MEDICINAL MISHAP

Chronic lithium toxicity

Case

A 66-year-old man presented to hospital following two weeks of diarrhoea and worsening confusion, unsteady gait and muscle twitching. His oral intake and urine output were markedly reduced. The medical history included bipolar disorder, class III obesity, type 2 diabetes, hypertension and dyslipidaemia. He was being treated with venlafaxine, mirtazapine, lithium, aripiprazole, metformin, empagliflozin, olmesartan and rosuvastatin, which he continued while unwell. He had been on lithium for nearly 20 years with no recent change of dose. Serum trough concentrations of lithium were maintained around 0.6 mmol/L (target range 0.6–0.8 mmol/L). Renal function was normal when measured three months earlier.

On examination, the man was lethargic and not orientated to time or place. His blood pressure was 100/65 mmHg with otherwise normal vital signs. He had a coarse tremor, myoclonic jerks and generalised hyperreflexia, but no focal neurological deficit.

Investigations revealed normal serum sodium, potassium and glucose concentrations, but urea was 25 mmol/L and creatinine was 1130 micromol/L. Serum lithium had increased to 2.7 mmol/L. There was a moderately severe anion gap metabolic acidosis but a normal lactate. An ECG showed a normal sinus rhythm. CT of the abdomen excluded structural abnormalities that may have accounted for impaired kidney function or diarrhoea.

The patient was diagnosed with severe acute kidney injury precipitated by hypovolaemia and subsequent neurotoxicity from lithium accumulation. All drugs were temporarily ceased, intravenous fluids were given and he was admitted to intensive care. Continuous renal replacement therapy was provided under vasopressor support until serum lithium concentrations approached 1 mmol/L and renal function improved. The diarrhoea settled, but the man's neurological recovery was slow and complicated by hypernatraemia, ileus and hospital-acquired pneumonia.

After four weeks, the patient was transferred to a rehabilitation facility and lithium recommenced at half the usual dose. His daily urine output remained greater than 3 L which was consistent with nephrogenic diabetes insipidus.

Comment

Lithium is an effective mood-stabilising drug that requires monitoring to avoid toxicity.[1] Long-term treatment can cause nephrogenic diabetes insipidus, where resistance to antidiuretic hormone produces polyuria. Patients usually compensate by increasing their water intake, but an inability to maintain hydration can lead to acute kidney injury.

Lithium shares characteristics with sodium. Both are monovalent cations distributed through total body water and eliminated by the kidneys. Lithium's usual half-life of 12 hours can be much longer in renal impairment.[2] Drugs that reduce glomerular filtration, such as ACE inhibitors, angiotensin receptor blockers and non-steroidal anti-inflammatory drugs, as well as dehydration caused by diuretics and diabetes insipidus, can therefore lead to accumulation of lithium. The patient's venlafaxine, metformin and olmesartan are also renally excreted.

Exposure to elevated lithium concentrations over days to weeks, known as chronic lithium toxicity, can manifest as worsening tremor, lethargy, confusion, ataxia, myoclonic jerks and seizures.[3] Elderly patients are particularly susceptible due to reductions in renal function, body water and cognitive reserve. Treatment includes lithium elimination, through restoration or replacement of renal function, and supportive care. Resolution of neurotoxic effects may take weeks and can be incomplete.[4]

Conclusion

To prevent chronic lithium toxicity, drug concentrations and kidney function should be checked during intercurrent illness. Patients with diabetes insipidus and the elderly require particularly close monitoring. In renal impairment, exposure to lithium and other nephrotoxic drugs must be reduced or avoided. A sick-day plan should direct patients to seek medical attention if symptoms of chronic lithium toxicity develop.

Physicians experienced in pharmacology or a Poisons Information Centre can advise on the management of chronic lithium toxicity. In mild cases, lithium is stopped until clinical resolution and then reintroduced at a lower dose, while patients with severe toxicity require admission to hospital.

Conflicts of interest: none declared

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