Real-time continuous glucose monitoring in people with type 2 diabetes

In this section, a panel of multidisciplinary team members give their opinions on a recently published paper. In this issue, we focus on the issue of using real-time continuous glucose monitoring versus self-monitoring of blood glucose in people with type 2 diabetes not on prandial insulin therapy.

GP and Associate Clinical Professor, Warwick Medical School, University of Warwick; Visiting Professor at the Institute of Diabetes in Older People (IDOP), University of Bedfordshire

This is an interesting article comparing the effect of short-term, real-time continuous glucose monitoring (RT-CGM) with self-monitoring of blood glucose (SMBG) in 100 adults with type 2 diabetes not on prandial insulin.

Those randomised to RT-CGM used a DexCom® SEVEN device for four cycles of 2 weeks on, 1 week off, for 12 weeks, and also performed SMBG before meals, at bedtime and at the time of symptoms of hypo- or hyperglycaemia. After 12 weeks, participants continued with SMBG until 52 weeks, as recommended by their usual provider. The SMBG group were asked to perform SMBG before meals, at bedtime and at times of symptoms of hypo- or hyperglycaemia for the first 12 weeks and then to 52 weeks as recommended by their usual provider. Participants in both groups continued usual care for their diabetes and were instructed to contact their primary care provider for all treatment decisions.

The results showed a significantly greater decline in HbA_{1c} level over the course of the study for the RT-CGM group than for the SMBG group. Those who used the RT-COM per protocol improved the most. The magnitude of the improvement in HbA_{1c} level was comparable to that reported for adding on a further blood glucose-lowering agent, but it occurred without any greater intensification of pharmacotherapy compared with the SMBG group.

So do these results suggest that this technique of RT-CGM be adopted widely in the UK? I have a number of concerns about the data and its applicability to the UK and so I would say NO!

The authors state that this is the first study to use RT-CGM technology in a population reflective of the majority of people with type 2 diabetes. They reference this to USA diabetes statistics. It is not a population that is reflective of the majority of people with type 2 diabetes in the UK.

Participants were military healthcare beneficiaries of whom 38–46% were on glucagon-like peptide-1 (GLP-1) or insulin therapy. The intervention of intensive RT-CGM was against a background of intensive SMBG. The majority of people with type 2 diabetes in the UK are not on GLP-1 or insulin therapy to this extent and they do not use SMBG to this extent (NHS Information Centre, 2011).

Guidelines in the UK suggest a very limited place for SMBG in people with type 2 diabetes on lifestyle and oral antidiabetes agents (excluding sulphonylurea therapy) and/or GLP-1 receptor agonists, where the risks of hypoglycaemia are very low (NHS Diabetes, 2009).

The present article, however, does not give any costs for RT-CGM. It is likely that the intervention of RT-CGM on a background of intensive SMBG would be very expensive. The intervention is reported to produce HbA_{1c}-lowering equivalent to adding a further blood glucose-lowering agent. If this could be done by adding an agent at generic prices (£1–3/month) or even at new blood glucose-lowering agent prices (£30–35/month) it is likely that such an intervention would be much more cost-effective than reducing HbA_{1c} by the same amount using RT-CGM, at present-day prices in the UK.

NHS Diabetes (2009) *Self Monitoring of Blood Glucose in Non-Insulin-Treated Type 2 Diabetes: A Report Prepared by an NHS Diabetes Working Group*. NHS Diabetes, Newcastle Upon Tyne. Available at: http://bit.ly/zkFmO3 (accessed 30.01.12)

NHS Information Centre (2011) *Prescribing for Diabetes in England: 2005/6 to 2010/11*. NHS Information Centre, London. Available at: http://bit.ly/zf1IZe (accessed 30.01.12)

Short- and long-term effects of real-time continuous glucose monitoring in patients with type 2 diabetes

Vigersky RA, Fonda SJ, Chellappa M et al (2011) *Diabetes Care* **35**: 32–8

DIABETES CARE

Real-time CGM improves glycaemic control in people with T2D not on prandial insulin

1 Real-time continuous glucose monitoring (RT-CGM) has been shown to improve glycemic control and/or reduce the frequency of hypoglycemic events in children and adults with type 1 diabetes (T1D), and in adults with type 2 diabetes (T2D) on a prandial insulin regimen. However, RT-CGM has not been used for people with T2D who are not taking prandial insulin, who rely on self-monitoring of blood glucose (SMBG) to inform on their glycaemic control.

2 This USA-based randomised controlled trial aimed to determine whether short-time RT-CGM has long-term beneficial effects on glycemic control in people with T2D who are not on prandial insulin.

3 One hundred adults with T2D who were not on prandial insulin were recruited to the study. Inclusion criteria comprised: age ≥18 years, diagnosis of

T2D of at least 3 months, initial HbA_{1c} level of ≥53 mmol/mol (≥7%) but ≤108 mmol/mol (≤12%), treated with diet and exercise alone or other blood glucose-lowering therapies except prandial insulin, able to independently measure and read fingerstick blood glucose levels, and willing to perform SMBG four times daily.

4 The study compared the effects of 12 weeks of intermittent RT-CGM with SMBG on glycemic control over a 40-week follow-up period.

5 By week 12, a significant difference in HbA_{1c} level was observed in the intervention group, which was sustained during follow-up. At weeks 12, 24, 38 and 52, the mean HbA_{1c} level in the RT-CGM group had decreased by 10.9 (1.0), 13.1 (1.2), 8.7 (0.8), and 8.7 mmol/mol (0.8%), respectively, compared with 5.5 (0.5), 5.5 (0.5), 5.5 (0.5), and 2.2 mmol/mol (0.2%), respectively, in the SMBG group (P=0.04).

6 The decline in HbA_{1c} level over the course of the study was significantly greater in the RT-CGM group versus the SMBG group, after adjusting for covariates (P<0.0001).

7 Improvement was greatest in participants who used RT-CGM per protocol (≥48 days; P<0.0001). Moreover, improvement in the RT-CGM group occurred without a greater intensification of medication compared with the SMBG group.

8 It was concluded glycaemic control was significantly improved at 12 weeks in participants with T2D not on prandial insulin who used RT-CGM intermittently for 12 weeks, and that this improvement was sustained without RT-CGM during the 40-week follow-up period, compared with those who used only SMBG.

Peter Hammond, Consultant in General Medicine, Harrogate

Continuous glucose monitoring (CGM) has been largely perceived as an adjunct to optimise intensive insulin therapy in people with type 1 diabetes. However, there are now reports of its value in those with type 2 diabetes (T2D), and the article from Vigersky et al (2011; summarised alongside) suggests that 12 weeks of CGM in those with T2D and not using intensified insulin has a continuing positive benefit in terms of HbA_{1c} reduction for 12 weeks after use, and with lasting improvement at 1 year compared with a group using self-monitoring of blood glucose (SMBG) alone.

What lessons can we take from this study? CGM is expensive, at upwards of £500 for 12 weeks of continuous sensing, and this is certainly the case when compared with SMBG in a population where the latter intervention is likely to be recommended for relatively infrequent use, if at all. However, this study hints at two important aspects of using CGM:

1. First, that short-term usage, in this case at least 48 days in 12 weeks, can result in sustained improvement in glycaemic control. Furthermore, no advice was given to the user as to how to interpret CGM outputs, so it was presumably self-learning that translated into improved control.
2. Second, that it is not necessarily intensification of therapy that is responsible for the HbA_{1c} reduction, so it is likely that lifestyle adjustments prompted by CGM make a significant contribution. This is further supported by the fact that, since there was no difference in pre-prandial SMBG in the two groups, the authors concluded that lower post-prandial glucose levels in the CGM group must explain the improved HbA_{1c}. This observation is considered in more detail in the group's original report of the study (Ehrhardt et al, 2011).

I would therefore conclude that this study supports short-term use of CGM as an effective intervention for improving glycaemic control; and that its use should be targeted, in those with T2D, at people who are likely to benefit from greater insight into how lifestyle change could lower post-prandial blood glucose levels.

Ehrhardt N-M, Chellappa M, Walker MS et al (2011) The effect of real-time continuous glucose monitoring on glycemic control in patients with type 2 diabetes mellitus. *J Diabetes Sci Technol* **5**: 668–75

Pratik Choudhary, Senior Lecturer and Consultant in Diabetes, King's College London

This study of 100 adults with type 2 diabetes (T2D) on oral medications with or without basal insulin evaluated the effect of 3 months' intermittent continuous glucose monitoring (CGM) against SMBG (Vigersky et al; summarised alongside). At 12 months, those randomised to CGM showed benefits in terms of a greater drop in HbA_{1c} level compared with the control group (0.7% vs 0.3%; P=0.04) and a greater proportion with some weight loss, but there was no difference in time spent in hypoglycaemia, Problem Areas in Diabetes scores or changes to medication.

From the article, it is not clear if the frequency of blood glucose tests was different between groups, and it is not clear how much extra contact those with CGM received. However, the differences between the groups were apparent from the outset, and were maintained. Those in the CGM arm achieved a 0.5% lower HbA_{1c} despite no increase in weight and no change in therapy, suggesting that this benefit came from lifestyle changes, which is a novel finding.

This article also showed some trends seen in almost all studies with CGM. First, there is a clear dose–response relationship with CGM, with a threshold of about 60% time below which intermittent CGM does not seem to hold any benefit. Also, this study conforms with other data suggesting that a significant proportion of people are unable to tolerate CGM for one reason or another, reminding us to choose our patients carefully and to check that they are indeed using the equipment.

The use of CGM in T2D needs to be understood in the context of the ongoing debate around the value of SMBG in those on oral medications. Any potential benefit in HbA_{1c} has to be considered in terms of both clinical as well as cost-effectiveness. It will be important to perform qualitative investigation into changes generated by CGM in these people with T2D. The educational and behavioural impact of CGM is a largely overlooked area that deserves more investigation.