Use of HbA$_{1c}$ in the diagnosis of diabetes mellitus: A response from the Scottish Clinical Biochemistry Managed Diagnostic Network.

Situation

The World Health Organisation has recently recommended that: “HbA$_{1c}$ can be used as a diagnostic test for diabetes providing that stringent quality assurance tests are in place and assays are standardized to criteria aligned to the international reference values, and there are no conditions present that preclude its accurate measurement.” In November 2012 a consensus statement on the approach was published on behalf of the Department of Health Advisory Committee on Diabetes Mellitus on the use of HbA$_{1c}$ diagnostically within the UK. Details of the envisaged mode of application are given in the Appendix. This will lead to a significant cost pressure for Clinical Biochemistry budgets in Scotland (conservatively estimated at £600k per annum) and provide significant operational pressures in delivery of increased HbA$_{1c}$ workloads. The adoption of this approach across Scotland will not only have significant resource implications for SCBMDN laboratories, but may give rise to potential clinical governance issues if not managed appropriately in a co-ordinated manner. There is a need for health boards to develop an initial position on this development while all stakeholders consider the implications for diagnosis and management of diabetes in Scotland and secure the resources to deliver the approach safely and effectively.

Background

The biochemical diagnosis of diabetes mellitus has relied in the past on measurement of blood glucose and also the use of oral glucose tolerance testing. Glucose measurements are highly automated in Scottish laboratories and can be delivered at a cost of circa 6 pence per test. To monitor diabetic control glycated haemoglobin (Haemoglobin A$_{1c}$) is measured, usually on standalone chromatographic systems that are comparatively much more labour intensive at a cost ranging from £1.20 to £1.50 per test. These costs relates to reagents and costs of instrumentation only.

World Health Organisation (WHO) identified the approach that underpins current practice employing glucose measurements. However in 2011 WHO concluded that HbA$_{1c}$ could be used diagnostically as a diagnostic test which has subsequently led to the publication of an expert position paper (consensus statement) from the Department of Health Advisory Committee on Diabetes Mellitus on the use of HbA$_{1c}$ diagnostically within the UK. In the summary of that paper the following is stated: -

“This new method of diagnosing diabetes will identify a different cohort as having diabetes than is currently being diagnosed; but the process of investigation that does not require a fasting sample makes investigation easier, allowing more people to be investigated”.

This statement clearly identifies that an increasing workload might result from adoption of the new diagnostic approach and it is also clear that there are degrees of complexity in its application as a consequence of the number of situations in which HbA$_{1c}$ cannot be applied (see appendix). The situations in which it is suggested that HbA$_{1c}$ should be used to effectively screen for diabetes is also potentially very large. Primary care physicians are keen on the approach to diagnosis, since it removes the requirement for fasting patients, and reduces the need for oral glucose tolerance testing. However it is clear that they will require significant preparative education requiring not only wide dissemination of the flow diagrams contained within the consensus statement, but also appropriate narrative, if the test is to be used appropriately.

SCBMDN anticipates that adoption of the consensus statement recommendations will lead to a significant increase in laboratory workload for HbA$_{1c}$. A conservative estimate is that this will exceed 100% (according to anecdotal evidence from other European labs and early adopters in the UK). This will have a significant impact on analytical capacity and cost. In 2011, 434,000 HbA$_{1c}$ tests were performed by Scottish biochemistry laboratories (data from Keele National Pathology Benchmarking Service and data collected by SCBMDN). At a cost of £1.20-£1.50 a test, the cost of the anticipated workload increase to Scottish laboratories could be in excess of £600,000.
**Assessment**

This approach to diagnosis of diabetes represents a significant change to current practice and needs to be managed accordingly. There is recognition that a different population of diabetics will be identified, and that there will consequently still be a need for the conventional approach to diagnosis in a range of patients. It is also recognised that ease of testing a large target population will all lead to increased workloads for laboratories both in terms of initial diagnosis and follow up of patients. There will be a need for education of users requiring close co-operation of the various stakeholders. This might be better achieved by a nationally co-ordinated approach that is linked to delivery of capacity in terms of diagnostics and in managing the impacts at the point of care around.

There will be significant cost pressures on laboratory budgets when this diagnostic approach is adopted. It is recognised that across the whole Healthcare economy that this development will potentially be accompanied by reductions in the costs of administering oral glucose tolerance tests (OGTT) and of repeated patient appointments (to ensure provision of a fasting sample), which in turn leads to a better experience for patients. Savings accrued however will be primarily outside of the laboratory and not accrue in laboratory budgets given that the relative costs of HbA1c testing is so much more than that for glucose (£1.20 versus £0.06 per reportable test). The impacts on laboratories serving the biggest populations will be considerable financially and will prove particularly challenging in terms of delivery of the analytical capacity given current technologies used. This may require laboratories to reconfigure their service provision to enable delivery of the increased volume of testing. There are likely to be impacts on reagent costs, equipment requirements and staffing.

There will be a requirement for active management of demand for HbA1c, to ensure that the consensus algorithms are followed appropriately. There is not only potential here for significant volume growth, but also for significant rise in inappropriate use in contexts where the testing is unreliable and therefore unsafe. The impacts on diabetes clinics and other diabetes related resources needs to be identified and scoped.

To ensure successful adoption and benefits realisation of a safe transition to HbA1c measurement for diagnosis of diabetes mellitus, the SCBMDN believes that there is a need for provision of appropriate guidance on interpretation for users, education relating specifically to clinical conditions which preclude the use of HbA1c as a diagnostic test, development of demand management strategies, and delivery of appropriate resources to laboratories to enable the service delivery. The laboratory services will need to give some consideration as to methodological requirements and address any differences in approach across Scottish Health Boards that might complicate the move.

There is a danger that this diagnostic approach to diabetes might be introduced by stealth as GPs and patients become increasingly aware of it following the publication of the consensus statement. It is therefore a matter of some urgency that health boards develop a position on its introduction to enable a controlled, safe and appropriately funded deployment.

**Recommendations**

1. SCBMDN laboratories familiarise themselves with the consensus statement and attempt to assess the likely impact on their service provision in terms of cost and other resources.
2. SCBMDN collates the information gathered and raises the issue through the Diagnostic Steering Group as a pressure on systems nationally.
3. SCBMDN laboratories advise their Medical Directors of the difficulties that may ensue from a piecemeal and ad hoc adoption of the use of HbA1c as a diagnostic test for diabetes. This should be highlighted as a clinical governance issue.
4. SCBMDN laboratories highlight to local management the pressures on resources that are likely to arise from the introduction of HbA1c as a diagnostic test and advise against progression without appropriate resource allocation.
5. SCBMDN develops a co-ordinated approach to the adoption of HbA1c as a diagnostic test, engaging with relevant stakeholders (e.g. GP groups, Local Diabetes Networks, local diabetes specialists) to ensure appropriate preparation for, identification of potential for virement of funds, and resourcing of the move.

6. SCBMDN works with stakeholders to develop and agree appropriate demand strategies to enable delivery of maximum benefit from the move while minimising waste and harm.

7. SCBMDN advocates and facilitates formation of a short life working group consisting of members of the network and relevant stakeholders to address this issue.

8. SCBMDN recommends maintenance of the status quo, and continues to provide glucose measurements as a front line diagnostic test for diabetes until such time as the scope of the resource implications of using HbA1c have been identified and provided for.

References


2. Hitman GA. Finally, a UK consensus on the use of HbA1c. Diabetic medicine 2012;29(11):1349. Full text available free:  

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Appendix

The World Health Organisation has recently recommended that: “HbA1c can be used as a diagnostic test for diabetes providing that stringent quality assurance tests are in place and assays are standardized to criteria aligned to the international reference values, and there are no conditions present that preclude its accurate measurement.”

An HbA1c of 48 mmol/mol is recommended as the cut-off point for diagnosing diabetes. A value of less than 48 mmol/mol does not exclude diabetes diagnosed using glucose tests.

In symptomatic patients (in whom conditions precluding accurate measurement of HbA1c have been excluded) a single HbA1c result of ≥48 mmol/mol would be sufficient to diagnose diabetes. In asymptomatic patients a second sample (taken within 2 weeks) is recommended and diabetes only diagnosed if both results are ≥48 mmol/mol.

Advantages of HbA1c

There is no need for patients to fast prior to sampling.
The inconvenience for patients of oral glucose tolerance tests is avoided.
HbA1c is stable and is not affected if analysis is delayed, reducing the pre-analytical variation compared to plasma glucose.

Disadvantages of HbA1c

It currently has greater analytical variation than glucose.
It cannot be used for certain groups of patients (see below).
It is affected by age and ethnicity and other factors.
It may identify a different group of patients to those identified with plasma glucose.

HbA1c cannot be used for diagnosis…

- For children and young people
- During pregnancy
- For suspected Type I diabetes
- If diabetes symptoms are of short duration
- If patients are acutely unwell
- For patients taking medication that may cause rapid glucose rise (e.g. corticosteroids, antipsychotic drugs)
- If patients have acute pancreatic damage
- In renal failure
- In HIV infection

Other Factors

Variant haemoglobins – Measurement of HbA1c is affected by the presence of haemoglobin variants. The ability of analytical methods to identify and account for abnormal haemoglobins varies.

Anaemia – Haemolytic anaemia reduces HbA1c values due to decreased red cell survival. Iron deficiency anaemia causes an inappropriate rise in HbA1c.

Altered red cell lifespan – Decreased red cell lifespan (in some haemoglobinopathies, splenomegaly, rheumatoid arthritis or with drugs such as antiretrovirals, ribavirin and dapsone, recent commencement of erythropoietin) results in a decrease in HbA1c. Increased erythrocyte lifespan (e.g. with splenectomy) results in increased HbA1c.

Ageing – Older people without diabetes have higher HbA1c values than younger individuals resulting in fewer elderly patients with HbA1c ≥48 mmol/mol having glucose-defined diabetes.

Ethnicity – Afro-Caribbeans and Asians have higher HbA1c levels than white Europeans, resulting in a lower proportion of subjects with HbA1c ≥48 mmol/mol having glucose-diagnosed diabetes.