

lithium toxicity

general

- Lithium toxicity occurs in two main settings: acute ingestion of a large dose or, more commonly, chronic accumulation of the drug during prescribed maintenance therapy.

pharmacology

Parameter	Value
Molecule	Monovalent cation; radius, 0.6 Å; weight, 7 Da
Dose (adult)	900-1800 mg/day in 3-4 doses (less in sustained-release form)
Therapeutic serum level	0.7-1.2 mEq/L
Toxic levels	>1.5 mEq/L (narrow therapeutic index)
Bioavailability	>95%
Volume of distribution	0.7-0.9 L/kg in steady state
Half-life	12-27 hr after single dose (longer with chronic therapy and in elderly patients)
Time to peak plasma level	2-4 hr after ingestion
Elimination	Primarily renal; excreted unchanged in urine

clinical manifestations

1. Central nervous system
 - a. State of consciousness (confusion to coma)
 - b. Cerebellar symptoms
 1. Dysarthria
 2. Ataxia
 3. Nystagmus
 4. Tremor
 - c. Basal ganglia
 1. Choreiform movements
 2. Parkinson-like movements
 - d. Seizures
 - e. Death
2. Gastrointestinal
 - a. Nausea/vomiting
 - b. Bloating
3. Cardiac
 - a. Syncope
4. Renal
 - a. Polyuria
 - b. Polydipsia
 - c. Renal insufficiency
5. Neuromuscular
 - a. Peripheral neuropathy
 - b. Myopathy
6. Endocrine
 - a. Hypothermia
 - b. Hyperthermia

management

resuscitation

- patient who have severe impairment of consciousness require airway protection
 - Activated charcoal is an ineffective gastrointestinal decontaminant in lithium overdose because it does not absorb strongly ionized chemicals. In contrast, polyethylene glycol (CoLyte, GoLYTELY) has been shown to be effective in acute lithium intoxication

electrolytes & acid base

- Volume status should be assessed, because significant volume depletion can occur as a result of urinary concentrating defects. Many of these patients have volume-responsive decreases in renal function.

- hyponatraemia decreases renal lithium clearance and should be avoided

- The management of lithium intoxication is determined by the degree of intoxication (serum level), a history of acute versus chronic lithium exposure, the clinical symptoms, and the adequacy of renal function.

specific interventions

- Lithium[®] removal**
- a. Serum lithium[®] level >3.5-4 mEq/L-Most patients require hemodialysis.
 - b. Serum lithium[®] levels 2-4 mEq/L-Unstable patients and patients with severe neurologic signs (seizures, stupor, coma) require hemodialysis.
 - c. Serum lithium[®] levels 1.5-2.5 mEq/L-Fluid therapy or forced diuresis treatment should be recommended only for patients with early signs of lithium[®] intoxication and normal renal function, and when it is certain that serum lithium[®] has been elevated for only a few days and not higher than 2.5 mEq/L; dialysis should be instituted if a serum lithium[®] concentration of 1 mEq/L is not reached within 30 hr.

Mode	Lithium [®] Clearance (mL/min)
Renal excretion	10-40
Forced diuresis	0.9-39
Peritoneal dialysis	9-15
Hemodialysis (blood flow, 126-250 mL/min)	70-170
Continuous renal replacement therapies	Variable, about 20.5

factors predisposing to lithium toxicity include:

1. Infection
2. Volume depletion
3. Gastroenteritis
4. Overdose (e.g., suicide attempt)
5. Chronic kidney disease
6. Surgery
7. Decreased "effective arterial volume"
 - a. Congestive heart failure
 - b. Cirrhosis
 - c. Nephrosis
8. Drugs
 - a. Nonsteroidal antiinflammatory drugs
 - b. Diuretics
 - c. Tetracycline
 - d. Cyclosporine[®]
9. Decreased dietary sodium intake
10. Anorexia

underlying causes

prognosis

- The outcome after lithium intoxication is favorable; most patients exhibit reversible neurologic deficits. However, long-lasting neurologic sequelae may occur.
 - Permanent neurologic changes appear to stem primarily from cerebellar deficits