Diabetes Management in a Point of Care Setting

By Professor Chris Price, Visiting Professor in Clinical Biochemistry, Department of Primary Care Health Sciences, University of Oxford and Dr Gary Dowthwaite, Product Manager, EKF Diagnostics.

Why point of care testing?

The objective of point-of-care testing (POCT) is the rapid provision of diagnostic information to enable clinical decisions to be made at the earliest opportunity during patient care and treatment. Such rapid provision of information facilitates optimistaion of the care process. The potential utility for any application of POCT can therefore be judged in terms of its contribution to decision making and to the process of care – the latter including access to care. However it is also important to be aware of the potential impact of the analytical performance of POCT measurement systems compared with laboratory analytical systems, as the majority of the core evidence on the utility of a test will have been established using laboratory based systems.

A chequered history

The role of HbA1c testing in the management of patients with diabetes has been established for several decades, whilst its role in the diagnosis has been recognised more recently. These utilities are based on the fact that the HbA1c concentration reflects the average circulating glucose concentration over the lifespan of the red cell, and the evidence that HbA1c concentration is a good predictor of the complications of diabetes e.g. cardiovascular disease (1-3). Early experience with the use of HbA1c measurement was based on laboratory-based methods including ion exchange and affinity chromatography methods, with alternative affinity and immunological methods following later. An early study of biological variation indicated that intra- and inter individual variation between non-diabetics was 1.7 and 4.0% respectively (4). Another study found an intra-individual variation of HbA1c as 1.2% in non-diabetics, with a figure of 1.75% in patients with Type 1 diabetes. Interestingly, the respective figures for fasting blood glucose were 5 and 30% (5); this illustrates one of the attractive features for using the HbA1c measurement in screening for, and management of, diabetes. A more recent evaluation of the biological variation of HbA1c in healthy individuals using an IFCC-calibrated assay found intra- and inter individual variation of 2.5 and 7.1% respectively.

These authors used this data to calculate the desirable analytical goals for imprecision, bias and total error as 1.3%, 1.9% and 3.9% respectively (6). Using similar performance criteria Lestra Winters et al (7) found that only two out of eight POCT systems for the measurement of HbA1c met the required performance criteria whilst Bruns and Boyd (8) commented on the implication of poor analytical performance on clinical decision making. In the Lenters-Westra report, it is apparent that there was variation among the laboratory reference methods, although they were all controlled and calibrated in the authors' laboratory. Indeed, one reference is cited as a source of concern regarding the accuracy of POC instruments, yet this reference describes an accuracy drift over time that was as large in the central laboratory instrument as it was in the POC device (9). Survey results from the College of American Pathologists (10) indicate that in the field, variation within and between laboratory-based methods can be comparable to or greater than some of the POC results reported by Lenters-Westra and an analysis of these trends was given in the report by Holmes et al (9).

Digging deeper into the analysis

A recent systematic review of the use of POCT for HbA1c in the management of patients with diabetes concluded that there was "an absence of evidence in clinical trial data to date for the effectiveness of POCT for Hb A1c in the management of diabetes" (11). Whilst this might be considered disappointing, it is helpful to explore how the authors came to these conclusions. Firstly, whilst there were seven studies included in the review (12-17), two approaches to the surrogate outcome measure were employed (mean change in HbA1c level, and change in proportion of patients with HbA1c ≤7.0%) reducing the opportunity for meta-analysis of the full cohort of patients. Secondly there was considerable heterogeneity in the patient populations studied, including both Type 1 and Type 2 diabetics in some studies, as well as the proportion of patients with HbA1c values ≤7.0% at the outset of the studies (baseline), thus limiting the opportunity for pooling of data and meta-analysis.

In addition there was very little documentation of the treatment protocols employed, and therefore no indication as to whether patients had been stratified in relation to the care they were given. Thirdly there was no indication in some of the studies as to whether the results were discussed with the patients at the time the results were generated, and in one instance it was documented that the results using POCT had not been discussed at the time of generation (14). However there was some evidence of greater treatment intensification in patients with HbA1c >7.0% in those receiving POCT.

The authors drew attention to key features in the use of POCT, which are equally applicable to routine practice as well as in research studies, namely (i) the need to stratify patients [and their treatment] according to baseline HbA1c values; (ii) define and adhere to a revised process of care using POCT; and (iii) ensure that results of POCT are discussed with patients when generated and that treatment decisions are documented and implemented. Interestingly, four observational studies, of over 5700 patients with diabetes, in which there was immediate feedback of results to patients all showed significant reductions in the HbA1c results (17-20). Indeed, one of these studies demonstrated maintenance of improved HbA1c concentrations for a period of four years (19). A recent systematic view of quality improvement (QI) strategies in the management of diabetes has shown that QIs, involving greater adherence to guidelines can help to improve HbA1c levels (20). Data mining of primary care records has shown that there is evidence of both over- and under utilisation of HbA1c tests (21). On the other hand there is good evidence to show that patient satisfaction is improved using POCT, and personal knowledge of an individual's HbA1c levels is associated with better outcomes (as judged by HbA1c levels) (22-24).

The case for testing HbA1c in POCT settings

The attributes of the HbA1c measurement for the management of diabetes are equally applicable for its use in the diagnosis of diabetes. Furthermore the performance has been shown to be equal to that of the fasting blood glucose commonly used as a screening test for Type 2 diabetes (25). The World Health Organisation has recommended the use of HbA1c for the diagnosis of diabetes (26) and similar guidance has now followed in several countries (e.g. 27,28).

However the test should be used with a degree of caution. The test should not be used in children, young people, pregnant women, individuals in whom type 1 diabetes is suspected, in individuals where symptoms have been of short duration, or in patients who are acutely ill (29, 30). Furthermore the test should not be used in patients on drugs that might cause a rapid rise in the blood glucose, patients in whom pancreatic damage might be present, patients with renal failure, or HIV infection. It is also suggested that the cut-off value generally quoted (48 mmol/mol (6.5% DCCT)) may not be appropriate for all populations and may require further study in populations that have not featured in studies to date. However it should also be noted that individuals within the range 42 -47mmol/mol, should be considered at high risk of developing diabetes, given appropriate lifestyle guidance and retested annually and that those with values less than 42 mmol/mol, should be tested every three years (30).

Concerns have been expressed about the use of HbA1c in screening for diabetes including the issue of access to the test in terms of instrument and consumables costs (31). Further, in studies of opportunistic screening for Type 2 diabetes in Emergency Departments, a high prevalence has been found. However there were significant problems associated with patient follow-up for diagnostic testing and lifestyle guidance (32,33). Current guidance supports the employment of HbA1c measurement in both screening for type 2 diabetes and in the management of patients with diabetes.

Summary

There are strong arguments for the use of POCT for HbA1c where the performance characteristics of the systems are equivalent to those employed in the central laboratory. POCT offers improved access to testing, as well as enabling immediate clinical decision making, discussion with the patient and implementation of appropriate treatment and/or lifestyle advice. Furthermore POCT enables testing to be undertaken closer to the patient, affords greater convenience for the patient, thereby improving the likelihood of treatment compliance. EKF Diagnostics provides point of care HbA1c analysers certified to international standards (IFCC and NGSP) for point of care testing during screening and monitoring of diabetes.

Bibliography

1. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med 2004;141:413–20.
2. Selvin E, Marinopoulos S, Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann of Internal Medicine 2004;141:421–31.
3. ten Brinke R, Dekker N, de Groot M, Ikkersheim D. Lowering HbA1c in type 2 diabetics results in reduced risk of coronary heart disease and all cause mortality. Prim Care Diabetes 2008;2:45–9.
4. Rohlfing C, Wiedmeyer H-M, Little R, Grotz L, Tennill A, England J, et al. Biological Variation of Glycohemoglobin. Clin Chem 2002;48:1116-8.
5. Carlsen S, Petersen PH, Skeie S, Skadberg Ø, Sandberg S. Within-subject biological variation of glucose and HbA(1c) in healthy persons and in type 1 diabetes patients. Clin Chem Lab Med. 2011;49:1501-7.
6. Braga F, Dolci A, Montagnana M, Pagani F, Paleari R, Guidi GC, et al. Revaluation of biological variation of glycated hemoglobin (HbA(1c)) using an accurately designed protocol and an assay traceable to the IFCC reference system. Clin Chim Acta 2011;412:1412-6
7. Lenters-Westra E, Slingerland RJ. Six of eight hemoglobin A1c point-of-care instruments do not meet the general accepted analytical performance criteria. Clin Chem 2010;56:44 –52.
8. Holmes EW, Ersahin C, Augustine GJ, Charnogursky GA, Gryzbac M, Murrell JV, McKenna KM, Nabhan F and Kahm SE. Analytic bias among certified methods for the measurememnt of haemoglobin A1c. A cause for concern? Am J Clin Pathol 2008, 129, 540-547
9. College of American Pathologists (CAP) Survey Data. http://www.ngsp.org/CAPdata.asp
10. Bruns DE, James C. Boyd JC. Few point-of-care hemoglobin A1c assay methods meet clinical needs. Clin Chem 2010;56:4–6.
11. Al-Ansary L, Farmer A, Hirst J, Roberts N, Glasziou P, Perera R, Price CP. Point-of-Care Testing for Hb A1c in the Management of Diabetes: A Systematic Review and Metaanalysis. Clin Chem 2011;57:568-76.
12. Bubner TK, Laurence CO, Gialamas A, Yelland LN, Ryan P, Willson KJ, et al. Effectiveness of point-of-care testing for therapeutic control of chronic conditions: results from the PoCT in General Practice Trial. MJA 2009;190:624–6.
13. Cagliero E, Levina EV, Nathan DM. Immediate feedback of HbA1c levels improves glycemic control in type 1 and insulin-treated type 2 diabetic patients. Diabetes Care 1999;22:1785-9.
14. Khunti K, Stone MA, Burden AC, Turner D, Raymond NT, Burden M, et al. Randomised controlled trial of near-patient testing for glycated haemoglobin in people with type 2 diabetes mellitus. Br J Gen Prac 2006;56:511–7.
15. Kennedy L, Herman WH, Strange P, Harris A, GOAL A1C team. Impact of active versus usual algorithmic titration of basal insulin and point-of-care versus laboratory measurement of HbA1c on glycemic control in patients with type 2 diabetes: the Glycemic Optimization with Algorithms and Labs at Point of Care (GOAL A1C) trial. Diabetes Care. 2006;29:1– 8.
16. Agus MS, Alexander JL, Wolfsdorf JI. Utility of immediate hemoglobin A1c in children with type I diabetes mellitus. Pediatr Diabetes 2010;11:450–4.
17. Grieve R, Beech R, Vincent J, Mazurkiewicz J. Near patient testing in diabetes clinics: appraising the costs and outcomes. Health Technol Assess 1999;3:1–74.
18. Ferenczi A, Reddy K, Lorber DL. Effect of immediate hemoglobin A1c results on treatment decisions in office practice. Endocr Pract 2001;7:85–8.
19. Petersen JR, Finley JB, Okorodudu AO, Mohammad AA, Grady JJ, Bajaj M. Effect of point-of-care on maintenance of glycemic control as measured by A1C. Diabetes Care 2007;30:713–5.
20. Rust G, Gailor M, Daniels E, McMillan-Persaud B, Strothers H, Mayberry R. Point of care testing to improve glycemic control. Int J Health Care Qual Assur 2008;21:325–35.
21. Driskell OJ, Holland D, Hanna FW, Jones PW, Pemberton RJ, Tran M, Fryer AA. Inappropriate requesting of glycated hemoglobin (Hb A1c) is widespread: assessment of prevalence, impact of national guidance, and practice-to-practice variability. Clin Chem 2012;58:906-15.
22. Levetan CS, Dawn KR, Robbins DC, Ratner RE. Impact of computer-generated personalized goals on HbA(1c). Diabetes Care 2002;25:2– 8.
23. Peterson KA, Radosevich DM, O'Connor PJ, Nyman JA, Prineas RJ, Smith SA, et al. Improving Diabetes Care in Practice: findings from the TRANSLATE trial. Diabetes Care 2008;31:2238-43
24. Laurence CO, Gialamas A, Bubner T, Yelland L, Willson K, Ryan P, Beilby J. Point of Care Testing in General Practice Trial Management Group. Patient satisfaction with point-of-care testing in general practice. Br J Gen Pract 2010;60:e98–104.
25. Bennett CM, Guo M, Dharmage SC. HbA(1c) as a screening tool for detection of Type 2 diabetes: a systematic review. Diabet Med 2007;24:333-43.
26. World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. 2011. www.who.int/diabetes/publications/report-hba1c_2011.pdf.
27. National Institute for Health and Clinical Excellence. Preventing type 2 diabetes: risk identification and interventions for individuals at high risk. 2012. www.nice.org.uk/nicemedia/live/13791/59951/59951.pdf.
28. ADA guidelines
29. Inzucchi SE. Clinical practice. Diagnosis of diabetes. N Engl J Med 2012;367:542-50.
30. Farmer A. Use of HbA1c in the diagnosis of diabetes. BMJ 2012;345:e7293.
31. Higgins T. HbA(1c) for screening and diagnosis of diabetes mellitus. Endocrine. 2012 Aug 21. [Epub ahead of print].
32. Ginde AA, Cagliero E, Nathan DM, Camargo CA Jr. Point-of-care glucose and hemoglobin A1c in emergency department patients without known diabetes: implications for opportunistic screening. Acad Emerg Med. 2008;15:1241-7.
33. Jelinek GA, Weiland TJ, Moore G, Tan G, Maslin M, Bowman K, et al. Screening for type 2 diabetes with random finger-prick glucose and bedside HbA1c in an Australian emergency department. Emerg Med Australas 2010;22:427-34.

EKF DIAGNOSTICS

SCIENCE MADE SIMPLE