Starvation Ketoacidosis: a rare but significant metabolic condition

Dr S Nardeosingh, Amy Savage and Dr M Banerjee | Department Diabetes and endocrinology, Royal Bolton Hospital

Introduction

Ketoacidosis is defined as metabolic acidosis associated with an accumulation of ketone bodies[1]. Causes include diabetes, pregnancy, alcohol excess, and malnutrition[1,2,3,4,5]. Ketonaemia following starvation has been documented in the literature. However, developing acidosis secondary to the build up on ketone bodies in a starved state is rare[6,7].

Here, we review two cases of starvation ketoacidoss.

Case 1

A 63 years old gentleman with no history of diabetes, presented with persistent vomiting for 48 hours. Admission bloods:

pH 7.19
pCO2 2.7
Base excess -17.8
Serum bicarbonate 8
Plasma glucose 5.2 mmol/l
Serum alcohol <100
Serum ketones 3.4 mmol/l.

He was managed with intravenous (IV) fluids, mainly dextrose and 0.9% saline. His symptoms, serum ketones and pH levels normalised while his blood glucose remained stable and he was discharge after 3 days.

Case 2

A 67 year old lady with past history of COPD, excess alcohol intake and osteoporosis, presented with feeling unwell, since she stopped eating for 5 days due to low mood.

Admission bloods

pH 7.43
pCO2 3.5
Base excess -4.7
serum bicarbonate 14
Plasma glucose 6.7 mmol/l
Serum alcohol <100
Serum ketones 3.4 mmol/l.

She was managed with IV fluids with dextrose and IV Vitamin B complex. Her symptoms, serum ketones and pH levels normalised while her blood glucose remained stable over next day and was discharged home.

Discussion

In tissues except the brain, red blood cells and liver:

- Fatty acids combine with co-enzyme A to form acyl-CoA chains.
- Break down of these chains by β-oxidation leads to the production of acetyl-CoA.
- Acetyl-CoA enters the citric acts cycle and reacts with oxaloacetate to produce citrate.
- This reaction leads the the production of carbon dioxide, water, 1 GTP and 11 ATP molecules per acetyl group[1,8].

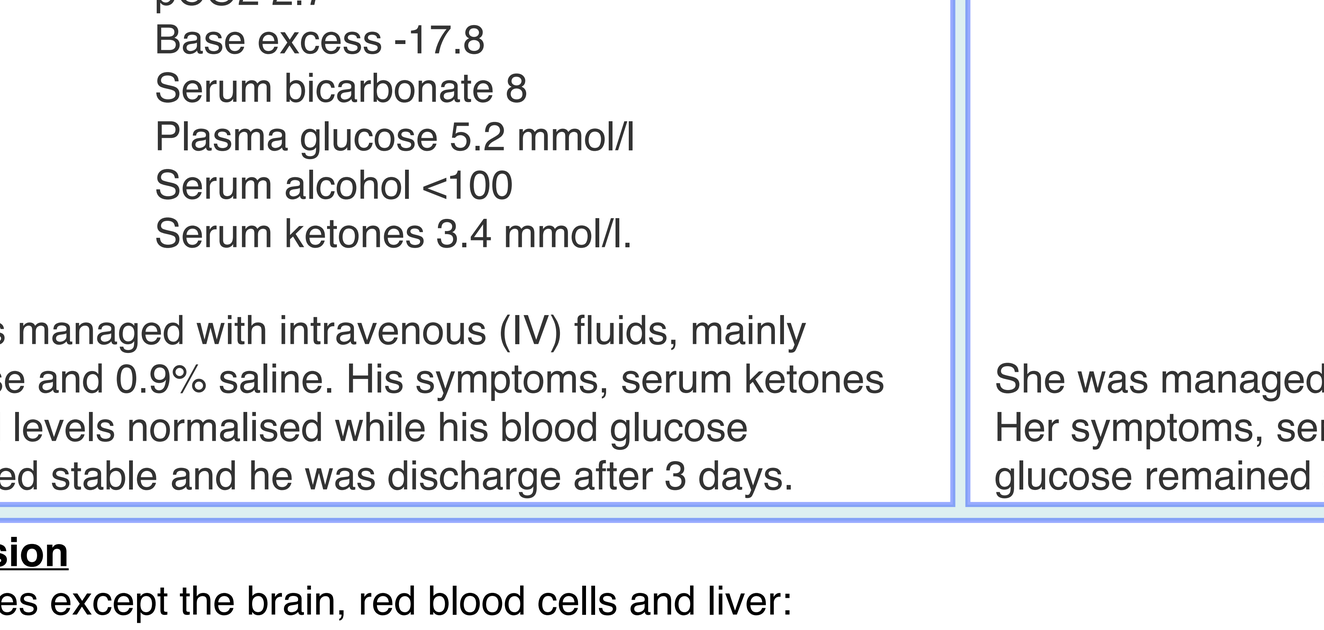

Figure 1: The formation of ketone bodies in the liver. The citric acid cycle can not oxidise all of the acetyl CoA as it is being produced. Excess acetyl CoA is diverted into the cytosol from the mitochondria, where ketone bodies are formed. Adapted from *The Digestive System by M.Smith and D. Morton*[9].

In the starved state:

- Oxaloacetate, is diverted to the gluconeogenic pathway.
- Oxaloacetate is hydrogenated to malate, which is removed from the mitochondrion and transferred to the cytoplasm where it is converted to glucose to be be released into the blood stream[1,9,10].
- Due to the reduced levels of oxaloacetate, acetyl-CoA is diverted to form ketone bodies (Figure 1).

Ketone bodies are released into the blood stream where they can be taken up by peripheral cells containing mitochondria. The ketone bodies are converted to acetyl-CoA to be used in the citric acts cycle to produce energy[6].

Build up of these ketone bodies results can result in metabolic acidosis as demonstrated by the two cases.

Conclusion

Starvation ketoacidosis is an under recognised condition. Prompt diagnosis and treatment targeted to correct volume and calorie deficit (mainly from carbohydrates) helped the two patients discussed, to go from a metabolic state based on fatty acid catabolism to a eumetabolic state. Distinction from diabetic ketoacidosis is extremely important. If misdiagnosed as euglycaemic diabetic ketoacidosis[11], consequent inappropriate insulin therapy would lead to hypoglycaemia in an already carbohydrate depleted individual.

References

1. Laffel, L. (1999). Ketone bodies: a review of physiology, pathophysiology and application of monitoring to diabetes. *Diabetes/Metabolism Research and Reviews*, 15(6), pp.412-426.
2. Menon, A. and Morton, A. (2015). Case of ketoacidosis in pregnancy. *Emergency Medicine Australasia*, 27(4), pp.373-374.
3. Smith, D. et al (1999). Alcoholic ketoacidosis presenting as diabetic ketoacidosis. *Irish Journal of Medical Science*, 168(3), pp.186-188.
4. Mostert, M. and Bonavia, A. (2016). Starvation Ketoacidosis as a Cause of Unexplained Metabolic Acidosis in the Perioperative Period. *American Journal of Case Reports*, 17, pp.755-758.
5. Sinha, N. et al (2014). Starvation Ketoacidosis: A Cause of Severe Anion Gap Metabolic Acidosis in Pregnancy. *Case Reports in Critical Care*, 2014, pp.1-4.
6. Metin Aksu et al (2017). Ketoacidosis due to Starvation. *Eurasian Journal of Emergency Medicine*.
7. Palmiere, C et al (2016). Postmortem biochemistry in suspected starvation-induced ketoacidosis. *Journal of Forensic and Legal Medicine*, 42, pp.51-55.
8. Veech, R. (2004). The therapeutic implications of ketone bodies: the effects of ketone bodies in pathological conditions: ketosis, ketogenic diet, redox states, insulin resistance, and mitochondrial metabolism. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 70(3), pp.309-319.
9. Frise, C. and Mackillop, L. (2016). Starvation ketoacidosis. *Journal of the Intensive Care Society*, 17(4)(356).
10. Laverde-Sabogal, C. et al (2014). A rare cause of severe metabolic acidosis: Presurgical fasting. *Colombian Journal of Anesthesiology*, 42(4), pp.312-316.