Horizon Scan Report 0007 **31 July 2009**

Diagnostic Technology: Point of Care test (POCT) for glycosylated haemoglobin HbA_{1c}

Clinical Question: In the diagnosis and monitoring of patients with type 1 and type 2 diabetes, what advantages does point of care HbA_{1c} testing provide over current practice?

Devices:
A1cNow+ (Chirus Ltd), Afinion and NycoCard (Axis-Shield UK), DCA Vantage (Siemens Healthcare Diagnostics Ltd), in2it (Biorad Laboratories Ltd). These devices have been evaluated and compared in a Buyers' guide prepared by the NHS Purchasing and Supplies Agency (PASA) (June 2009) (1).

Advantages over Existing Technology:
The advantage of point of care testing is that test results are available rapidly, facilitating more immediate therapeutic decisions. This is particularly important in managing long-term conditions, such as diabetes. The Diabetes Control and Complication Trial (DCCT) (US and Canada) (5) and the United Kingdom Prospective Diabetes Study (UKPDS) (4) showed long-term health and economic benefits from tight glycaemic control. Monitoring glycaemic control patients with existing diabetes using HbA_{1c} is performed every 3-6 months in primary care. It typically involves a visit to the nurse or phlebotomist for venepuncture, with a follow up visit with a Practice Nurse or GP 1-2 weeks later to discuss results. Point of care testing for HbA_{1c} could provide immediate results, resulting in more immediate therapeutic decisions and fewer patient visits. This might result in improved diabetic control. For screening and/or diagnosis of diabetes, currently fasting plasma glucose test (FPG) is used, which requires a fasting sample and two patient visits/contacts (one to obtain the sample, one for the results). There is substantial ethnic variability in the sensitivity and specificity of the current diagnostic approach and a study has shown that combining FPG and HbA_{1c} improves identification of diabetics (positive likelihood ratio: 14.4) (13). Using point of care HbA_{1c} testing instead of (or in addition to) FPG could therefore offer a more effective screening procedure for diabetes. The American Diabetes Association (ADA) has published new recommendations for the diagnosis of diabetesand risk categories for diabetes using glycated haemoglobin (HbA1c).

Details of Technology:
Blood glucose adheres to haemoglobin in red blood cells, making glycosylated haemoglobin, called haemoglobin A_{1c} or HbA_{1c}. The HbA_{1c} gives a long-term measure of blood glucose levels in patients with diabetes, indicating the blood glucose control over the preceding 3 month period. A drop of blood from a fingerstick sample is applied to a sample cartridge, which is then analysed over 5-10 minutes (depending on the device) in a desk top analyser, which measures the percentage HbA_{1c}.

Patient Group and Use:
- Patients with type 1 or type 2 diabetes mellitus to monitor glycaemic control
- Patients being screening for diabetes

Importance:
Diabetes UK reports 2.5 million people diagnosed with diabetes in the UK in 2008 (3.8% prevalence) (2). A recent study reported an increase in the incidence of diabetes amongst children in Europe, with an average annual increase of 3.9% (3). The study also predicted a 70% increase in the incidence amongst children younger than 15 years by 2020.
A report on the progress of the National Services Framework for Diabetes by the Department of Health highlights the importance of managing diabetes in primary care (12). In the National Diabetes Audit for 2008-2009, 88% of records

from people with Type 1 and 94% of Type 2 diabetes included an HbA1c measurement, emphasising the importance of this test in diabetes management (8).

A recent meta-analysis of randomised controlled trials confirmed that intensive control of glucose significantly reduced coronary events in patients with diabetes (6). An NHS guidance on vascular risk assessment and management highlights that even within the non-diabetic range, HbA_{1c} has been shown to be a risk marker for vascular events and can be used to assess risk of diabetes (9, 15). HbA_{1c} testing does not require fasting blood samples, and this guidance recommends that it should therefore be used where fasting is not possible. Furthermore, blood could potentially be tested from the same finger prick sample as one taken for other POCT tests potentially, for example a cholesterol test.

Previous Research:

Accuracy compared to existing technology:

The PASA buyers' guide recommends A1cNow+ for use in GP surgeries (1). The recommendation is based on the ease of use, convenience (brief operator time) and small sample size required. However the report noted that this device underestimates values relative to laboratory tests and may result in under-treatment of patients. One study comparing point-of-care (POC) analysis (Metrika A1c Now, Bayer Health Care) with laboratory analysis on 99 paired samples, showed that the POC method yielded a mean HbA_{1c} of 7.4%, which was equivalent to the mean of 7.5% produced with all combined standard laboratory analyses (20). The Pearson correlation between POC and the laboratory analysis test results was 0.9 ($P < .001$). POC test sensitivity was 81% and specificity was 93%. Eighteen percent of patients with an $HbA_{1c} >=$ 7% by laboratory analysis were not identified by the POC test. Comparison of A1c Now monitor (Chirus) showed good correlation ($r = 0.758$) to the standardized laboratory test, with the most accurate A1c Now values falling within a range of 6-8% (21).

A recent study comparing 8 HbA1c measurement devices using three Clinical Laboratory Standards Institute Protocols to investigate to investigate imprecision, accuracy and bias reported that only DCA Vantage and Afinion met the acceptance criteria (coefficient of variation <3%) in the clinically relevant range (24).

Impact compared to existing technology:

A single RCT which randomized patients with type 1 and type 2 diabetes attending an academic diabetes centre to immediate feedback of HbA_{1c} results compared to standard care, found significant improvement in glycaemic control at 6 and 12 months in patients receiving immediate feedback (7). The introduction of POCT in this study was positively received by both patients and physicians. A prospective controlled trial comparing POCT and standard laboratory testing in an urban primary care clinic showed that POC HbA_{1c} availability resulted in more frequent intensification of therapy when A1c was >/=7.0% at the baseline visit (51 vs. 32% of patients, $P = 0.01$). In 275 patients with two follow-up visits, HbA1c fell significantly in the POCT group (from 8.4 to 8.1%, $P = 0.04$) but not in the standard care group (from 8.1 to 8.0%, $P = 0.31$) (19). One study in primary care among patients receiving active insulin titration (weekly monitoring) showed that POCT resulted in a greater portion achieving HbA_{1c} <7.0% compared to those where HbA_{1c} was measured in the laboratory (16). However, in another RCT, the proportion of patients with $HbA_{1c} < 7.0\%$ did not differ significantly between groups receiving laboratory testing and those receiving POCT (37 versus 38%, odds ratio 0.95 [95% confidence interval = 0.69 to 1.31]) at 12 months follow up (18). This study also included an economic assessment and showed that the total cost for diabetes-related care was £390 per patient for the control group (usual care) and £370 for the POCT group; this difference was not statistically significant.

Regarding patient satisfaction, a study in general practice in Leicestershire (UK) indicated that the POC test was highly acceptable to patients and staff and confirmed that there may be potential benefits such as time saving, reduced anxiety and impact on patient management and job satisfaction (17). However, the study identified high pre-existing levels of satisfaction with diabetes care and the survey failed to confirm increased patient satisfaction as a result of rapid testing.

A systematic review of HbA_{1c} as a tool for screening for type 2 diabetes concluded that HbA_{1c} and fasting plasma glucose (FPG) screening tests have similar sensitivities and specificities for early detection (11). The combined use of FPG and HbA_{1c} in the diagnosis of diabetes has also been investigated. A recent study in the UK and Australia has

shown that using a combination of both tests would reduce the number of additional tests performed in the UK cohort by 33% and by 66% in the Australian patients studied (14).

Health Technology Assessments:
Two relevant HTA reports were identified:

1. A report on screening for type 2 diabetes was published in 2007, which also discusses laboratory HbA_{1c} testing in terms of utility and cost effectiveness (22). The report compares three tests for screening – FPG, OGTT and HbA1c. Their conclusions were as follows: All are safe, precise and validated; however, each has advantages and disadvantages. OGGT is inconvenient and poorly reproducible. FPG requires people to fast, compliance may be imperfect. HbA1c is more expensive but can be done at any time of day and reflects glycaemia over a period of several months.
2. A report on near patient testing (NPT) in diabetes clinics indicated that providing HbA_{1c} results by NPT seems to improve the process of care and aspects of patient satisfaction. The report recommended a prospective RCT of NPT in diabetes clinics.

Cost-effectiveness and economic impact:
Limited evidence currently exists on the cost-effectiveness of POCT for HbA1c. In fact a recent review on the evidence-based practice for POCT suggested that more detailed studies are required which focus on the wider economic costs and benefits of POCT, beyond the immediate cost of providing the test and the change in clinic attendance (25). Where evidence exists it is equivocal, Grieve and colleagues (23) compared laboratory and nurse near patient testing compared to conventional testing for several diagnostic tests of which HbA1c was included, they found that POCT led to improvements in the care process, significantly greater patient satisfaction and lower mean levels of HbA1c but higher visit costs reflecting the greater number of test and higher equipment costs. A Swedish before-and-after study compared the economic costs and benefits of implementing HbA1c home testing (26). They found a reduction in costs due to fewer clinic visits, reduction in total treatment costs, time saved and reduced labour costs in administration and sampling, reduced travel costs and a reduction in mean HbA1c levels. Khunti and colleagues (18) in a pragmatic RCT where patients were randomised to receive instant results for HbA1c or routine care found a non-statistical total cost difference of diabetes related care; £390 in the control group and £370 in the POCT group.

Research Questions:
To what extent has the use of HbA_{1c} testing been implemented in primary care?
In primary care settings, what are the effects of immediate feedback of HbA_{1c} results on control of diabetes, patient and provide satisfaction, and provider/clinic time?
How do immediate and standard HbA_{1c} compare in terms of cost effectiveness?
What are the potential barriers to introduction of point of care HbA_{1c} testing in primary care, e.g. Consumables, quality control, reproducibility, QC, linking to practice IT, training, time involved, sample throughput etc? *(although these are generic POCT issues, not specific to HbA_{1c})*
Screening for DM: To what extent would POC HbA_{1c} testing reduce false positive samples?
What are the implications of over or under estimation of $HbA_{1c}$with the POCT devices?

Suggested next step:
Recommendation to the HTA
Systematic review of the use of HbA_{1c} testing in primary care
Pilot study on the use of HbA_{1c} testing in primary care for the diagnosis and screening of type 2 diabetes
Randomised controlled trial of near patient testing of HbA_{1c} in primary care

Expected outcomes:
HbA_{1c} testing at point of care in primary care would provide better control of diabetes, greater patient satisfaction, and be more cost effective than current management by eliminating the time required for tests to be returned from the laboratory.

Comments:

The following systematic review, published after completion of this report, is relevant to this topic:
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