Paediatrics

Prolonging the honeymoon from hypoglycaemia

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Hypoglycaemia has long been considered a significant limitation to the intensification of diabetes treatment especially in young children. The DCCT (Diabetes Control and Complications Trial; 1995) showed that as HbA_{1c} went down, the risk of severe hypoglycaemia (SH) increased especially in the adolescent cohort, yet the DCCT was published 20 years ago, before analogue insulin, increased use of insulin pump therapy, improvements in glucose monitoring technology and the professionalisation of diabetes healthcare teams. So how much of a problem is hypoglycaemia for children and young people with modern diabetes care?

Two studies have recently examined SH in childhood. One study from Australia has examined clinic visit data from 1770 patients under the age of 16 years from 2000 to 2011 (Cooper et al, 2013; summarised on the next page). This study suggested that rates of SH have decreased over the last 12 years, with a peak incidence of 21.8 episodes per 100 patient-years in 2002 to a stable level of 5.5 episodes per 100 patient-years from 2006 to 2011. There were no associations between the risk of SH and glycaemic control during the 12-year period of observation. Children less than 6 years of age did not have a significantly increased risk compared to other age groups. Links between the risk of SH and the mode of insulin delivery were only seen in adolescents where insulin pump therapy was related to a lower risk of SH, and multiple injection therapy to a higher risk. Interestingly in older children (>6 years of age) and adolescents, there was a significant increase in SH risk after the first year of diagnosis. This was most pronounced in adolescents where the risk of an episode of SH increased four-fold between 1 and 3 years post-diagnosis, seven-fold between 3 and 6 years after diagnosis and 10-fold for those with a disease duration greater than 6 years. The authors postulated that this may be due to the development of hypoglycaemia-related autonomic failure, well described in adolescents, or due to decreased patient vigilance.

Another study suggests that residual beta-cell function (RBF) may provide a supportive role both in terms of facilitating good glycaemic control, as well as in avoiding SH (Sorensen et al, 2013; summarised alongside). This study from Denmark assessed meal-stimulated C-peptide levels in 342 children aged 4.8–18.9 years of age. Patients with RBF of <0.04 nmol/L were found to be significantly more likely to have SH than patients with RBF of >0.04 nmol/L with an odds ratio of 2.5 (95% CI, 1.10–7.08; $P<0.03$) despite having a lower HbA_{1c} (69.3 ± 0.9 mmol/mol [8.5 ± 0.1%] versus 63.1 ± 1.4 mmol/mol [7.9 ± 0.1%]; $P<0.01$). This could explain why rates of SH start to climb as the honeymoon period starts to wane.

These data are encouraging as they suggest that glycaemic control can be intensified even in young children without an increased risk of SH with modern approaches to diabetes management. Further study is necessary to examine the optimum combination of care processes to achieve this outcome, and this may include methods to prolong the honeymoon period for as long as possible.

Diabetes Control and Complications Trial (DCCT) Research Group (1995) Adverse events and their association with treatment regimens in the Diabetes Control and Complications Trial. *Diabetes Care* **18**: 1415–27

Krystyna Matyka

Dr Krystyna Matyka has been Section Editor for the Paediatrics section in *Diabetes Digest* since 2005. Dr David Kerr and the Publisher would like to thank Krystyna for her valuable contribution to the journal and her thoughts on the literature; we wish her all the very best. In the new year, we welcome Dr Chizo Agwu (Sandwell and West Birmingham Hospital Trust) as the Editor for this section.

DIABETES CARE

Residual beta-cell function is beneficial for severe hypoglycaemia

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

1 Data examining the level of residual beta-cell function (RBF) in children who have had diabetes for multiple years are scarce. There is also little evidence quantifying the effect of RBF on metabolic control and the development of later complications.

2 The authors assessed RBF (meal-stimulated C-peptide concentration), HbA_{1c}, severe hypoglycaemia incidence and insulin requirements in 342 children and young people diagnosed with T1D for 3 to 6 years. Participants were aged between 4.8 and 18.9 years.

3 RBF was greater than 0.04 nmol/L in 27% of children. Those with RBF<0.04 nmol/L had an increased likelihood of experiencing severe hypoglycaemia (odds ratio [OR] 2.59; 95%CI, 1.10–7.08; $P<0.03$) compared to those with RBF >0.04 nmol/L.

4 Participants with RBF <0.04 nmol/L had a significantly higher HbA_{1c} compared with those with RBF >0.04 nmol/L ($P< 0.01$). Individuals with RBF >0.2 nmol/L, however, had significantly lower insulin requirements (U/kg/day ± standard error [SE]; 1.07 ±0.02 versus 0.93 ± 0.07; $P<0.04$).

5 The authors concluded that RBF was considerably varied amongst children with T1D lasting 3 to 6 years. A threshold RBF value of ~0.04 nmol/L was found to be associated with a lower risk of severe hypoglycaemia and improved metabolic control.

Sorensen JS, Johannesen J, Pociot F et al (2013) Residual beta-cell function 3 to 6 years after onset of type 1 diabetes reduces risk of severe hypoglycemia in children and adolescents. *Diabetes Care* 29 Aug [Epub ahead of print]

DIABETOLOGIA

Do changes in diabetes therapy affect severe hypoglycaemia incidence?

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

1 The risk of severe hypoglycaemia is an important factor to consider when optimising glycaemic control. Recent studies suggest that the epidemiology of severe hypoglycaemia may have been altered due to changes in diabetes therapy.

2 The authors sought to determine the incidence of severe hypoglycaemia and its associated factors in a population of young people under 16 years of age with T1D (n=1770).

3 Clinical data were prospectively collected from participants at clinic visits every 3 months. In total, 8214 patient-years of data were analysed.

4 Throughout the study follow-up, 841 episodes of severe hypoglycaemia were reported. The risk of severe hypoglycaemia did not differ between age groups.

5 The average HbA_{1c} within the cohort was 64–75 mmol/mol (8–9%). Good glycaemic control (HbA_{1c}<53 mmol/mol [7%]) did not convey an increased risk of hypoglycaemia.

6 In participants aged 12–18 years, insulin pump therapy was associated with a lower rate of severe hypoglycaemia, when compared with injection regimens (incidence risk ratio 0.6; 95%CI, 0.4 ± 0.9).

7 The authors concluded that modern diabetes therapy was associated with a change in the incidence of severe hypoglycaemia in this cohort of young people with T1D.

Cooper MN, O'Connell SM, Davis EA et al (2013) A population-based study of risk factors for severe hypoglycaemia in a contemporary cohort of childhood-onset type 1 diabetes. *Diabetologia* **56**: 2164–70

DIABETES

Plasma 25(OH)D and glucose tolerance

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

1 The authors aimed to investigate whether concentrations of plasma 25-hydroxyvitamin D (25[OH]D) differ between obese youth with normal glucose tolerance (NGT), prediabetes and T2D. The secondary aim of the study was to determine if 25(OH)D was associated with *in vivo* insulin sensitivity and beta-cell function.

2 Concentrations of plasma 25(OH)D were determined in blood samples from 175 obese youth with a mean age of 14.3 ± 2.1 years and a mean BMI of 35.7 ± 5.6 kg/m^2.

3 No difference in plasma 25(OH)D was detected between glucose tolerance groups. There was no significant relationship between 25(OH)D and *in vivo* insulin sensitivity or beta-cell function.

4 The authors concluded that concentrations of plasma 25(OH)D were not correlated with different subsets of glucose tolerance in obese youth.

de las Heras J, Rajakumar K, Lee S et al (2013) 25-hydroxyvitamin D in obese youth across the spectrum of glucose tolerance from normal to prediabetes to type 2 diabetes. *Diabetes* **36**: 2048–53

DIABETES CARE

Increased energy intake causes increased insulin resistance

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

1 The aim of this study was to evaluate the relationship between total energy intake, energy density, dietary nutrient intake and risk markers for T2D in a multi-ethnic cohort of 2017 children aged 9–10 years.

2 A positive association was identified between energy intake, insulin resistance, blood glucose and fat mass index, even after adjustment for age and sex.

3 There was no significant association between individual nutrient intake and markers of T2D risk.

4 The authors concluded that elevated total energy intake was strongly correlated with increased levels of insulin resistance, which may explain the mechanisms behind childhood T2D risk.

Donin AS, Nightingale CM, Owen CG et al (2013) Dietary energy intake is associated with type 2 diabetes risk markers in children. *Diabetes Care* 12 Aug [Epub ahead of print].

DIABETES CARE

Effects of personality on HbA_{1c} and glucose monitoring behaviour

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

1 The authors performed a 3-year longitudinal study to determine the effects of personality traits such as conscientiousness, agreeableness and emotional regulation on glycaemic control and blood glucose monitoring in 142 young people aged 8–19 years with T1D.

2 Personality was characterised using the Five Factor Personality Inventory for Children. Regression models and mixed-design ANOVA were applied to investigate the association between personality, HbA_{1c} and glucose monitoring.

3 Conscientiousness was significantly associated with blood glucose monitoring behaviours. Those with high or low emotional regulation had poorer glycaemic control over the 3-year period.

4 The authors concluded that personality was associated with diabetes management in youth with T1D.

Waller D, Johnston C, Molyneaux L et al (2013) Glycemic control and blood glucose monitoring over time in a sample of young Australians with type 1 diabetes. *Diabetes Care* 8 Jul [Epub ahead of print]

> *"The authors concluded that personality was associated with diabetes management in youth with T1D."*