removed by the kidney (2, 4). This metal holds a limited therapeutic index (therapeutic range: 0.6 to 1.5 meq/L), and its toxicity is prevalent in people who use it. An increase in blood lithium concentration is used to identify lithium intoxication. However, it is important to realize that its serum level and clinical symptoms do not always coincide (5, 6). It might develop as a result of an acute intentional intake or as an unintended result of a therapeutic misadventure triggered by

a number of causes, resulting in chronic poisoning. Drug interactions, prescription or dispensing mistakes, concurrent diseases that compromise renal functions, or more chronic triggers of fluid depletion, including dehydration and nephrogenic diabetes insipidus induced by lithium, are examples of such causes (7). Lithium overdose may lead to life-threatening toxicity requiring hospitalization in the intensive care unit (ICU) (8). Lithium can also lead to serotonin syndrome due to overdose or drug interactions and in some cases, it is ignored owing to the lack of attention to its symptoms (9, 10).

There are three kinds of lithium intoxication: acute, acute-on-chronic, and chronic, which vary in symptomatology because of lithium pharmacokinetics. Acute lithium poisoning is often characterized by gastrointestinal symptoms, cardiotoxic consequences, and late-developing neurological indications, while chronic variants are characterized largely by neurological symptoms such as confusion, seizures, and myoclonus (3).

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There is no particular antidote available for coping with toxic complications resulting from lithium. The most effective therapy for acute lithium toxicity is hemodialysis. Peritoneal dialysis might be an option, but less successful therapy for patients with compromised or possibly impaired renal function. In most cases, preventing intoxication requires collaboration between patient and physician, as well as consuming lower doses with low levels of risks (11).

The purpose of this study was to investigate the risks related to lithium poisoning and its complications in poisoned patients with lithium referred to Razi Hospital in 2015-2018. In this study, we determined the frequency of lithium poisoning based on age, sex, cause of poisoning, duration of hospitalization, clinical signs, serum lithium concentration, use of dialysis in treatment, hospitalization in ICU, and the relationship between these variables.

METHODS

In this cross-sectional study, after acquiring approval from Ahvaz Jundishapur University of Medical Sciences Ethical Committee, we collected data from case files of patients with lithium poisoning who referred to Razi Hospital located in Ahvaz, Khuzestan Province, southwest of Iran in 2015 to 2018. Overall, 21 cases related to lithium poisoning patients admitted to Razi Hospital were investigated.

After studying the records of lithium poisoning patients, the checklist was adjusted based on age, gender, cause of poisoning, need for dialysis, duration of hospitalization, ICU admission, the onset of symptoms, clinical signs, concomitant use with other drugs, underlying disease, and mortality. Descriptive statistics and chi-square tests were used to analyze the gleaned data. More specifically, the data were analyzed using the SPSS software, version 18.0, and the significant level of the test was considered less than 0.05.

RESULTS

Among 21 subjects, 10 patients (47.6%) were men and 11 (52.4%) were women. In addition, 3 (14.3%), 10 (47.6%), and 4 (19%) patients were in the age range of <20, 20-29, and 30-49 years, respectively. The others (4, 19%) were older than 50 years. Also, 2 cases (9.5%) of poisoning occurred accidentally, while suicide was reported as the cause of 19 other ones (90.5%) (Table 1). Among all patients younger than 50 years, poisoning was caused by suicide, and a significant relationship was observed between age and cause of poisoning. ($P<0.05$).

Table 2 indicates the clinical characteristics of 21 patients with lithium poisoning. The serum lithium level of 9 subjects was not measured and reported in their record, while that of 9 (42.9%), 2 (9.5%), and 1 (4.8%) patients was <1, 1-2, and >2, respectively. Furthermore, 2 cases (9.5%) had the blood urea nitrogen (BUN) above 20 (mg/dl), and the creatinine level of one subject (4.8%) was higher than 2.1 (mg/dl).

In the present study, 16 patients (76.2%) were hospitalized in the ICU. All patients who underwent dialysis (4, 19%) referred with neurological symptoms, while none of those presented with the gastrointestinal symptoms of lithium poisoning required dialysis, although no statistically significant difference was obtained between the first symptom and dialysis ($P=0.117$).

Table 1. Demographic Characteristics of 21 Patients with Lithium Poisoning Admitted to Razi Hospital in 2015-2018.

Variable	Frequency (n=21)	Percentage (%)
Male	10	47.6
Female	11	52.4
<i>Age range:</i>		
< 20	3	14.3
20-29	10	47.6
30-49	4	19
>50	4	19
<i>Cause of poisoning:</i>		
Suicide	19	90.5
Accidental	2	9.5

Table 2. Clinical Aspects of 21 Patients with Lithium Poisoning Admitted to Razi Hospital in 2015-2018.

Variable	Frequency (n=21)	Percentage (%)
<i>Onset of symptoms after ingestion (hour):</i>		
<6	18	85.7
6-24	2	9.5
>24	1	4.8
<i>Duration of hospitalization:</i>		
<24 h	2	9.5
24-72 h	5	23.8
3-5 day	10	47.6
>5 day	4	19
<i>Serum lithium levels (meq/l):</i>		
No data	9	42.9
<1	9	42.9
1-2	2	9.5
>2	1	4.8
<i>Need for dialysis:</i>		
Yes	4	19
No	17	81
<i>ICU admission:</i>		
Yes	16	76.2
No	5	23.8
<i>Co-administration with other drugs:</i>		
Yes	15	71.4
no	6	28.6
<i>Underlying disease:</i>		
Yes	10	47.6
No	11	52.4
<i>Mortality:</i>		
Yes	1	4.8
No	20	95.2

Table 2. Continued.		
Variable	Frequency (n=21)	Percentage (%)
<i>Symptoms of poisoning:</i>		
Unconscious	10	47.6
Nausea	7	33.3
Abdominal pain	1	4.8
Diarrhea	2	9.5
Convulsion	1	4.8
<i>BUN levels (mg/dl):</i>		
>20	2	9.5
<20	19	90.5
<i>Creatinine levels (mg/dl):</i>		
>1.2	1	4.8
<1.2	20	95.2

Additionally, total mortality rate was one case (4.8%), which was associated with consuming antidepressants. In this study, decreased consciousness (47.6%) was the most common symptom of poisoning. There was no significant difference between the two variables of the first symptoms and the duration of hospitalization ($P=0.317$).

The most frequency of onset of symptoms was in 18 patients (85.7%), and the first 6 hours after ingestion. Furthermore, the maximum frequency of hospitalization was between 3-5 days in 10 patients (47.6%), of which 7 patients had their first symptoms less than 6 hours after intoxication, 2 patients, 6-24 hours, and one patient after 24 hours. However, no statistically significant difference was identified between symptom onset and duration of hospitalization ($P=0.697$).

Among 21 cases, 10 (47.6%) had the underlying neurological disease. In the study of concomitant lithium poisoning with other drugs, in 15 patients (71.4%), it was associated with the use of other drugs, the most common of which were hypnotics and antidepressants.

DISCUSSION

Based on the results, the highest and lowest prevalence of lithium poisoning was respectively obtained in the age range of 20-29 and < 20 years, and it was common equally among women and men. Neurological symptoms were found in 52.4% of cases (Figure 1), and no one died due to lithium poisoning. However, in the study of Meltzer et al., ten patients were studied, all of whom were women aged 55-78 years, and the mortality rate was 12.5%. Also, neurological symptoms were observed in all patients, which is inconsistent with the results of our study (12). Another study was conducted on 68 patients older than 16 years in the United States, the cause of poisoning in 63.3% of whom was suicide. In addition, one subject was dialyzed, and no mortality was observed (13). In the present study, four patients underwent dialysis, 90.5% of poisoning was caused by suicide, and one patient died, which was associated with

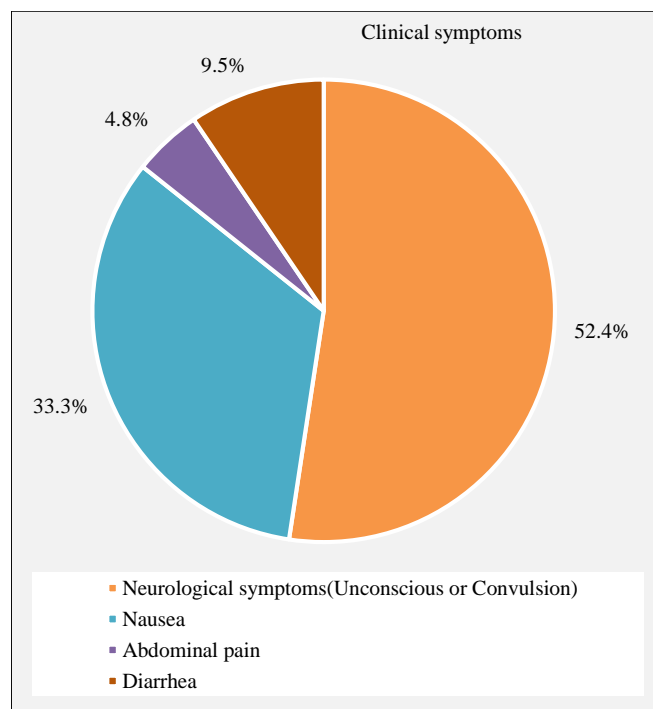


Figure 1. Clinical Signs of 21 Patients with Lithium Poisoning Admitted to Razi Hospital in 2015-2018.

consuming other medicines. The difference can be related to the presence of underlying neurological diseases among the subjects of this study.

Regarding the present study, 19% of patients were dialyzed, 47.6% suffered from the underlying neurological disorder, and 71.4% were poisoned with lithium while taking other medicines. Further, age was not significantly related to serum lithium level. The results of our study are in line with some previous studies. For example, a study performed in Taiwan during 2000-2009 reported an insignificant association between serum level with age and gender, as well as dialysis in 22.2% of patients (14). Furthermore, some researchers found the association of lithium poisoning with consuming other medicines in 69.7% of patients (15). Based on the results of a study of Pablo and colleagues with the sample size almost equal to that of the present study (58.3% women and 43.8% men), 87.5% of subjects had underlying neurological disorders and 37.5% needed dialysis (16), which are inconsistent with those of the present study. In the present study, 76.2% of patients were admitted to the ICU, which is in agreement with the results of Ott et al. (34%) in Sweden (17). They outlined the changes in consciousness as the most frequent symptom of poisoning (27.5%), as well as observed no mortality due to lithium poisoning. Some researchers examined those referred to Loghman Hakim hospital with antidepressant poisoning, and highlighted that 9.3% of cases were caused by lithium, and women were poisoned twice the men (18), while the number of women was equal to that of men in the present study. In terms of mortality rate, the results are in line with those of a study in England (19). The study suggested the serum levels of

lithium of 1.7-3.3 mmol/L in 9.9% of the acutely poisoned patients grouped as moderate-severe, while the level above 2 meq/L was observed only in one case in the present study. Other researchers referred to the lack of a relationship between serum levels of lithium and symptoms (20), which is consistent with the results of the present study which reflected that the serum levels were not significantly related to symptom onset. However, Chen et al. found a significant difference between the level and symptom severity ($P < 0.01$) (15).

Other results of the present study, such as symptom onset, creatinine level, and BUN, cannot be compared due to the limitation of resources and insufficiency of information on lithium poisoning in Iran, and lack of extensive and specialized research.

CONCLUSION

In the present study, the cause of lithium poisoning in 90.5% of cases was suicide. Additionally, the concomitant consumption of lithium with antidepressants and hypnotic drugs was obtained as a significant point in this study. Hence, further research should be seemingly performed in the psychological and social fields for preventive measures, as well as planning to reduce committing suicide and poisoning.

LIMITATIONS

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Conflict of interest: None to be declared.

REFERENCES

1. Benard V, Vaiva G, Masson M, Geoffroy P-A. Lithium and suicide prevention in bipolar disorder. *L'Encéphale*. 2016;42(3):234-41.
2. Lavonas EJ, Buchanan J. Hemodialysis for lithium poisoning. *Cochrane Database of Systematic Reviews*. 2015(9).
3. Haussmann R, Bauer M, von Bonin S, Grof P, Lewitzka U. Treatment of lithium intoxication: facing the need for evidence. *International journal of bipolar disorders*. 2015;3(1):1-10.
4. Dunne FJ. Lithium toxicity: the importance of clinical signs. *British Journal of Hospital Medicine* (2005). 2010;71(4):206-10.
5. Chien S-C, Liu K-T, Wu Y-H. Lithium intoxication presenting as altered consciousness and arrhythmia with cardiogenic shock: A case report. *Medicine*. 2018;97(45).
6. Erden A, Karagöz H, Başak M, Karahan S, Çetinkaya A, Avci D, et al. Lithium intoxication and nephrogenic diabetes insipidus: a case report and review of literature. *International journal of general medicine*. 2013;6:535.
7. Baird-Gunning J, Lea-Henry T, Hoegberg LC, Gosselin S, Roberts DM. Lithium poisoning. *Journal of intensive care medicine*. 2017;32(4):249-63.
8. Vodovar D, El Balkhi S, Curis E, Deye N, Mégarbane B. Lithium poisoning in the intensive care unit: predictive factors of severity and indications for extracorporeal toxin removal to improve outcome. *Clinical Toxicology*. 2016;54(8):615-23.
9. Monteith J, Jelinek G, Karro J, Cadogan M, Weiland T. Knowledge and Confidence of Emergency Clinicians in Managing Toxicological Presentations. 2016.
10. Mégarbane B. Toxidrome-based approach to common poisonings. *Asia Pacific Journal of Medical Toxicology*. 2014;3(1):2-12.
11. Amdisen A. Clinical features and management of lithium poisoning. *Medical toxicology and adverse drug experience*. 1988;3(1):18-32.
12. Meltzer E, Stienlauf S. The clinical manifestations of lithium intoxication. *The Israel Medical Association journal : IMAJ*. 2002;4:265-7.
13. Dyson E, Simpson D, Prescott L, Proudfoot A. Self-poisoning and therapeutic intoxication with lithium. *Human toxicology*. 1987;6(4):325-9.
14. Lee Y-C, Lin J-L, Lee S-Y, Hsu C-W, Weng C-H, Chen Y-h, et al. Outcome of patients with lithium poisoning at a far-east poison center. *Human & experimental toxicology*. 2011;30:528-34.
15. Chen KP, Shen WW, Lu ML. Implication of serum concentration monitoring in patients with lithium intoxication. *Psychiatry and clinical neurosciences*. 2004;58(1):25-9.
16. Herrera de Pablo E, Climent B, Herrera A, editors. Analysis of the poisonings by lithium in a department of internal medicine. *Anales de medicina interna (Madrid, Spain: 1984); 2008*.
17. Ott M, Stegmayr B, Salander Renberg E, Werneke U. Lithium intoxication: incidence, clinical course and renal function—a population-based retrospective cohort study. *Journal of Psychopharmacology*. 2016;30(10):1008-19.
18. Naderi-Heiden A, Shadnia S, Salimi A-R, Naderi A, Naderi MM, Schmid D, et al. Self-poisonings with tricyclic antidepressants and selective serotonin reuptake inhibitors in Tehran, Iran. *The World Journal of Biological Psychiatry*. 2009;10(4):302-12.
19. Waring W, Laing W, Good A, Bateman D. Pattern of lithium exposure predicts poisoning severity: evaluation of referrals to a regional poisons unit. *Journal of the Association of Physicians*. 2007;100(5):271-6.
20. Waring W, Good A, Bateman D. Acute lithium toxicity is commonly reported as a mixed overdose: prospective evaluation of enquiries to a regional poisons centre. *Journal of Toxicology: Clinical Toxicology*. 2004;42(4):529.