Lithium

Atomic number 3
Atomic weight 6.94

Collection

Serum/Plasma	2 mL	Plastic container. No anticoagulant Check that blood has not been collected into lithium-heparin tubes. Serum should be separated as soon as possible (within 1 hour) to avoid movement of lithium into erythrocytes.
Blood	2 mL	Plastic container. EDTA anticoagulant
Urine	20 mL	Sterile Universal

Reference ranges

			Reference
Serum/plasma	nmol/L	8-270	1
Blood	nmol/L	Less than 201	1
Urine	mmol/L	4.1	3
	mmol/24 h		
	mmol/mol creatinine	0.52 95th percentile	3

	Serum/plasma [2] (µmol/L)
Prophylactic therapy	0.4-0.8
Treatment of acute mania	0.8-1.2
Increased risk of toxicity	Greater than 1.4
Life threatening toxicity	Greater than 3.5

References

1. Cesbron A, Saussereau E, Mahieu L, Couland I, Guerbet M,Jean-Pierre Goulle´ JP. Metallic Profile of Whole Blood and Plasma in a Series of 106 Healthy Volunteers. Journal of Analytical Toxicology 2013, 37, 401-405.
2. Aronson JK and Reynolds DJM. ABC of monitoring drug therapy; Lithium. *BMJ*, 1992; 305: 1273-1276
3. Morton J, Leese E, Tan E, Cocker J. Determination of 61 elements in urine samples collected from a non-occupationally exposed UK adult population, Toxicol. Letters 2014; 231: 179-193.

Clinical

Lithium salts are used predominantly in the acute and short-term treatment of manic states and as prophylactic long-term treatment of recurrent manic and depressive illness. The mechanism appears to involve modulation of the reuptake of glutamate neurotransmitter from the synapse back to the neuron. The metal is administered orally as either the carbonate or citrate in doses of 10 to 80 mmol per day. Absorption from the gut is complete within 8 hours and peak plasma concentrations are seen 2-4 hours

after dosage. The distribution volume of lithium approximates to the body water volume, although concentrations in white matter, thyroid and bones are several-fold higher than the plasma concentration. Penetration into the cerebrospinal fluid takes place at a relatively slow rate and at equilibrium the concentration is about 40% of that in plasma. There is no binding to plasma proteins and excretion is almost entirely by the kidneys. Lithium is handled like sodium in the proximal tubule with about 80% being reabsorbed. The elimination half-life varies with age and ranges from 8-20 hours in younger patients with normal renal function to 30-40 hours in elderly patients or in those with renal impairment.

The optimum maintenance dosage is usually established by monitoring the serum lithium concentrations and these are measured subsequently to check compliance, prevent sub-therapeutic dosing and to diagnose impending or manifest lithium toxicity.

Toxicity

Lithium therapy is frequently associated with mild side effects such as weight gain, polyuria, tremor, diarrhoea and oedema of the face and legs which resolve when the treatment stops. A small proportion of patients develop a benign enlargement of the thyroid and it is recommended that thyroid function tests are carried out when treatment starts and at six month intervals thereafter. Usually there is a fall in total and free thyroxine levels and a rise in thyroid stimulating hormone (TSH), but hypothyroidism is rarely so severe as to need thyroxine therapy. Lithium has diuretic properties due to its antagonism of the renal response to ADH and can induce nephrogenic diabetes insipidus, although the full pathogenesis of the condition, which persists for some time after medication is withdrawn, is uncertain.

Since lithium is excreted almost exclusively by the kidneys, any impairment of this route induced by, for example, mild dehydration, reduced salt intake, sliming diets, intercurrent kidney disease and the use of interacting medications such as diuretics or non-steroidal anti-inflammatory drugs, can lead to intoxication at any stage during long-term treatment. If moderate renal impairment is not detected or drugs are given which reduce lithium excretion and lithium intake continues, the intoxication escalates so that the patient may develop a life threatening illness within a few days.

The clinical effects of acute and chronic lithium poisoning are similar, although these tend to be milder in overdose cases despite higher plasma levels and diminish more rapidly. The prime effect is on the central nervous system and the kidneys. At an early stage the patient may look ill with a greyish yellow complexion. Other characteristic features include nausea, vomiting, diarrhoea, drowsiness, ataxia, blurred vision, seizures and coma. These may be accompanied by progressive acute renal failure with oliguria. The symptoms are reversible with haemodialysis if instituted in time, but usually persist for a prolonged period and there is a danger that these patients will be left with permanent neurological damage.

Laboratory Indices of Lithium Therapy and Toxicity

When monitoring lithium therapy, it is most important to measure the serum lithium concentration as close as possible to 12 hours after the last dose by which time the drug's absorption is complete and distribution will have stabilised. This standardised measurement is commonly referred to as the 12h-stSLi and should preferably be taken always at the same time of day to mitigate the effect of diurnal variation of serum lithium levels. When a patient begins therapy, it is usual to carry out one or two 12h-stSLi measurements with appropriate adjustment of the dose regime and to check the serum lithium concentration one week after any change of dose or formulation. If treatment with diuretics and other drugs which affect renal function is instituted or the patient moves to a low salt diet, more intensive monitoring is indicated.

There is substantial inter individual variation in the relationship between serum lithium concentrations and effective therapy. However, it is generally accepted that in patients with acute mania levels of up to 1.3 mmol/L may be needed to gain a satisfactory response, whereas effective prophylaxis with minimum side effects can be achieved in most patients with serum lithium concentrations in the range 0.5 to 0.8 mmol/L.

There is a marked risk of oliguria and acute renal failure if the serum lithium concentration rises above 1.4 mmol/L and levels of over 3.5 mmol/L after chronic accumulation are associated with serious and possibly fatal toxicity.

References

Aronson JK and Reynolds DJM. ABC of monitoring drug therapy; Lithium. *BMJ*, 1992; **305**: 1273-1276