An 82 year old woman was admitted with worsening dyspnoea. Arterial blood gases were taken on air and revealed a pH of 7.39, with a partial pressure of CO₂ (pCO₂) of 1.2 kPa, pO₂ of 19.3 kPa, HCO₃⁻ of 13.8 mmol/litre, and base excess of −16.3 mmol/litre: a compensated metabolic acidosis with hyperventilation induced hypocapnia, which is known to be a feature of lactic acidosis. There was also an increased anion gap ([(Na⁺140 + K⁺4.0) – (Cl⁻ 106 + HCO₃⁻ 13.8)] = 24.2 mEq/litre (reference range, 7–16)), consistent with unmeasured cation. Lactate was measured and found to be raised at 3.33 mmol/litre (reference range, 0.9–1.7). After exclusion of common causes of lactic acidosis Atorvastatin was stopped and her acid-base balance returned to normal. Subsequently, thiamine was also shown to be deficient. The acidosis was thought to have been the result of a mitochondrial defect caused by a deficiency of two cofactors, namely: ubiquinone (as a result of inhibition by statin) and thiamine (as a result of dietary deficiency).

An 82 year old woman was admitted after six weeks of worsening dyspnoea. She was breathless at rest and unable to carry out her normal daily activities. She reported no fever, cough, chest pain, or orthopnoea. She had a history of chronic obstructive pulmonary disease, mild hypertension, and had suffered a deep vein thrombosis 12 months previously. Drug regimen on admission was hypertension, and had suffered a deep vein thrombosis 12 months previously. Drug regimen on admission was:

- Beclomethosone inhaler, 200 months previously.
- Drug regimen on admission was hypertension, and had suffered a deep vein thrombosis 12 months previously. Drug regimen on admission was:

- Atorvastatin was stopped and her acid-base balance returned to normal.
- The patient was started on antibiotics and nebulised bronchodilators.
- Examination revealed a respiratory rate of 30 and no other inflammatory markers were assessed. Chest radiograph showed no focal abnormality.
- The only likely remaining causes were a metabolic myopathy and thiamine deficiency.
- It is well known that statins can cause myopathy and rhabdomyolysis.
- The patient was taking Atorvastatin at 10 mg/day. This was stopped and she immediately improved clinically.

**Abbreviations:** ABGs, arterial blood gases; bd, twice daily; coQ10, coenzyme Q10; HMGCoA, hydroxymethylglutaryl CoA; od, once daily; qds, four times daily; P, partial pressure
DISCUSSION

We have reported an unusual case of lactic acidosis that appeared to resolve as a result of cessation of statin treatment. Possible causes for lactic acidosis included thiamine deficiency, vitamin D deficiency, myeloma, or abnormal renin–aldosterone functioning. It was later found that thiamine deficiency was also present and this may have acted in tandem with the statin to cause lactic acidosis, when neither element individually would have been sufficient.

Statins work by inhibiting hydroxymethylglutaryl-CoA (HMGCoA) reductase, but in addition to reducing cholesterol synthesis there is a decrease in the production of other non-sterols, such as coenzyme Q₁₀ (coQ₁₀: ubiquinone), and HMGCoA reductase inhibitors have been shown to reduce coQ₁₀ concentrations. CoQ₁₀ is an essential carrier in the mitochondrial respiratory chain that participates in oxidative phosphorylation. Consequently, there is decreased activity of mitochondrial complex I with inadequate substrate (acetyl-CoA and α-ketoglutarate tricarboxylic acid cycle effect) and reduced electron carrier transport (coQ₁₀ effect). One other possible case has been reported, although that patient also had signs of hepatitis, which was not present in our patient.

Thus, both statin treatment, via decreased coQ₁₀, and thiamine deficiency, via reduced α-ketoglutarate dehydrogenase complex activity, can result in impairment of mitochondrial oxidative phosphorylation. It is possible that the lactic acidosis was the result of the combination of both thiamine deficiency and statin treatment, such that removal of one element was sufficient to resolve the metabolic stress and result in the resolution of acidosis.

Take home messages

- We report an unusual case of lactic acidosis thought to be caused by a mitochondrial defect resulting from a deficiency of two cofactors: ubiquinone and thiamine
- The deficiency in ubiquinone was a result of inhibition by treatment with Atorvastatin and the thiamine deficiency was dietary in origin
- When treatment with Atorvastatin was stopped the patient’s acid–base balance returned to normal

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