Lithium Intoxication Cases at the Arizona Poison and Drug Information Center: Analysis of the Use of Hemodialysis as Treatment

Goldberg L, França N, Boesen KJ PharmD, CSPI, Shirazi FM MD, PhD, FACEP, FACMT
Arizona Health Sciences Center

Arizona Poison and Drug Information Center 1-800-222-1222

CTPER | Center for Toxicology and Pharmacology Education and Research

CIÊNCIA SEM FRONTEIRAS

THE UNIVERSITY OF ARIZONA College of Pharmacy

Introduction

LITHIUM (Li)
A mood stabilizer used in clinical psychiatry, primarily to treat bipolar disorder.

NARROW THERAPEUTIC WINDOW (0.6 - 1.2 mmol/L)
The disadvantage of lithium [4], with toxic effects as low as 1.5 mmol/L [5]. The etiology of the toxicity may vary [1] and there is no antidote for the toxic effects of lithium. [3]

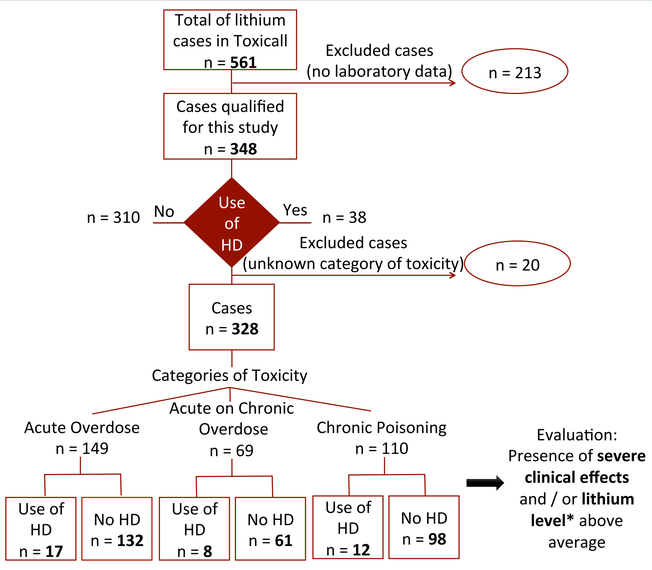
HEMODIALYSIS (HD)
An effective intervention: enhances clearance and decreases half-life of lithium. However, HD is costly and associated with a 1% risk of significant complications, including catheter-related complications and neurological injury induced by fluid and electrolyte shifts. [2]

USE OF HEMODIALYSIS FOR TOXICITY MANAGEMENT
The decision to perform hemodialysis is clinical and variable as an intervention in the treatment of lithium poisoning. [6] Lithium levels of ≥ 4 mmol/l in any category and lithium levels of ≥ 2.5 mmol/l in chronic exposure have been described as indications for HD.

Objectives

To analyze cases of lithium intoxication received by the Arizona Poison and Drug Information Center (APDIC) between 2002 and 2014; and assess patients' laboratory data (i.e. lithium and serum creatinine levels), clinical symptomatology and the use of hemodialysis to improve lithium clearance.

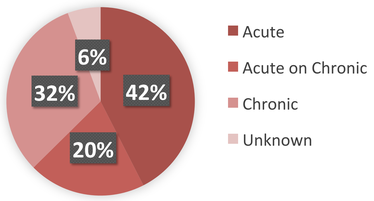
Methods



In this study, "lithium level" represents the highest reported level. The mean highest lithium level was calculated for each category.

Results

Reported Toxicity



Overall

Median age: 43.5 ± 18.0 years
60% were female

Mean highest lithium level
348 cases = 2.4 ± 1.2. mmol/l
HD group = 4.1 ± 1.4mmol/l
No HD group = 2.2 ± 1.0 mmol/l
p < 0.0005

Mean highest serum creatinine
348 cases = 1.5 ± 1.1mmol/l
HD group = 2.1 ± 1.5mmol/l
No HD = 1.4 ± 0.9 mmol/l
p < 0.05

89.1 % of patients treated without HD
No deaths in any of the groups

ACUTE OVERDOSE

HD Group

n =17	%	1 /more severe clinical effect	[Li] equal or above average 4.1	[Li] average in the subgroup
7	41.2	Yes	Yes	4.9mmol/l
8	47.0	Yes	No	3.2 mmol/l
2	11.8	No	Yes	5.2 mmol/l
0	0	No	No	

No HD group
52.3% → at least one severe clinical effect and [Li] < 4.1mmol/l
47.7% → no severe clinical effect and [Li] < 4.1mmol/l

No HD Group

n=132	%	1 / more severe clinical effect	[Li] equal or above average 2.2	[Li] average in the subgroup
38	28.8	Yes	Yes	**3.1 mmol/l**
31	23.5	Yes	No	1.5 mmol/l
27	20.4	No	Yes	2.9 mmol/l
36	27.3	No	No	1.2 mmol/l

Similarity of [Li] average in HD vs. no HD groups
8 patients with [Li] average = 3.2mmol/l were dialyzed
38 patients with [Li] average = 3.1mmol/l were not dialyzed
No HD group: drowsiness/lethargy and confusion
HD group: no pattern; up to six different serious clinical effects

ACUTE ON CHRONIC OVERDOSE

HD Group

n=8	%	1 or more severe clinical effect	[Li] equal or above average 5.0	[Li] average in the subgroup
2	25.0	Yes	Yes	6.5 mmol/l
4	50.0	Yes	No	3.5 mmol/l
1	12.5	No	Yes	8.1 mmol/l
1	12.5	No	No	4.4 mmol/l

No HD group
One case in which the [Li] was 4.1mmol/l but only a gastrointestinal clinical effect was manifest (i.e. vomiting).

No HD Group

n=61	%	1 /more severe clinical effect	[Li] equal or above average 2.2	[Li] average in the subgroup
19	31.1	Yes	Yes	2.7 mmol/l
13	21.3	Yes	No	1.5 mmol/l
12	19.7	No	Yes	3.0 mmol/l
17	27.9	No	No	1.4 mmol/l

In the other cases of this subgroup, the [Li] was ≤ 3.9mmol/l. The predominant symptoms were agitation, drowsiness/lethargy and confusion.

CHRONIC POISONING

HD Group

n=12	%	1 /more severe clinical effect	[Li] equal or above average 3.5	[Li] average in the subgroup
6	50	Yes	Yes	4.1 mmol/l
6	50	Yes	No	3.0 mmol/l
0	0	No	Yes	
0	0	No	No	

No HD group
34.7% → one or more severe clinical effect and [Li] ≥ 2.1mmol/l
27.6% → [Li] ≥ 2.5mmol/l

No HD Group

n=12	%	1 /more severe clinical effect	[Li] equal or above average 2.1	[Li] average in the subgroup
34	34.7	Yes	Yes	2.9 mmol/l
33	33.7	Yes	No	1.5 mmol/l
10	10.2	No	Yes	2.7 mmol/l
21	21.4	No	No	1.6 mmol/l

Some "no HD" cases had high [Li] (4.2; 4.5 and 10.0mmol/l) associated with severe clinical effects (i.e. fasciculations, drowsiness/lethargy, coma)

Conclusions

Literature recommendations for HD are inconsistent. Overall, HD is indicated when the patient meets one or more of the following criteria: [6]

a) [Li] ≥ 4.0mmol/l in any category and [Li] ≥ 2.5 or 4.0mmol/l in chronic toxicity
b) Presence of at least one severe clinical effects (neurological symptoms)
c) Contraindications for volume expansion

In general, when comparing HD to that of conservative therapy, HD was utilized when patients had higher values of lithium level.

Acute Overdose: Patients who were dialyzed had [Li] ≥ 4.0mmol/l and / or presence of one or more severe clinical effect. Only 2% of patients in this category met the above condition but were not dialyzed.

Acute on Chronic Overdose: Patients with higher [Li] were more likely to get dialyzed. Contrary to literature recommendations, patients with severe clinical effects and low [Li] were not always dialyzed.

Chronic Poisoning: In this category, the severity of lithium intoxication may correlate directly with blood level concentration and [Li] >2.5mmol/l is characterized as serious [3]. However, in the practice we did not always observe that patients with [Li] ≥ 2.5mmol/l were dialyzed.

Limitations:
-Limited data in HD groups
-Inconsistent laboratory data
-Lack of follow up to discharge in each case
-Lack of documented contraindications for volume expansion
-Accuracy of database with regards to symptomatology documentation

Based on our data we were unable to evaluate the effectiveness of HD in reducing the morbidity or mortality of patients. Further research is required in order to determine which patients may benefit from HD in lithium toxicity.

References

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