Limitations to using point of care blood ketone testing to monitor DKA treatment

Sir, After recommendations from the Joint British Diabetes Societies to use bedside monitoring of blood ketones in the management of diabetic ketoacidosis (DKA),[1] a number of UK hospitals have introduced point of care testing (POCT) for measurement of blood ketones. The guidelines state that the method of choice for monitoring the response to treatment is bedside measurement of capillary blood ketones. Many of the devices used in hospitals to measure blood glucose at the patient's bedside are also able to measure ketones; specifically, betahydroxybutyrate (BHB) which is the predominant ketone present in DKA. The guidelines also recommend that one of the main therapeutic targets should be a reduction in blood ketones by 0.5mmol/L per hour. If this target is not reached, it is recommended that the insulin infusion rate should be increased.

We introduced bedside blood ketone testing using the Abbott Precision Xceed Pro meter with Precision Xceed Pro β ketone test strips. We decided to evaluate and introduce a laboratory method for BHB as it is advisable that for all POCT there should be a laboratory method available if the result is outside the measurable range of the device, if the result does not fit clinically or if there are contraindications to using the POCT device in particular patients. As part of the evaluation, we compared a laboratory BHB method (Randox RanBut D-3 hydroxybutyrate reagents on the Roche P Module) to the POCT capillary blood ketone results. Venous serum samples collected within 1 hour of the POCT capillary blood ketone test were analysed using the laboratory BHB method. Additionally, we compared the results obtained using the laboratory and POCT method on the same venous sample (Figure 1).

There was good agreement between the POCT capillary blood ketone results and laboratory venous serum BHB results up to a BHB concentration of 3mmol/L. Above 3mmol/L, the POCT capillary blood ketone results were consistently lower than the laboratory venous serum results. Janssen *et al.* also advise caution on results above 3mmol/L.[2] However, when the venous samples were tested using the Abbott meter, there was very good correlation between the laboratory results and the POCT results. Therefore, the lower results observed in the capillary whole blood samples are most likely to be a problem with the capillary sample rather than the POCT ketone test itself. We hypothesise that dehydration and decreased peripheral circulation, often seen in DKA patients, are factors affecting the quality of the capillary blood sample and the ketone concentration above 3mmol/L.

These findings have implications when trying to use POCT capillary blood ketone tests to monitor patients with DKA. Using the target reduction of 0.5mmol/L per hour will be acceptable if the ketone concentration is <3mmol/L. However, due to the underestimation of POCT ketones using capillary samples, a reduction in ketones may not be demonstrated using the meter if the ketone concentration is >3mmol/L. In some of our patients, the capillary POCT ketones stayed at about the same level for several hours whereas the laboratory results were decreasing rapidly. There is a danger that, in these patients, the rate of the

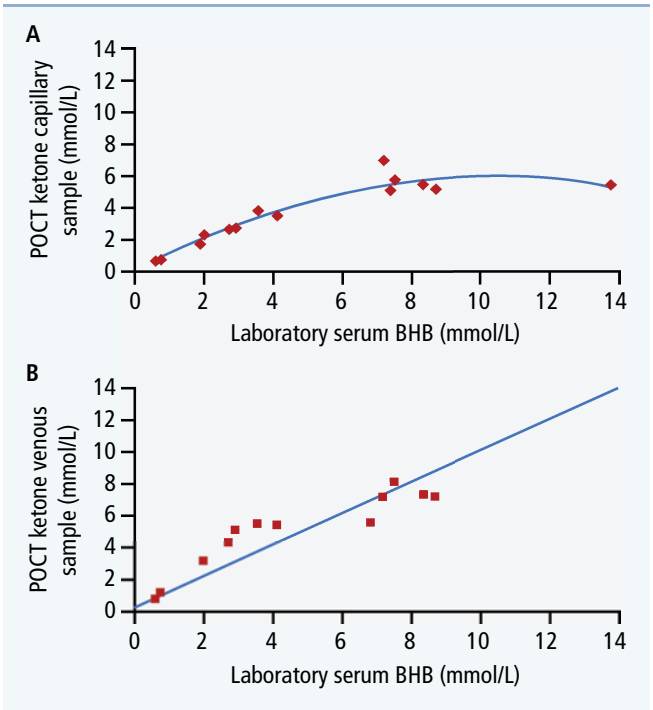

Figure 1. (A) the comparison between the serum betahydroxybutyrate (BHB) results using the Randox method on venous samples and the POCT ketone results (using the Abbott Precision Xceed Pro meter with Precision Xceed Pro β ketone test strips) on capillary samples. (B) the comparison between the serum BHB results (Randox method) and POCT ketone results (using the same Abbott meter with test strips) on the same venous samples. Note that the measuring range of the POCT ketone tests is up to 8mmol/L (using the Abbott Precision Xceed Pro meter with Precision Xceed Pro β ketone test strips)

insulin infusion would have been increased unnecessarily, increasing the risk of hypoglycaemia and hypokalaemia.

Our local guideline for DKA has been updated to include the use of venous BHB measurements. We recommend that BHB should be measured in the laboratory on the venous sample collected at 0, 2, 4 and 8 hours. We have also put a cautionary statement in our guideline to ensure that the insulin administration rate is not increased on the basis of an apparent inadequate reduction of blood ketones alone. The guideline states that: 'when blood ketones are >3mmol/L, ketone meter using capillary blood may underestimate actual value and rate of change may also be falsely low. Review venous ketone results and also assess change in capillary glucose and venous bicarbonate to help determine if IV insulin rate needs to be changed.'

The POCT and laboratory methods compared well on venous samples but the POCT capillary results were an underestimate of the laboratory venous result if the ketone concentration was >3mmol/L. This suggests that the falsely low results observed with capillary samples are due to the characteristics of the capillary blood rather than the methodology of this particular meter. This is not surprising as the MHRA advises the collection of a venous sample instead of capillary glucose testing in patients with severe dehydration or in hyperglycaemic states with or without ketosis.[3] This is a potential problem for users of any type of bedside ketone meter to monitor patients with DKA. We advise all users of POCT blood ketone tests to compare their results on capillary samples to venous samples using

a laboratory method and advise caution if using capillary ketone results alone to guide patient management.

Jane Armer, Clinical Biochemistry
Natalie Hunt, Clinical Biochemistry
Kalpana Kaushal, Diabetes and Endocrinology
Martin Myers, Clinical Biochemistry
Lancashire Teaching Hospitals NHS Foundation Trust, UK

References

1. Savage MW, *et al.* Joint British Societies guideline for the management of diabetic ketoacidosis. *Diabet Med* 2011;28:508–15.
2. Janssen MJ, *et al.* Accuracy of the Precision point of care ketone test examined by liquid chromatography tandem mass spectrometry (LC-MS/MS) in the same fingerstick sample. *Clin Chem Lab Med* 2010;48:1781–4.
3. MHRA Point of Care Testing Blood Glucose Meters – Advice for Healthcare Professionals 2011. Available at www.mhra.gov.uk/Publications/Postersand leaflets/CON2015499 [last accessed October 2013].

Response

Sir, We are grateful to the authors for their important observation that capillary POCM ketone measurements may not parallel venous blood measurement assessed by POCM and laboratory methods. They suggest that POCT results of >3mmol/L underestimate true venous levels, and that this may relate to dehydration and decreased perfusion. It would be helpful if the correspondents were to provide more detailed figures to help understand the degree of discrepancy at ketone levels >3mmol/L. Their observations may be important but need to be confirmed by others. Nevertheless, at this stage their observations need to be considered in the context of the current guidelines.

It is important to recognise that blood ketone values are highly unlikely to be measured in isolation and that all those on fixed or variable rate IV insulin infusion will also have hourly bedside glucose monitoring. Thus, their concern that hypoglycaemia may occur by 'blindly' increasing insulin infusion rates is unlikely. If, after an increase in infusion, glucose does not fall by at least 3mmol/L, then, as the guidelines state, checks should be made to ensure that the insulin infusion pump is working and that the correct insulin residual volume is present. Thus these checks are likely to prompt the health care professional to err on the side of safety.

Additionally, the guidelines state that venous blood gas samples should be taken at regular intervals to check potassium levels. Many, if not most, blood gas analysers also automatically measure ketone levels, thus providing the additional check that the correspondents suggest. It may be appropriate for future versions of the guidelines to incorporate checks on venous ketone levels when capillary levels are above 3mmol/L; this will be dependent, we suggest, on technological developments. In addition, while we accept the premise of the argument, previous work has shown that, despite these sources of potential interference, ketone meter performance is robust enough to be used in clinical scenarios.[1] A further use is the ability to distinguish between the acidosis of ketonaemia and that of hyperchloraemia secondary to saline use. Furthermore, we have anecdotal reports that the use of bedside ketone monitors has reduced hospital length of stay.

The guidelines have been widely adopted or adapted across most hospitals in the UK with most teams finding them 'useful' or 'very useful'. To date, we have had no correspondence from other teams highlighting this issue and would welcome any information letting us know if amendments are required. As with the other guidelines produced by the Joint British Diabetes Societies, they are dynamic documents, subject to regular review and change. The latest version of the DKA guidelines was put on the ABCD website in October 2013. We would encourage other teams to analyse their results and compare their point of care testing results with their laboratory results. If these teams collectively find that the problems associated with DKA treatments by these authors occurs elsewhere, then the JBDS guidelines will be changed to reflect this.

In the meantime, it is important to know your point of care testing device and its limitations, and work closely with your point of care testing team.

Ketan Dhatariya, Consultant in Diabetes, Endocrinology and General Medicine, on behalf of the JBDS DKA guidelines writing group

Reference

1. Khan AS, *et al*. Evaluation of a bedside blood ketone sensor: the effects of acidosis, hyperglycaemia and acetoacetate on sensor performance. *Diabetic Med* 2004; 21:782–5.

Tribute to Mary MacKinnon, RGN, MMedSci

It is with much sadness that we report the recent loss of our friend and colleague, Mary MacKinnon, the outstanding Diabetes Nurse Specialist of her generation. For many years Mary was a hugely valued editorial board member of *Practical Diabetes*, contributing wise counsel from her immense experience of working with diabetes, especially in the community, and her exceptional empathy for people living with diabetes.

Mary's roots were firmly placed in Sheffield, where she held a number of distinguished diabetes appointments, but it was on the national and international stage that her legacy will be remembered, enabling individuals with diabetes to become 'experts', confident in managing their condition. Mary wrote extensively, including her definitive guide on 'Providing Diabetes Care in General Practice' published in 1993, which led to her participation as a founder member of the organisation Primary Care Diabetes UK. She was Lecturer and Director of Education on the Warwick Diabetes Postgraduate Course, and a contributor to a number of diabetes task force initiatives, one of many being the St Vincent Declaration.

Recognising Mary MacKinnon's singular commitment to diabetes care, Diabetes UK endowed a prestigious annual lecture to her name. Indeed, many of us will remember the privilege of listening to her own delivery of the first MacKinnon Lecture in 1999, reflecting on her personal research of the life of Florence Nightingale and its relevance to nursing today. Dedicated to diabetes in every dimension of care delivery, Mary MacKinnon will be much remembered for her professional achievements, but above all for being the person who championed tirelessly on behalf of everyone living with diabetes.

