J R Coll Physicians Edinb 2012; 42:228
http://dx.doi.org/10.4997/JRCPE.2012.309

CLINICAL

Treating type 2 diabetes in youth: a depressing picture

ER Pearson
Clinical Reader, Division of Cardiovascular and Diabetes Medicine, Medical Research Institute, University of Dundee, Scotland, UK

TITLE A clinical trial to maintain glycemic control in youth with type 2 diabetes.

AUTHORS Zeitler P, Hirst K, Pyle L et al.

JOURNAL *New Engl J Med* 2012; 366:2247–56. http://dx.doi.org/10.1056/NEJMoa1109333

DECLARATION OF INTERESTS No conflicts of interest declared.

Correspondence to **ER Pearson**
Medical Research Institute,
University of Dundee,
Nethergate, Dundee DD1 4HN
Scotland, UK

tel. **+44 (0)1382 383387**
e-mail **e.z.pearson@dundee.ac.uk**

SUMMARY

There is an increase in type 2 diabetes (T2D) in children, yet little evidence to guide management. The TODAY study aimed to assess the impact of three treatment interventions in this demographic group.[1] In this study 927 children were converted from their current medication to metformin monotherapy. This run-in phase proceeded to randomisation if an HbA1c <8% (64 millimoles per mole [mmol/mol]) was achieved with adherence to medication ≥80% for at least six weeks. The randomisation cohort consisted of 699 children, aged between 10 and 17 years with T2D diagnosed within the past two years and a body mass index (BMI) >85th percentile. The ethnicity split was 41% Hispanic, 31.5% non-Hispanic Black, and 20% non-Hispanic White. The children were randomly assigned to stay on metformin alone, to have rosiglitazone added to their regime, or to continue on metformin and undergo a family based behavioural weight loss programme. This consisted of weekly visits for the first six months, then biweekly for six months, then bimonthly for the remainder of the study. The primary endpoint was either an HbA1c >8% for more than six months, or sustained insulin treatment for more than three months.

Treatment failure was observed in 45.6% of children; 50% by 11.5 months after randomisation. Treatment failure was seen less in those with rosiglitazone added (38.6%) compared to those who stayed on metformin alone (51.7%, p=0.006). Intensive lifestyle intervention had an intermediate result (46.6% failure) but this did not differ significantly from those taking metformin alone. The authors conclude that whatever the intervention, progression of diabetes is rapid in this age group and that multiple oral treatments or insulin will be required within a few years for the majority of this group.

OPINION

With the increase in obesity rates in children, there is increasing prevalence of T2D in young people. While still relatively uncommon in the UK, in some ethnic groups in the US the incidence of T2D in children aged over 10 years old exceeds that of type 1 diabetes.[2] These children present a major challenge to healthcare systems due to the long duration of diabetes and other co-morbidities related to their obesity and insulin resistance. The TODAY study was a valiant attempt to develop an evidence base for management of this problematic group.

This was a challenging study to undertake due to the characteristics of children who develop T2D. This is highlighted by some striking figures – during the study period 19.2% of the children had a serious adverse event, which was mostly due to hospitalisation; 41.5% of the participants had a household income <US$25,000 and 61% did not live with both their parents.[3] The TODAY study group spent considerable effort in engaging with this group, yet adherence to treatment was just 57% by month 60, and only 54% of participants randomised to lifestyle intervention attended for more than 75% of visits.[1]

The results overall present a depressing picture. Roughly half of the children required additional treatment, half of these within one year. Despite what is clearly a disease driven by obesity, intensive lifestyle intervention – much more intensive than can be achieved in clinical practice – did not alter progression rates of diabetes or other parameters such as blood pressure or cholesterol level. The only effective intervention was to add more pharmacological therapy, and even here the progression rates remained high. The solution, of course, is for children to avoid 'diabesity' in the first place – easier said than done.

REFERENCES

1 Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. *New Engl J Med* 2012; 366:2247–56. http://dx.doi.org/10.1056/NEJMoa1109333
2 Centers for Disease Control and Prevention. *Fast facts on diabetes: national estimates and general information on diabetes and prediabetes in the United States*. Atlanta, GA: US Department of Health and Human Services; 2011.
3 Copeland KC, Zeitler P, Geffner M et al. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. *J Clin Endocrinol Metab* 2011; 96:159-67. http://dx.doi.org/10.1210/jc.2010-1642