Management of type 1 diabetes

Biological HbA_{1c} variation predicts microvascular risk

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Think back to the last time you looked at a patient's home blood glucose monitoring record and noted that the values seemed to bear little resemblance to their recent HbA_{1c} of 11 %. Usually we assume the 'recorded blood glucose' has been interpreted with a generous rounding down. Less often we see the reverse – where the HbA_{1c} seems remarkably good in comparison to their own blood glucose readings.

The study from McCarter et al suggests that these discrepancies are not all due to measurement 'errors' but may in part be due to biological variation between individuals. This is not the first time this has been suggested – a recent twin study showed that genetics explained 62 % of the population variance in HbA_{1c}. This is important as it means that glycosylation rates vary between individuals, such that a mean 28-day plasma glucose of 10 mmol/l may result in a range of HbA_{1c} values as wide as 6.2–10.8 % in different subjects. Similarly, an HbA_{1c} of 7.0 % corresponds to a range of mean 28-day plasma glucose estimates between 8 mmol/l and 11 mmol/l in different subjects.

This study used the Diabetes Control and Complications Trial (DCCT) database to look at this more closely, to see how it may relate to the development of complications. The mean blood glucose was used to predict HbA_{1c}, and an index derived from the difference between this and the actual HbA_{1c} at each time point. Where this discrepancy was large the risk of developing retinopathy or nephropathy was greater.

What this means in practice is that two individuals with the same mean blood glucose may have a different HbA_{1c}. This difference is genetically determined and the higher is at greater risk of microvascular complications. This has huge implications since, for some, lowering blood glucose may simply not be enough. Interpreting HbA_{1c} for an individual is becoming more complex and this paper is one of a growing number suggesting that we may either need a different marker of glycaemic control or additional data (such as the haemoglobin glycation index) when assessing an individual's risk of developing microvascular complications.

DIABETES CARE

Insulin glargine: SC infusion vs multiple daily injections

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 This study aimed to establish the efficacy of continuous subcutaneous insulin infusion (CSII) and insulin analogues available for multiple daily injection (MDI) in adolescents and children with type 1 diabetes.

2 The 32 participants aged between eight and 21 were given either CSII and insulin aspart or MDI treatment with once-daily glargine and premeal/snack insulin aspart.

3 Those randomised to CSII had a significant drop in HbA_{1c} level from 8.1 % to 7.7 % after 16 weeks, while there was little change in the glargine group (8.2 % to 8.1 %).

4 Total daily insulin dose dropped significantly in the CSII group ($p<0.01$) but was unchanged in the glargine group.

5 While fasting self-monitored blood glucose levels were similar for both groups, in the CSII group lunch, dinner and bedtime readings were significantly lower ($p<0.01$).

6 CSII enabled lower premeal glucose and HbA_{1c} levels to be attained than did glargine-based MDI, suggesting it is an effective treatment for young people with type 1 diabetes.

Doyle EA, Weinzimer SA, Steffen AT, Ahern JAH, Vincent M, Tamborlane WV (2004) A randomized, prospective trial comparing the efficacy of continuous subcutaneous insulin infusion with multiple daily injections using insulin glargine. *Diabetes Care* **27**: 1554–58

DIABETES CARE

Biological variation in HbA_{1c} predicts complication risk

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓ ✓

1 Chronic hyperglycaemia (measured by HbA_{1c} or mean blood glucose [MBG]) has been linked to microvascular complication development and progression in diabetes.

2 The aim of this study was to determine whether biological variation in HbA_{1c} might predict diabetes-related microvascular complications in the DCCT.

3 HbA_{1c} levels and MBG, measured every three months in the 1441 people participating in the DCCT, were used to create a longitudinal multiple regression model.

4 Biological variation was assessed at each visit with a haemoglobin glycation index (HGI), based on directional deviation between actual HbA_{1c} and predicted MBG from the regression model.

5 Patients' mean HGI during the study was used to subdivide them into three groups: high, medium and low HGI.

6 Retinopathy and nephropathy development or progression risk was calculated for each group using Cox proportional hazard analysis.

7 Results showed HbA_{1c} levels were not determined by MBG alone. Compared to the low HGI group, the high HGI group had a six times greater risk of nephropathy and three times greater risk of retinopathy after seven years.

8 In patients with type 1 diabetes, between-individual biological variation of HbA_{1c} (distinct from that attributable to MBG) was a strong predictor of complication risk.

McCarter RJ, Hempe JM, Gomez R, Chalew SA (2004) Biological variation in HbA_{1c} predicts risk of retinopathy and nephropathy in type 1 diabetes. *Diabetes Care* **27**: 1259–64

Type 1 diabetes

DIABETES AND METABOLISM

Pre-pubertal T1D contributes to retinopathy

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 Correlations between retinopathy prevalence and duration of type 1 diabetes in people who developed diabetes before and after puberty were compared.

2 Patients (200 of whom developed diabetes before puberty and 428 after puberty) were screened by ophthalmoscopy and digital photography or 33 mm photography.

3 Those with pre-pubertal diabetes of 10–14 years and 15–19 years duration had a lower retinopathy prevalence than those with post-pubertal diabetes but after 20 years duration rates were similar.

4 Retinopathy is probably mild and infrequent during childhood due to short duration of diabetes and not a pre-pubertal protective effect suggesting pre-pubertal years contribute to retinopathy onset.

Porta M, Dalmasso P, Grassi G, et al (2004) Pre-pubertal onset of type 1 diabetes and appearance of retinopathy. *Diabetes and Metabolism* **30**: 229–33

DIABETOLOGIA

Follow-up of out-patient programme

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 Long-term outcomes of an intensified insulin therapy structured outpatient diabetes teaching and treatment programme (DTTP) in 123 outpatients with type 1 diabetes was analysed. Follow-up was at three, six and 12 years.

2 At three years there was a reduction in mean HbA_{1c} levels from 7.9 % to 7.1 % ($p<0.01$), but after six and 12 years the difference was not significant (7.8 %).

3 Episodes of hypoglycaemia per patient per year were reduced from 0.49 to 0.14 at three, 0.19 at six and 0.16 at 12 years.

4 HbA_{1c} could be lowered without severe episodes of hypoglycaemia in 41 % of patients over the 12 years.

5 Over a 12-year period after participation in a DTTP, patients had a sustained reduction in severe hypoglycaemia incidence.

Plank J, Köhler G, Rakovac I, et al (2004) Long-term evaluation of a structured outpatient education programme for intensified insulin therapy in patients with type 1 diabetes: a 12-year follow-up. *Diabetologia* **47**: 1370–75

DIABETES AND METABOLISM

Smoking: increased microalbuminuria and HbA_{1c}

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓

1 In the Swedish National Diabetes Register in 1996–2000, 12–15% of patients with type 1 and 10–12 % of patients with type 2 diabetes smoked. These patients had higher mean HbA_{1c}, lower mean body mass index (BMI) and higher frequencies of microalbuminuria than non-smokers with diabetes.

2 In patients with both type 1 and type 2 diabetes, smoking was independently associated with microalbuminuria ($p<0.001$), and elevated HbA_{1c} levels ($p<0.001$), and negatively associated with BMI.

3 Smoking was particularly prevalent in young women with type 1, and middle aged people with type 1 and 2 diabetes. Cessation campaigns should target these groups.

4 Smoking was widespread and associated with microalbuminuria and poor glycaemic control.

Nilsson PM, Gudbjörnsdottir, Eliasson B, Cederholm J, et al (2004) Smoking is associated with increased HbA_{1c} values and microalbuminuria from the National Diabetes Register in Sweden. *Diabetes and Metabolism* **30**: 261–68