NHS
South London and Maudsley
NHS Foundation Trust

COVID-19 and lithium

Additional precautions and special measures

Lithium

Lithium has a narrow therapeutic range, meaning the serum level needed for response and the level that causes toxicity are very close together.

Target lithium levels are 0.6-0.8 mmol/L (0.4mmol may be enough for some patients and indications). Blood samples should be taken 12 hours after the last dose (1).

Lithium is exclusively excreted by the kidneys and can build up in the blood if kidney function is impaired. Lithium has been associated with a gradual decline in estimated glomerular filtration rate (eGFR) over time, particularly if levels are maintained near or above the maximum recommended level. Longer exposure to supra-therapeutic lithium levels is possibly more toxic than short exposure to high levels (2).

Lithium in COVID-19

Recent reports from Wuhan, China suggested that "kidney disease on admission and acute kidney injury (AKI) during hospitalization were associated with an increased risk of in-hospital death" in patients with COVID-19 disease (3). Therefore, the possible effect of lithium on kidney function must be borne in mind when treating patients who develop the disease.

Lithium toxicity

Drug interactions are an important cause of increased lithium levels and subsequent decline in renal function. NSAIDs, diuretics and ACE inhibitors/ARBs are the most common drug causes of lithium toxicity. (Note that NSAIDS and drugs acting on ACE may be withdrawn during COVID-19 infection, causing a fall in lithium levels.)

Dehydration or reduced fluid intake is another important cause of lithium toxicity (see below).

In many cases of slowly developing lithium toxicity, symptoms can be relatively bland, non-specific or non-existent. Signs of moderate to severe lithium toxicity may include diarrhoea, vomiting, mental state changes, coarse tremor or falls due to ataxia.

General guidelines and precautions

All patients

Remind all patients:

- To seek medical attention if they develop diarrhoea or vomiting, or feel acutely unwell for any reason
- To ensure they maintain their fluid intake, particularly if they have a fever, if they are immobile for long periods or if they develop a chest infection or pneumonia
- To inform their care team of any changes to their drug treatment
- Not to take over-the-counter non-steroidal anti-inflammatory drugs (e.g. ibuprofen), but to take paracetamol instead.
- Not to stop lithium abruptly unless advised to do so.

Patients without symptoms of COVID-19

Patients who are self-isolating should not attend the clinic or GP surgery for routine lithium monitoring tests. The appointment should be re-booked for a later date unless the patient falls under the high-risk group outlined below.

Patients with symptoms of COVID-19

Patients presenting with new cough and/or fever: ask the patient to continue taking lithium but take blood sample for lithium serum level and U&Es. Remind patient of need to maintain their fluid intake. If lithium levels are elevated or kidney function is compromised, seek urgent specialist advice.

If there is any delay in obtaining a lithium level, it may be reasonable to pause treatment and await the result of the lithium level. Blood levels should govern on-going treatment and the dose used. Be aware that sudden discontinuation of lithium can be associated with a rapid relapse of symptoms, particularly mania. Use caution until the patient has regained physical health, with increased frequency of monitoring of lithium levels and renal function.

Patients presenting with flu-like/COVID-19 symptoms and symptoms of lithium toxicity (e.g. diarrhoea, vomiting, tremor, mental state changes, or falls): WITHOLD lithium, take URGENT lithium serum level and U&Es.

NHS
South London and Maudsley
NHS Foundation Trust

At-risk patients

People who require more frequent lithium monitoring

These patients MUST continue to have their regular lithium monitoring

Elderly
Initiating or stopping drugs that interact with lithium*
Established chronic kidney disease
Evidence of impaired thyroid function
Raised calcium level
Poor symptom control
Poor adherence
Has a lithium serum level $\geq$ 0.8mmol/L

*NSAIDS, ACE inhibitors, ARBs, diuretics

Standard blood tests for lithium monitoring (4)

	Checks	Base-line	1 week after initiation	1 week after dose changes	Weekly until stable	Every 3 months once stable (for the first year)	Every 6 months from initiation*
Renal	Urea	✓					
	Creatinine	✓					
	U&Es	✓					✓
	eGFR	✓					✓
Endocrine	TFTs	✓					✓
	Calcium	✓					✓
Physical	ECG	✓					
	Weight	✓					✓
Serum level	(12 hours post dose)		✓	✓	✓	✓	✓

*3-monthly in certain groups of people (see 'at-risk patients')

Professor David Taylor

Director of Pharmacy

March 25th 2020

References

1. Taylor DM, Young AH, Barnes TRE. The Maudsley Prescribing Guidelines in Psychiatry 13th Edition. Vol. 13, Wiley Blackwell. 2018. 1–854.
2. Ott M, Stegmayr B, Salander Renberg E, Werneke U. Lithium intoxication: incidence, clinical course and renal function a population-based retrospective cohort study. J Psychopharmacol (Oxford, England) 2016;30(10):1008–1019.
3. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, Li J, Yao Y, Ge S, Xu G, Kidney disease is associated with in-hospital death of patients with COVID-19, Kidney International (2020), doi: https://doi.org/10.1016/j.kint.2020.03.005.
4. National Institute for Health and Care Excellence (2014). *Bipolar disorder: assessment and management.* (NICE Guideline 185). Updated February 2020. Available at: https://www.nice.org.uk/guidance/cg185