Glycaemic intervention studies – the case for early and intensive therapy

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Professor Bailey

Introduction

The recommended targets for HbA_{1c} in people with type 2 diabetes are less tight in the UK than the US or Europe. There is evidence that for each additional reduction in HbA_{1c} of 1%, there is a significant reduction in risk of complications of diabetes. In his presentation, Cliff Bailey recommended more intensive therapy for people with type 2 diabetes.

Treat the disease early, treat it intensively and try to reduce the HbA_{1c} by an extra 1% are the three key points to remember when providing good care for people with type 2 diabetes. This is according to Professor Cliff Bailey, the Head of Diabetes Research and Professor of Clinical Science at Aston University, Birmingham.

HbA_{1c} targets

There are different targets for HbA_{1c} all around the world, he said, so which should we choose? In the UK, we probably have more targets than anywhere else. The favourite target in the world, and the one in use in Europe today, seems to be a HbA_{1c} of about 6.5% (Nathan et al, 2006). There is a lot of published information about a target HbA_{1c} of 7.0%, as this is what the US was working to until recently, although they seem to be moving towards a 6.5% target as well. Professor Bailey then suggested that the National Institute for Health and Clinical Excellence (NICE) target of up to 7.5% (NICE, 2002) is too high. Professor Bailey said there were sensible arguments for pursuing a lower HbA_{1c}.

Reduce HbA_{1c} more

Irrespective of how far you drop the HbA_{1c} (i.e., from 9% to 8%, or 8% to 7%, or 7% to 6%), there is always a substantial reduction in deaths from diabetes, risk of heart attack and microvascular complications (Stratton et al, 2000). Professor Bailey suggested that in poorly motivated patients it would be beneficial to help them to understand these data. Over a 10-year period, a 1% reduction in HbA_{1c} reduces risk of retinopathy by a third and peripheral vascular disease by about half (Stratton et al, 2000). 'There is no lower threshold for HbA_{1c} [below which we do not see extra benefit], we should aim for as close to normal as possible,' said Professor Bailey.

Cardiovascular targets

This presentation focused on keeping glucose levels under control as this is the primary driver for microvascular disease, said Professor Bailey. At the

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Speakers (left to right) Cliff Bailey, Steve Cleland and symposium chairman Martin Hadley-Brown

same time, he said, we must bear in mind the components of metabolic syndrome which are cardiovascular risk factors. Generally speaking, we are good at achieving these cardiovascular targets. This is demonstrated by the 8-year STENO 2 trial in which the investigators attempted to deal with as many cardiovascular risk factors as possible. They were able to reduce the relative risk of cardiovascular disease by about 50 %. Large numbers of people in this trial reached targets for cholesterol, blood pressure and triglycerides. However, the big problem was HbA_{1c}. Even with intensive therapy, few patients actually reached their target (Gaede et al, 2003).

Lower life expectancy

Diabetes UK has said that 1.8 million people in the UK have been diagnosed with diabetes and a further 0.8 million are unaware that they have the disease (Diabetes UK, 2004). The prevalence appears to be doubled in areas of the country where there are many people of Asian origin (DoH, 2005). This is very significant, suggested Professor Bailey, because the life expectancy of people with diabetes can be reduced by 10 years. Another indication of the significance of the problem is that 40 % of the people on the dialysis register have diabetes [mainly caused by diabetic nephropathy].

The risk of cardiovascular death increases with rising 2-hour post-glucose tolerance test results. In fact, when the result is within the range representing impaired glucose tolerance, the risk of cardiovascular death is almost as high as that for people with newly diagnosed type 2 diabetes (DECODE study group and the European Diabetes Epidemiology Group, 2003). It is important to recognise the increased risk of macrovascular disease which occurs in people with impaired glucose tolerance, said Professor Bailey. In reality, patients may have been experiencing a raised risk of complications for 10 years when diabetes is diagnosed (Diabetes UK, 2000). There is therefore no room to delay treatment when we spot the disease. The UK Prospective Diabetes Study (UKPDS) showed that over a third of people already have raised blood pressure at diagnosis (Turner et al, 1999).

In the US, one-third of people with diabetes are below the target of HbA_{1c} at 7.0 % (Saydah et al, 2004). Just under one-third of patients in Europe meet the target of 6.5 % (Liebl et al, 2002). Even if we do not always reach the target with all our patients, at least if we are trying to reduce HbA_{1c} further we are moving in the right direction, said Professor Bailey.

Progressive disease

Diabetes is a progressive disease. The UKPDS showed us that, irrespective of the agent used, there is still going to be a gradual increase in hyperglycaemia over time. The percentage of patients on monotherapy that achieve and maintain a target HbA_{1c} of 7.0 % 3 years after diagnosis is less than half, at 6 years it is only a third and by 9 years only about a quarter. Therefore, 75 % of these patients should be on more than one therapy after 9 years (Turner at al, 1999). In other medical conditions, we routinely give more than one treatment to maintain people within target, but this is the evidence that in diabetes extra treatment should be given, said Professor Bailey.

More intensive treatment

Professor Bailey explained that current treatment practice often involves waiting until the HbA_{1c} has risen above the target before more therapies are added. He suggested a more intensive approach to treatment whereby additional therapy should be started before the HbA_{1c} rises to the target level, so that the person is always able to stay within range. Referring to his earlier comments, he reminded participants that reducing average HbA_{1c} by just 1 % can be of significant benefit over time to people with diabetes. ■

'A more intensive approach to treatment [is recommended] whereby additional therapy should be started before the HbA_{1c} rises to the target level.'
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