Long-term effects of continuous glucose monitoring on HbA$_{1c}$ levels: An audit

Julie Brake

Continuous glucose monitoring (CGM) has become a common and useful tool in diabetes care. To understand whether a 72-hour glucose profile can provide information to improve glycaemic control and to assess the long-term effects on HbA$_{1c}$ levels, an audit was undertaken in Liverpool in a small cohort of people with type 1 diabetes. The results were used to make recommendations about lifestyle, diet or regimen changes. Participants’ HbA$_{1c}$ levels were subsequently monitored over 36 months, and by study end the mean HbA$_{1c}$ level of the group had decreased significantly from 8.8% (73 mmol/mol) to 7.5% (58 mmol/mol). This article describes the audit, its findings and the recommendations made as a result.

The most common way for people with diabetes and their healthcare team to assess glycaemic control is through keeping HbA$_{1c}$ and fingerprick test diaries. However, this information alone is sometimes not enough to adjust treatment effectively.

Situations requiring detailed information about blood glucose fluctuations that only continuous glucose monitoring (CGM) can provide include: when adjusting therapy; quantifying the response in a trial of a diabetes therapy; assessing the impact of lifestyle modifications on glycaemic control; monitoring conditions where tighter control without hypoglycaemia is sought (for example, gestational diabetes); diagnosing and then preventing hypoglycaemia (for example, during sleep); and diagnosing and preventing postprandial hypoglycaemia.

The most important use of CGM is to facilitate adjustments in therapy to improve glycaemic control and/or quality of life (Sabbah et al, 2000; Kaufman et al, 2001). When deeper insight into glycaemic patterns is needed, CGM can help supplement HbA$_{1c}$ and fingerprick values, thus providing a complete picture of a person’s metabolic state. CGM is also a powerful tool for education and motivation.

Using continuous glucose monitoring

CGM devices work by measuring the glucose in the interstitial fluid rather than in capillary blood. Interstitial fluid is the main component of the extracellular fluid, and is found in the interstitial spaces. On average, a person has about 11 litres of interstitial fluid, which provide the cells of the body with nutrients and a means of waste removal.

When using CGM, a sensor is inserted into subcutaneous tissue, usually on the abdomen or upper arm, which feeds the information to

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Article points

1. There are certain situations, such as gestational diabetes, where detailed information about a person’s blood glucose fluctuations is needed.

2. Continuous glucose monitoring can provide up to 288 readings per day, providing a level of detail about a person’s glycaemic pattern that would otherwise be unattainable.

3. Better long-term management of diabetes can be achieved by adjusting lifestyle and diet to fluctuations in blood glucose levels.

4. Continuous glucose monitoring can help achieve low long-term HbA$_{1c}$ levels.

Key words

- Audit
- Continuous glucose monitoring
- Glycaemic control
- HbA$_{1c}$ level

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Page points

1. Most continuous glucose monitoring (CGM) systems provide up to 288 glucose readings per day (average of one test every 5 minutes), providing a level of detail about a person's glycaemic pattern that would otherwise be unattainable.

2. CGM allows early detection of glucose trends and identification of previously undetected glucose patterns. For example, CGM would allow detection of unrecognised nocturnal hypoglycaemia.

3. Glucose levels in interstitial fluid lag behind blood glucose values by about 5 minutes, therefore people are required to undertake fingerprick measurements for CGM system calibration and are often advised to use fingerprick measurements to confirm hypo- or hyperglycaemic status before taking corrective action.

4. CGM systems require up to four fingerprick blood glucose measurements per day for calibration. The ideal time to calibrate is either after fasting or at least 3 hours postprandially, but not immediately after exercise or when the blood glucose level is likely to be rising or falling due to the lag-time with interstitial fluid.

Advantages and disadvantages of CGM

Advantages

Most CGM systems provide up to 288 glucose readings per day (average of one test every 5 minutes), providing a level of detail about a person's glycaemic pattern that would otherwise be unattainable. CGM allows early detection of glucose trends and identification of previously undetected glucose patterns. For example, CGM would allow detection of unrecognised nocturnal hypoglycaemia. In this case, therapy or lifestyle can then be adjusted for improved glycaemic control (Kaufman et al, 2001; Pirzer et al, 2001).

CGM allows examination of how blood glucose levels react to insulin, exercise, food, and other factors. These data can be useful for setting correct insulin dosage for food intake and correction of hyperglycaemia (Sabbah et al, 2000). Monitors may also be equipped with alarms to alert people of hyper- or hypoglycaemia so that they can take corrective action even in cases where they do not yet feel any symptoms.

CGM detects four times more high and low blood glucose levels than fingerprick tests alone, and studies have demonstrated that people with continuous sensors experience less hyperglycaemia (Schiaffini et al, 2002; Weintrob et al, 2004; Garg et al, 2004; 2006), and can generally maintain lower HbA1c levels compared with fingerprick test management alone (Bode et al, 1999; Kaufman et al, 2001; Pirzer et al, 2001; Ludvigsson and Hans, 2003; Deiss et al, 2006; Garg and Jovanovic, 2006; Mastrorotaro et al, 2006).

Some CGM systems are available with real-time values displayed for the person to see, or with stored values only – which means the results can only be viewed after removal of the sensor and downloading the results onto a computer. There are benefits to both systems. Real-time systems can show the person, at the time, the effects of insulin doses and lifestyle changes, whereas monitors that store the readings are useful if trends are to be viewed over a period of days without the person making any corrections.

Disadvantages

Glucose levels in interstitial fluid lag behind blood glucose values by about 5 minutes (Steil et al, 2003; Wentholt et al, 2005; Wilhelm et al, 2006), therefore people are required to undertake fingerprick measurements for CGM system calibration and are often advised to use fingerprick measurements to confirm hypo- or hyperglycaemic status before taking corrective action.

CGM systems require up to four fingerprick blood glucose measurements per day for calibration. The ideal time to calibrate is either after fasting or at least 3 hours postprandially, but not immediately after exercise or when the blood glucose level is likely to be rising or falling due to the lag-time with interstitial fluid. Without such calibration, continuous readings may be incorrect. People with diabetes require a thorough training programme to calibrate and operate a CGM system.

Blood glucose levels, when changing rapidly, may read as being in a normal range on a CGM system while in reality the person is already experiencing symptoms of an out-of-range blood glucose value and may require treatment. People using CGM are therefore advised to consider both the absolute value of the blood glucose level given by the system as well as any trend in the blood glucose levels. For example, a person using CGM with a blood glucose of 5 mmol/L might take no action if their blood glucose has been consistent for several readings, while a person with the same blood glucose level but whose blood glucose has been dropping in a short period of time might be advised to perform a fingerprick test to check for hypoglycaemia.

Audit

Aim

An audit was undertaken at the author's institution to determine whether a 72-hour
glucose profile can provide information to improve diabetes control and to assess the long-term effects on HbA1c levels. Ethical approval was not needed for this study as it was designed and conducted to produce information to inform delivery of best care and is therefore classed as a clinical audit (National Patient Safety Agency, 2009).

The study recruited 12 people (seven women and five men) with type 1 diabetes being treated with multidose insulin therapy. Mean age was 57 years (age range 27–80 years). Inclusion criteria were:

- Age 18 years or older.
- Type 1 diabetes.
- Currently on a basal–bolus regimen.
- Those whose diabetes control did not appear to be improving despite regular review and ongoing management under the outpatient care of the author’s diabetes centre.

Method
People with diabetes attending the diabetes clinic who fulfilled the inclusion criteria were offered CGM to determine if any additional information would lead towards improvements in their diabetes control. Those who agreed to undergo CGM completed a food and insulin diary for the duration of the monitoring and followed a care pathway, which comprised:

- Training on the use of the CGM and insertion of the sensor.
- Removing the device either at the clinic or by themselves at home. They were advised to bring their food and insulin diary with them when they returned the monitor to the clinic.
- Attending a session with the DSN and diabetes specialist dietitian to discuss their results and compare them with their diary. Recommendations would then be made for lifestyle and nutrition changes.
- Completing a short questionnaire on their experience of using CGM.
- Follow-up at 3, 12, 24 and 36 months.

Results
HbA1c results at 3, 12, 24 and 36 months post-CGM were noted and compared with their initial pre-CGM result. Before CGM, the mean HbA1c level of the group was 8.8±1.4% (73±15.3 mmol/mol). The results of the monitoring showed previously unrecognised blood glucose excursions in all participants. Seven suffered unrecognised nocturnal hypoglycaemia, with an average of two asymptomatic nocturnal and early morning hypoglycaemic events per person (ranging between one and three episodes). Prolonged periods of hyperglycaemia (blood glucose levels >14 mmol/L for 5 hours) were also recorded in three people.

At 3-month follow-up, mean HbA1c levels had reduced from 8.8% (73 mmol/mol) to 8.2% (66 mmol/mol; P=0.028). This improvement was attributed to lifestyle and diet modification rather than changes in therapy. Mean HbA1c levels at 12, 24 and 36 months were 8.2% (66 mmol/mol; P=0.009), 8.0% (64 mmol/mol; P=0.009) and 7.5% (58 mmol/mol; P=0.004), respectively.

The lack of reduction in mean HbA1c level after 12 months compared with the mean level at 3 months was a result of one person’s HbA1c increase from 6.7% (50 mmol/mol) to 8.2% (66 mmol/mol), which had a significant effect on the mean HbA1c level of the group. The reason for this increase was unclear, but at 36 months this person’s HbA1c level had come back down to 5.9% (41 mmol/mol).

### Table 1. HbA1c results at baseline and 3, 12, 24 and 36 months after beginning continuous glucose monitoring.

<table>
<thead>
<tr>
<th>Person</th>
<th>Baseline</th>
<th>3 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8.3 (67)</td>
<td>8.2 (66)</td>
<td>8.4 (68)</td>
<td>8.2 (66)</td>
<td>8.2 (66)</td>
</tr>
<tr>
<td>B</td>
<td>10.2 (88)</td>
<td>8.5 (69)</td>
<td>8.1 (65)</td>
<td>8.0 (64)</td>
<td>8.8 (73)</td>
</tr>
<tr>
<td>C</td>
<td>9.7 (83)</td>
<td>6.7 (50)</td>
<td>8.2 (66)</td>
<td>8.4 (68)</td>
<td>5.9 (41)</td>
</tr>
<tr>
<td>D</td>
<td>10.3 (89)</td>
<td>9.4 (79)</td>
<td>8.8 (73)</td>
<td>7.8 (62)</td>
<td>6.9 (52)</td>
</tr>
<tr>
<td>E</td>
<td>7.0 (53)</td>
<td>7.0 (53)</td>
<td>6.9 (52)</td>
<td>6.9 (52)</td>
<td>6.9 (52)</td>
</tr>
<tr>
<td>F</td>
<td>9.5 (80)</td>
<td>8.9 (74)</td>
<td>9.0 (75)</td>
<td>9.6 (81)</td>
<td>9.4 (79)</td>
</tr>
<tr>
<td>G</td>
<td>8.8 (73)</td>
<td>8.4 (68)</td>
<td>8.5 (69)</td>
<td>7.8 (62)</td>
<td>7.3 (56)</td>
</tr>
<tr>
<td>H</td>
<td>7.9 (63)</td>
<td>7.9 (63)</td>
<td>7.1 (54)</td>
<td>6.5 (48)</td>
<td>6.5 (48)</td>
</tr>
<tr>
<td>I</td>
<td>7.8 (62)</td>
<td>7.0 (53)</td>
<td>7.9 (63)</td>
<td>8.1 (65)</td>
<td>7.8 (62)</td>
</tr>
<tr>
<td>J</td>
<td>8.7 (72)</td>
<td>8.2 (66)</td>
<td>8.2 (66)</td>
<td>8.6 (70)</td>
<td>7.2 (55)</td>
</tr>
<tr>
<td>K</td>
<td>9.0 (75)</td>
<td>8.9 (74)</td>
<td>8.5 (69)</td>
<td>7.8 (62)</td>
<td>7.6 (60)</td>
</tr>
<tr>
<td>L</td>
<td>8.7 (72)</td>
<td>8.9 (74)</td>
<td>8.6 (70)</td>
<td>8.2 (66)</td>
<td>7.8 (62)</td>
</tr>
<tr>
<td>Mean</td>
<td>8.8 (73)</td>
<td>8.2 (66)</td>
<td>8.2 (66)</td>
<td>8.0 (64)</td>
<td>7.5 (58)</td>
</tr>
</tbody>
</table>
By study end, 11 people had showed an improvement in their HbA1c level, while one person remained the same. Of the 11 who showed an improvement, four improved by up to 1 percentage point, five had improved by between 1.1 and 2 percentage points, and two people improved by over 2 percentage points.

Participants’ experience of CGM
During the initial 3-month assessment, participants completed a short questionnaire on their experience using the CGM system. Generally, they were positive about the experience. The results are shown in Table 1.

Discussion
CGM was performed for 72 hours and results were discussed with the participants. Discussion took place in a joint consultation with a DSN and a diabetes specialist dietitian. The participants completed a diet and lifestyle diary while on CGM, and this was used during the consultation to see how diet and other lifestyle issues such as exercise affected their glucose levels. Using this information, insulin or lifestyle adjustments were recommended.

It was found that CGM offered advantages over intermittent glucose monitoring when glycaemic patterns were poorly understood. The information about direction, magnitude, duration, frequency, and causes of fluctuations in blood glucose levels that can be obtained by CGM is simply not available with intermittent blood glucose monitoring; in this study this was most noticeable from the night-time glucose levels, after ingesting food, and during and after exercise or increased activity. When patterns are needed to adjust therapy or identify areas of hyper- or hypoglycaemia, CGM is useful.

A monitor that does not give real-time readings was used as this was the only one available to the team, and it was found that the information proved valuable for management decisions regarding peoples’ diabetes care.

Table 2. Results of a questionnaire on peoples’ experience of continuous glucose monitoring.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Participant responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ease of use of continuous glucose monitoring.</td>
<td>Eight people found it quite easy.</td>
</tr>
<tr>
<td></td>
<td>Four people found it neither easy or difficult.</td>
</tr>
<tr>
<td>2. Ease of use of diary.</td>
<td>Nine people found it very easy.</td>
</tr>
<tr>
<td></td>
<td>Three people found it quite easy.</td>
</tr>
<tr>
<td>3. Usefulness of information gained from continuous</td>
<td>Five people found it very helpful.</td>
</tr>
<tr>
<td>glucose monitoring.</td>
<td>Five people found it quite helpful.</td>
</tr>
<tr>
<td></td>
<td>One person found it neither helpful or unhelpful.</td>
</tr>
<tr>
<td></td>
<td>One person found it unhelpful.</td>
</tr>
<tr>
<td>4. Learning information previously unaware of from</td>
<td>Eleven people answered “yes”.</td>
</tr>
<tr>
<td>the continuous glucose monitoring.</td>
<td>One person answered “no”</td>
</tr>
<tr>
<td>5. Usefulness of experience.</td>
<td>Twelve people answered “yes” to useful.</td>
</tr>
<tr>
<td>6. Usefulness of advice from healthcare practitioner.</td>
<td>Eleven people answered “yes” to useful.</td>
</tr>
<tr>
<td></td>
<td>One person answered “no” to useful.</td>
</tr>
<tr>
<td>7. Intention of taking on advice given.</td>
<td>Eleven people answered “yes”.</td>
</tr>
<tr>
<td></td>
<td>One person answered “no”.</td>
</tr>
<tr>
<td>8. Advice given.</td>
<td>Eight people were given advice on dietary changes.</td>
</tr>
<tr>
<td></td>
<td>Three people were advised against taking ad hoc doses of insulin.</td>
</tr>
<tr>
<td></td>
<td>One person was given advice regarding changes in activity.</td>
</tr>
<tr>
<td></td>
<td>One person had no changes recommended.</td>
</tr>
<tr>
<td></td>
<td>One person was given advice regarding hypoglycaemia management.</td>
</tr>
</tbody>
</table>
During hypoglycaemia or periods of rapid fluctuation, values provided by CGM may be inaccurate and confirmation is needed by means of a fingerprick test. Clinical outcome studies suggest that measures of mean glycaemia and hypoglycaemic burden both improve with the use of CGM (Bode et al., 1999; Tanenberg et al., 2004).

Individualised care plans were made for each person, and agreed changes made and targets aimed for.

**Conclusion**

CGM is often seen as expensive, and the monitors and sensors can be costly. However, CGM can greatly improve a person with diabetes’ quality of life as a result of reduced risk of hypoglycaemia, improved glycaemic control and the subsequent reduced risk of long-term vascular complications.

CGM may become a routine part of diabetes management in the future, initially for people with difficult-to-control diabetes and eventually for most people with diabetes.

Retrospective reporting, as used in this small study, will eventually give way to real-time readings, and using a confirmatory fingerprick blood test will eventually give way to using without the requirement of such calibration. As methods for minimally invasive and non-invasive monitoring are developed, people with diabetes will use this technology more routinely. Data printouts from CGM will increasingly provide information for effective diabetes management in the future.

“**As methods for minimally invasive and non-invasive monitoring are developed, people with diabetes will use this technology more routinely.**”


