Study highlights possible role for insulin lispro in preventing nocturnal hypoglycaemia in children

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Research involving children is fraught with ethical challenges: consequently many drugs are not licensed for use in this group.

With this in mind, I was impressed by the paper from Ford-Adams and colleagues, who tried to investigate the value of using insulin lispro instead of soluble insulin in a group of children receiving three-times daily insulin. Splitting the evening injection so that the fast-acting insulin is given with the meal and the isophane at bedtime is used to reduce the frequency of night-time hypoglycaemia.

Studies in adults have shown that the use of analogues such as lispro and aspart instead of soluble insulin reduces this risk further. This was a demanding study for children and researchers as both study periods ended with admission for an overnight metabolic study.

Small differences between the regimens were observed with fewer low blood sugars (< 3.5 mmol/l) between 2200 and 0400. Interestingly, on either insulin 25% of children were hypoglycaemic between 0400 and 0700.

The disappointing aspects of the study were that there was no mention of carbohydrate counting, and no indication of the dose distribution of isophane – both important aspects of ensuring that any basal bolus regimen is safe and effective. The number of self-recorded symptomatic hypoglycaemic episodes were no different between the two regimens but most occurred late afternoon – as with the overnight data, this might suggest that doses of isophane were excessive.

DIABETIC MEDICINE

Preventing nocturnal hypoglycaemia in children with diabetes

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

1 Prevalence rates of nocturnal hypoglycaemia as high as 30–50% have been reported in children with type 1 diabetes. The long duration of action of soluble insulin given in the evening could contribute to this high prevalence.

2 This study examined whether replacement of soluble insulin with insulin lispro could reduce the risk of nocturnal hypoglycaemia in children on a three times daily insulin regimen.

3 In this randomised open crossover trial, 23 children received insulin lispro and soluble insulin. At the end of each 4 month treatment arm, an overnight 15-minute venous sampled blood glucose profile was done

4 Blood glucose levels on insulin lispro were lower despite similar levels pre-evening meal and post-meal.

5 Blood glucose levels in the early night were lower on lispro than on soluble insulin. However, in the early morning there was no difference between the treatments in terms of blood glucose levels.

6 Insulin lispro led to a decrease in the prevalence of early nocturnal low blood glucose without worsening HbA_{1c} levels.

7 Insulin lispro, or other rapid-acting insulin analogues, could be recommended as part of a three times daily insulin regimen to reduce the prevalence of early nocturnal hypoglycaemia.

Ford-Adams ME, Murphy NP, Moore EJ et al (2003) Insulin lispro: a potential role in preventing nocturnal hypoglycaemia in young children with diabetes mellitus. *Diabetic Medicine* **20**: 656–60

DIABETES

Duration of diabetes, age at onset and nephropathy

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

1 It is well established that the microvascular complications of diabetes increase with duration of the disease.

2 However, the effect of duration of diabetes on nephropathy and retinopathy may be modified by the age of onset of diabetes.

3 In particular, it is thought that the duration of diabetes after puberty has a greater effect than the same duration before puberty.

4 This article reports on the findings from the International Diabetic Nephropathy Study which looked at the effects of diabetes duration and age at onset on glomerular morphometry obtained from kidney biopsy in 243 patients with type 1 diabetes before the onset of microalbuminuria.

5 There were no significant differences in the effect of duration of diabetes among the three subgroups of patients with different ages of onset.

6 These results suggest that it is total duration of disease rather than duration before or after puberty which affects the rate of progression of the glomerular basement membrane and mesangial lesions characteristic of diabetic nephropathy.

Drummond KN, Kramer MS, Suissa S et al (2003) Effects of duration and age at onset of type 1 diabetes on preclinical manifestations of nephropathy. *Diabetes* **52**: 1818–24

'Abnormal urinary albumin excretion predicts an increase in mortality in people with a long duration of diabetes.'

DIABETES CARE

Who would benefit most from intensive therapy?

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

1 Intensive therapy is known to delay the onset of long-term complications of diabetes, but is costly and more difficult to implement in adolescents.

2 This study compares the prediction of HbA_{1c} in adolescents receiving intensive therapy *vs* usual care.

3 Participants (n=142) received a composite score for self-management competence (SMC) which combined standardised scores on baseline measures of diabetes knowledge, treatment adherence and quality of healthcare interactions.

4 It was hypothesised that patients with moderate SMC would benefit more from intensive therapy than those with high or low SMC.

5 Of those who had intensive therapy, mean HbA_{1c} levels were similar in the low, moderate and high SMC groups.

6 In those who received usual care, however, HbA_{1c} was increased in the low SMC group but not in the moderate and high SMC groups.

7 Patients should not be denied access to intensive therapy because they have a low SMC score.

Wysocki, Sadler M, Harris MA (2003) Self-management competence as a predictor of outcomes of intensive therapy or usual care in youth with type 1 diabetes. *Diabetes Care* **26**: 2043–7

DIABETES CARE

Microalbuminuria and mortality in long duration diabetes

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

1 Microalbuminuria is thought to be a stronger predictor of progression to diabetic nephropathy in patients with a duration of diabetes less than 17 years.

2 This study examined whether microalbuminuria remains a powerful predictor in patients with a longer duration of type 1 diabetes.

3 The 5-year clinical outcome of 190 patients with a disease duration of at least 30 years and variable levels of urinary albumin excretion was determined.

4 After 5 years, 11% of the 66% of participants who had been normoalbuminuric at baseline had died. At baseline, 22% of participants were microalbuminuric, and 26% of these had died by the study end. Of the 8% who had persistent proteinuria at baseline, 44% had died.

5 Abnormal urinary albumin excretion still predicts an increase in mortality in people with a long duration of diabetes.

Allen KV, Walker JD (2003) Microalbuminuria and mortality in long-duration type 1 diabetes. *Diabetes Care* **26**: 2389–91

DIABETIC MEDICINE

Quality of life on insulin aspart *vs* human insulin

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

1 Studies have shown a greater improvement in HbA_{1c} after treatment with insulin aspart compared with human insulin. However, there is a lack of data on quality of life and satisfaction with treatment.

2 This paper describes the psychometric assessment of 424 patients before and after randomisation to insulin aspart or human insulin.

3 Participants were assessed in terms of individual treatment goals, physical complaints, worries about the future, social relations, diet restrictions, fluctuations in blood glucose levels and fear of hypoglycaemia.

4 There were no significant differences between the groups in terms of HbA_{1c} levels or incidence of hypoglycaemia.

5 After 6 months, there was a greater improvement in treatment satisfaction and quality of life with regard to diet restrictions with insulin aspart than there was with human insulin.

Bott U, Ebrahim S, Hirschberger S, Skovlund SE et al (2003) Effect of the rapid-acting insulin analogue insulin aspart on quality of life and treatment satisfaction in patients with type 1 diabetes. *Diabetic Medicine* **20**: 626–34

'The optimal time for administration of insulin aspart is before meals. This is sometimes difficult in children since premeal dosing requires meal size adjustment to dose.'

DIABETES CARE

Postprandial vs preprandial insulin

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

1 The optimal time for administration of insulin aspart is before meals. This is sometimes difficult in children since premeal dosing requires meal size adjustment to dose.

2 The aim of this study was to compare the safety and efficacy of administration of insulin aspart postprandially in children with type 1 diabetes.

3 In this multicentre open-labelled crossover trial, 42 children and 34 adolescents were randomly assigned to preprandial or postprandial insulin aspart.

4 Overall glycaemic control was no worse with postprandial compared with preprandial administration. There was no significant difference in relative risk of hypoglycaemia.

5 Postprandial administration of insulin aspart is a safe and effective alternative.

Danne T, Jacobsen JL, Aman J et al (2002) A comparison of postprandial and preprandial administration of insulin aspart in children and adolescents with type 1 diabetes. *Diabetes Care* **26**: 2359–64