D-lactic acidosis: an application for urinary organic acid analysis outside the diagnosis and management of inborn errors of metabolism

D Peiris, P Cook

University Hospital Southampton NHS Foundation Trust, Department of Laboratory Medicine, SO16 6YD, UK

AIMS

- To demonstrate the value of **urinary organic acid analysis** in settings outside of inborn errors of metabolism (IEM): **D-lactic acidosis** (Fig.1)
- D-lactic acidosis is **currently diagnosed** based on a combination of:
  1. **Clinical presentation:** neurological symptoms such as confusion, ataxia, and slurred speech
  2. **Laboratory data:** blood gas results demonstrating a raised anion gap but normal lactate, and a D-lactate >3 mmol/L.

N.B. Not a widely available assay in the UK

Urinary organic acid analysis is an alternative, more readily available, reliable tool to diagnose D-lactic acidosis.

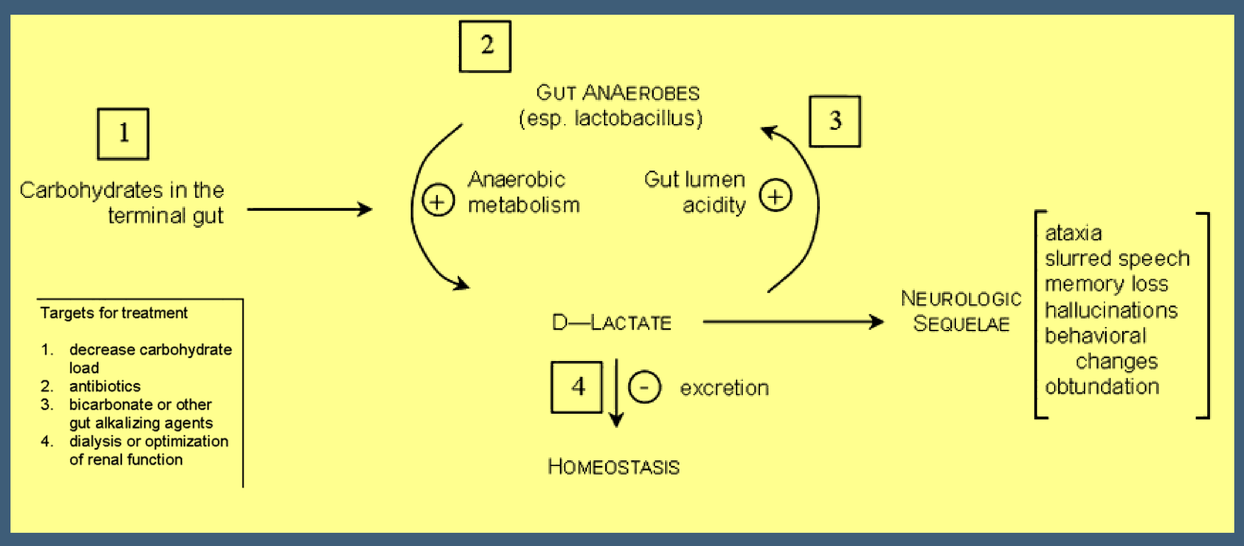

Fig 1. Pathogenesis of D-lactic acidosis[1], which involves substrate (carbohydrates), catalyst (terminal gut anaerobes, most importantly *Lactobacillus spp.)* and product (D-lactate), in the context of short bowel. The acidity of D-lactate contributes to a positive feedback loop promoting the growth of *Lactobacillus* in the gut lumen. Treatments listed, targeting either the substrate, catalyst and/or product, should lead to a subsequent symptomatic relief as D-lactate levels are reduced.

CASE

- 11 year old male
- Diagnosis of D-lactic acidosis secondary to short bowel syndrome (recognised association[2])
- Presented in A&E with stark changes in behaviour and confusion
- Request received in laboratory for quantification of D-lactate; urine organic analysis performed instead, as far quicker and readily available

METHODS

- Organic acid analysis of a random urine sample was performed using **gas chromatography-mass spectrometry (GC-MS)**:
- After oximation with hydroxylamine, organic acids were extracted with ethyl acetate and diethyl ether and separated as trimethylsilyl derivatives by gas chromatography on a non-polar fused silica capillary column.
- The organic acids were identified by elution time and mass spectra comparison to those compounds contained in an online library.

RESULTS

A huge peak of lactic acid was seen. This was **determined to be the D-lactate enantiomer** because of the presence of

- A normal plasma lactate
- Other characteristic features of D-lactic acidosis on urine organic acid analysis: **3OH-propionic, 3-phenyllactic and 4OH-phenylacetic acids**, and moderate increases in 2OH-3methylvaleric and 4OH-phenyllactic acids (compounds in bold highlighted on trace below; Fig. 2)

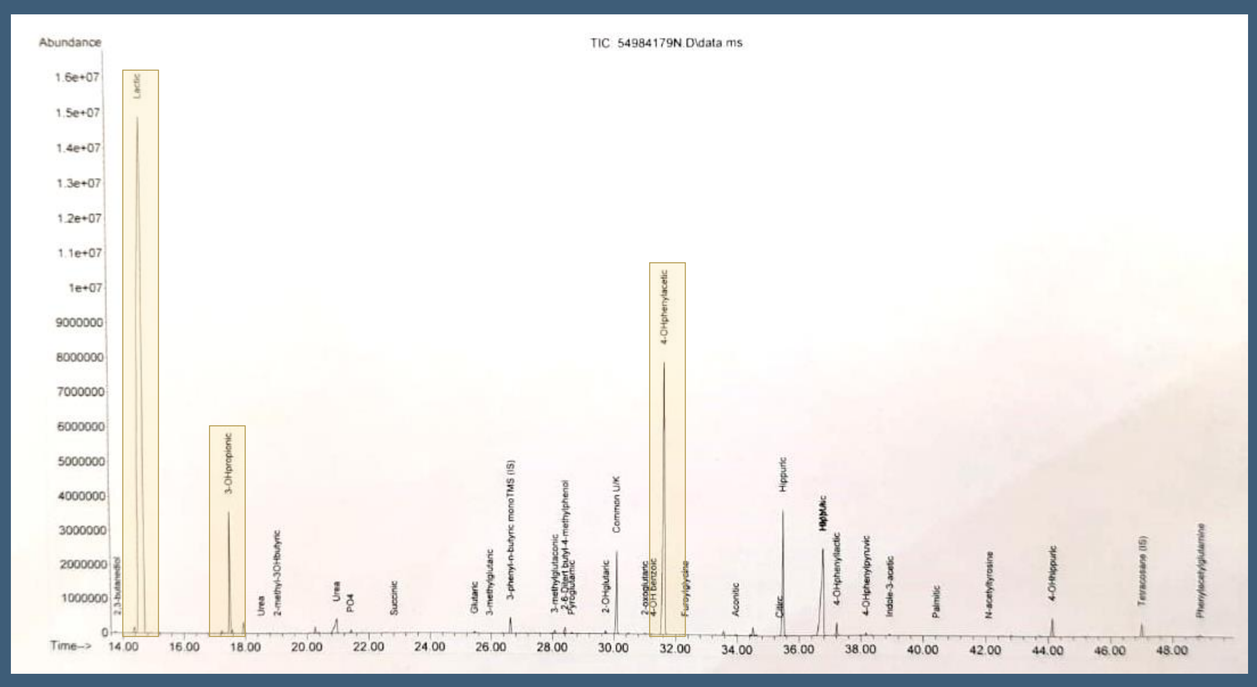

Fig 2. Urine organic acid analysis; chromatogram produced (GC-MS analysis) with key characteristic peaks in D-lactic acidosis highlighted

DISCUSSION & CONCLUSION

- This case demonstrates the **utility of urinary organic acid** analysis in the diagnosis of D-lactic acidosis
- We therefore **propose that it be used as a supporting diagnostic tool** in such suspected cases.
- It is also a reminder that urine organic acid analysis has **significant utility outside diagnosing IEM**.

REFERENCES

1. Htyte N, White L *et al.* 2011. An extreme and life-threatening case of recurrent D-lactate encephalopathy. *Nephrol Dial Transplant,* 4, 1432-1435.
2. Zhang DL, Jiang ZW *et al.* 2003. D-lactic acidosis secondary to short bowel syndrome. *Postgrad Med J,* 79, 110-112

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