Continuous glucose monitoring in children with type 1 diabetes

Rhonda Bleakly

Continuous glucose monitoring (CGM) can help people with diabetes to optimise their glycaemic control. Changes in treatment guided by the information obtained from CGM can result in improved HbA_{1c} levels and reduced risk of hypoglycaemia. In addition, CGM can be an educational and motivating tool if used appropriately with adequate support from healthcare professionals. In this article, the author carries out a literature review of studies on the use of CGM among children with type 1 diabetes and discusses the potential benefit of CGM in this population.

Type 1 diabetes is one of the most common chronic childhood illnesses affecting one in 550 children in the UK (Department of Health and Department for Education and Skills, 2005). The main goals of diabetes care include good metabolic control, minimisation of complications and maintaining a good quality of life (QOL). Failure to achieve these goals results not only in poor QOL for the person with diabetes, but is a huge strain on the health service, with the treatment of diabetes costing an estimated £5 million per day (Williams and Pickup, 2004). Much of this cost is attibutable to complications, which can be reduced with good professional care and self-management (Department of Health and Diabetes UK, 2005).

The introduction of continuous glucose monitoring (CGM) as a form of blood glucose monitoring has the potential to help people with diabetes achieve target HbA_{1c} levels while reducing the risk of severe hypoglycaemia. Although CGM has been in clinical use for approximately 12 years, the evidence surrounding its superiority over traditional blood glucose monitoring remains controversial. In this article, the author discusses the potential benefits of using CGM in children with type 1 diabetes.

Background

Despite the benefits of intensive insulin regimens, the potential benefits of new insulins and methods of delivery for overall metabolic control in children and adolescents has improved little in the UK in the past decade. For example, only 20% of children and young people with type 1 diabetes in Northern Ireland meet the recommended HbA_{1c} target of <7.5% (<58 mmol/mol; Cardwell et al, 2005). Furthermore, the fourth National Diabetes Audit has shown that paediatric care currently does not meet nationally agreed standards and will continue to cause health problems for young people with diabetes both now and in the future (Edge et al, 2005). Tight glycaemic control in people with type 1 diabetes is essential for delaying the progression of microvascular disease and improving long-term outcomes (DCCT [Diabetes Control and Complications Trial] Research Group, 1993).

Article points

1. The introduction of continuous glucose monitoring (CGM) as a form of blood glucose monitoring has the potential to help children with type 1 diabetes achieve target HbA_{1c} levels while reducing the risk of severe hypoglycaemia.
2. CGM reveals the fluctuations in glucose levels that often go unnoticed when only standard finger-stick blood glucose measurements are used.
3. This literature review showed that children who had most significant improvements in glycaemic control with CGM were those who had more consistent use of the sensors.

Key words

- Children
- Continuous glucose monitoring
- Glycaemic control
- Type 1 diabetes

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Page points

1. Continuous glucose monitoring (CGM) is capable of detecting unrecognised hypoglycaemia and other blood glucose patterns that are undetectable through conventional glucose monitoring.
2. By viewing continuous data and trend graphs, people with diabetes can react to high or low blood glucose levels before they become dangerous.
3. For CGM to be accepted for widespread use, the devices must be comfortable to wear, easy to operate and provide accurate results.
4. There are generally two types of CGM: one that records data to be analysed retrospectively and one that gives real-time glycaemic values.

Glycaemic control is even more challenging among children who have varying levels of activity and erratic eating patterns, leading to a great degree of blood glucose fluctuation. In recent years, the use of rapid and long-acting insulin analogues, improvements in insulin pump technology and increased frequency of blood glucose monitoring have gone some way in helping to achieve target HbA_{1c} levels in people with type 1 diabetes. However, the maintenance of euglycaemia with intensive insulin therapy is limited by the increased risk of hypoglycaemia. Fear of hypoglycaemia may lead to increased anxiety, non-adherence or under-dosing of insulin, resulting in poor glycaemic control (McAulay et al 2001; Davis and Alonso, 2004; Álvarez Guisasola et al, 2008; Labad et al, 2010). Even the most intense monitoring of blood glucose levels gives only a glimpse of the fuller picture and does not give information about glucose levels overnight.

Lock et al (2002) suggest that glycaemic control can be maintained through regular self-monitoring of blood glucose (SMBG) and appropriate action, to help prevent long-term complications. However, in addition to the discomfort associated, traditional finger-stick testing is limited by the fact that the readings simply represent distinct points in time. As individuals typically test no more than three or four times per day and generally do not test overnight, frequent glucose peaks and asymptomatic hypoglycaemia can be undetected leading to poor glucose control (Kaufman et al, 2002). Lack of information regarding trends in the glucose profile limit accurate adjustments of insulin therapy.

CGM is capable of detecting unrecognised hypoglycaemia and other blood glucose patterns that are undetectable through conventional glucose monitoring. The CGM sensor is inserted subcutaneously by a healthcare professional. Interstitial glucose measurements are recorded every 5 minutes for 72 hours, giving up to 288 daily glucose readings. There is a good correlation between interstitial glucose and plasma glucose levels (Sachedina and Pickup, 2003); however, results may not be accurate during rapidly changing blood glucose levels (Monsod et al, 2002). Calibration with capillary blood glucose levels is required during CGM use, requiring four finger-stick measurements per day. The individual is also asked to keep a food, insulin and event diary while wearing the CGM sensor. The downloaded glucose data are displayed in graph format and analysed to assist the individual in making optimal treatment decisions (Klonoff, 2005).

Literature review

A literature review was carried out using databases including MEDLINE and ProQuest. The search terms "continuous glucose monitoring", "children" and "type 1 diabetes" were used. Several key studies examining the benefits of CGM in both children and adults with type 1 diabetes were identified. These are summarised in *Table 1*.

Chase et al (2001) demonstrated marked increases in plasma glucose levels after meals, even in children with low HbA_{1c} levels. By viewing continuous data and trend graphs, people with diabetes can react to high or low blood glucose levels before they become dangerous. In addition, this information can provide insights into the underlying causes of glucose fluctuations, allowing further adjustments to insulin therapy to be made by healthcare professionals.

For CGM to be accepted for widespread use, the devices must be comfortable to wear, easy to operate and provide accurate results. There are generally two types of CGM: one that records data to be analysed retrospectively and one that gives real-time glycaemic values.

Chase et al (2001) and Kaufman et al (2002) were the first to report the use of CGM in children. Both studies demonstrated a significant improvement in HbA_{1c} levels in children using CGM for relatively short periods (30 days and 3 months, respectively). Similarly, Ludvigsson and Hanas (2003) reported that there were significant improvements in HbA_{1c} levels among the paediatric group studied (n=27) over a 12-week period (see *Table 1*). CGM was used for 3 days every 2 weeks over the 3-month period, leading to an improved

Table 1. Studies on the benefits of continuous glucose monitoring in adults and children with type 1 diabetes.

Year	Author	Sample size	Design and method	Outcomes
2003	Ludvigsson and Hanas	*n*=27	Children aged 5–19 years. Cross-over, double-blinded. Randomised SMBG or CGM over 12 weeks.	Improvement in HbA_{1c} level. Day-time hypoglycaemia (*n*=26). Night-time hypoglycaemia (*n*=27).
2004	Deiss et al	*n*=50	Children aged 1–16 years had CGM before and after 6 weeks after starting CSII. Simultaneous SMBG was performed. Cross-over, single-blind, parallel study.	CGM use improved HbA_{1c} level and provided additional information to SMBG. Less hyperglycaemia during the day. No increase in hypoglycaemia.
2006	Deiss et al	*n*=162	Randomised controlled trial. Real-time monitoring of SMBG. Children (*n*=81) and adults (*n*=81). Baseline HbA_{1c} >8.1% (>65 mmol/mol).	Gradual improvement in HbA_{1c} level measured at 1 month and further improvement at 3 months.
2006	Lagarde et al	*n*=27	Children aged 7–17 years. CGM every 2 months over 6 months. Single-blind, randomised, parallel.	Reduction in HbA_{1c} level without increase in hypoglycaemia.
2008	Hirsch et al	*n*=146	6-month study of people treated with CSII aged 12–72 years. Randomised, real-time CGM or SMBG used over 6 months. Baseline HbA_{1c} 7.5% (58 mmol/mol), aim for 7.0% (53 mmol/mol).	Greater sensor usage resulted in greater improvements in HbA_{1c} levels. No difference between groups. Both groups showed similar improvement in HbA_{1c} levels. Increased hypoglycaemia in the control group.
2008	JDRF CGM Study Group	*n*=322	26-week study of children and adults. Randomised, parallel SMBG or CGM real time. Age groups: 8–14, 15–24 and ≥25 years. Baseline HbA_{1c} 7.0% (53 mmol/mol).	Glycaemic control improved in the ≥25 age group. Not significant in children aged 8–14 or 15–24 years.
2009	Bode et al	*n*=129	Weekly use of CGM over a 26-week period in adults and children. Baseline HbA_{1c} <7.0% (<53 mmol/mol). Randomised SMBG or CGM real time.	Greatest improvements in HbA_{1c} levels in adults aged >25 years. Limited improvement in children and adolescent age group. Less hypoglycaemia in the CGM group.

CGM=continuous glucose monitoring; CSII=continuous subcutaneous insulin infusion; JDRF=Juvenile Diabetes Research Foundation; SMBG=self-monitoring of blood glucose.

mean HbA_{1c} level from 7.70% (61 mmol/mol) to 7.31% (56.1 mmol/mol). Deiss et al (2004) studied 50 children transferring to insulin pump therapy (continuous subcutaneous insulin infusion [CSII]) and demonstrated improvements in glycaemic control when using CGM (see *Table 1*). The most marked improvement was among those who had poor glycaemic control (HbA_{1c} level >8% [>64 mmol/mol]) prior to starting CSII. A randomised controlled trial (RCT) with CGM was performed by a European study consortium (Deiss et al, 2006) (see *Table 1*). Among the participants, 50% were children (*n*=81) and the study demonstrated significant reductions in HbA_{1c} level after 1 and 3 months of use.

The results of a 6-month trial by Lagarde et al (2006) (see *Table 1*) suggest CGM improves metabolic control and are consistent with previous studies. The study also examined whether improvements in HbA_{1c} levels occurred at the expense of frequent

Page points

1. The results of the study by the Juvenile Diabetes Research Foundation Continuous Glucose Monitoring (CGM) Study Group indicate that CGM improves HbA_{1c} levels in people with type 1 diabetes aged ≥25 years who have the necessary motivation to use the technology.
2. In addition to glycaemic benefits, CGM may help to encourage, motivate and empower people to take control of their diabetes. It has the potential to reinforce concepts that are taught in diabetes education and to reduce the fear of hypoglycaemia.
3. The CGM procedure should be carefully explained by an appropriately trained and competent healthcare professional. The diabetes team must then be able to interpret the recorded data and make informed decisions to assist the individual to maximise their glycaemic control.

episodes of hypoglycaemia. There were no significant differences between the frequencies of hypoglycaemia reported in the intervention and control groups. Therefore, improvements in HbA_{1c} levels were achieved without increasing risk of hypoglycaemia. However, it has been noted that CGM may be inaccurate during periods of hypoglycaemia (Monsod et al, 2002).

The results of an independent study carried out by the Juvenile Diabetes Research Foundation (JDRF) CGM Study Group et al (2008) contradict the reported positive results of earlier, smaller studies (see *Table 1*). This large study examined whether CGM can help people with type 1 diabetes to manage their condition. The RCT took place across 10 sites in the USA and involved people with type 1 diabetes aged 8–72 years (*n*=322). Participants were divided into three age bands (8–14, 15–24 and ≥25 years), with each age group being randomised to use a CGM device or to record information from standard finger-stick blood testing. The groups were followed for 26 weeks and changes in HbA_{1c} levels were used to assess the effectiveness of the different monitoring methods. At the commencement of the study, each participant had an HbA_{1c} level of 7–10% (53–86 mmol/mol). NICE (2004) guidelines recommend a target HbA_{1c} level of <7.5% (<58 mmol/mol) for adults and children.

The study showed that the benefits associated with CGM was strongly related to age (JDRF CGM Study Group et al, 2008). The group aged ≥25 years had improvements in all measures of glycaemic control, including a ≥10% relative reduction of the mean HbA_{1c} level compared with baseline. In contrast, the groups aged 8–14 and 15–24 years did not achieve statistically significant reductions in HbA_{1c} levels. The results of the study indicate that CGM improves HbA_{1c} levels in people with type 1 diabetes aged ≥25 years who have the necessary motivation to use the technology, as supported by Montagnana et al (2009). In contrast to findings previously reported by the DCCT Research Group (1993), which showed that improved control resulted in a three-fold increase in the frequency of severe hypoglycaemic episodes, JDRF reported fewer episodes of hypoglycaemia with improved glycaemic control (JDRF CGM Study Group et al, 2008).

The participants in the studies were generally those who were motivated and had good HbA_{1c} levels at baseline. Therefore, it is not possible to generalise the results to include the less-motivated individual. Individuals who had most significant improvements in glycaemic control were those who had more consistent use of the sensors. Subsequent follow-up of this study for 12 months demonstrated that improvements in glycaemic control were maintained in those who continued to use the sensor (Bode et al, 2009).

Psychological issues

Clinical use of CGM devices could have a significant impact on family management of paediatric diabetes. To date, psychological research on its use is limited. Only a few of the studies have used QOL as a measure of effectiveness and often this may be an important reason for people to use CGM in addition to their usual self-monitoring.

Reported results are inconclusive stating that CGM could potentially produce beneficial or adverse psychological reactions (Diabetes Research in Children Network Study Group, 2006). In addition to glycaemic benefits, CGM may help to encourage, motivate and empower people to take control of their diabetes. It has the potential to reinforce concepts that are taught in diabetes education and to reduce the fear of hypoglycaemia.

For some, the extra information obtained may cause additional stress. Such people may find it difficult to understand and feel burdened with the extra knowledge, while others may be naturally apprehensive about the invasiveness of the procedure. The procedure should be carefully explained by an appropriately trained and competent healthcare professional. The diabetes team must then be able to interpret the recorded data and make informed decisions to assist the individual to maximise their glycaemic control. Hammond et al (2010) state that the key to effective use of CGM is interpretation of the data.

It is important not to give people unrealistic expectations about CGM as some may believe that it could replace the need to carry out blood

Page points

1. It is apparent that one 3-day period of continuous glucose monitoring (CGM) is probably insufficient to translate into any meaningful improvement in diabetes control.
2. The availability of CGM is a significant advance that has the potential to assist diabetes care for those with poor metabolic control and those with suspected nocturnal hypoglycaemia.
3. In contrast to insulin adjustments made on self-monitoring of blood glucose alone, CGM-guided adjustments can improve glycaemia without increased risk of hypoglycaemia.

glucose measurements. A study by Ritholz (2008) found that those with high HbA_{1c} levels expected CGM to improve glycaemic control. In contrast, those with lower HbA_{1c} level understood that they themselves needed to work with the data consistently in order to make changes. A careful patient selection process is required, and as CGM is still a relatively new addition to the local service, a care pathway would be a useful tool to develop.

Limitations

The studies discussed above raise the question as to how frequently CGM needs to be used to achieve the desired outcome. The findings from a randomised study by Hirsch et al (2008) indicate that the more often people use CGM, the better glycaemic control they can achieve without the risk of hypoglycaemia (see *Table 1*).

A difficulty in comparing these studies was that each study used CGM for a different lengths of time and at various intervals. It is apparent that one 3-day period of CGM is probably insufficient to translate into any meaningful improvement in diabetes control. There may even be a tendency for the adolescent to change behaviour during sensor use; therefore, giving inconsistent CGM information for the 3-day period.

The fact that CGM data are retrospective can also be regarded as a limitation of the studies. The numbers and age groups of participants also varied greatly between studies, which were all short-term. The reduction in HbA_{1c} levels in children's studies may be attributable to parental input in adjustment of therapy. Further RCTs for extended time periods are needed to provide evidence of the benefits of CGM among children.

Conclusion

Type 1 diabetes in children and adolescents is characterised by variable blood glucose control, tendency to experience hypoglycaemia and difficulties in insulin adjustment. The need to protect this group against the long-term consequences of hypoglycaemia and hyperglycaemia is vital. The availability of CGM is a significant advance that has the potential to assist diabetes care for those with poor metabolic control and those with suspected nocturnal hypoglycaemia. This review of the literature has demonstrated positive outcomes in glycaemia while using CGM, although the sample sizes of the studies have been small. In contrast to insulin adjustments made on SMBG alone, CGM-guided adjustments can improve glycaemia without increased risk of hypoglycaemia (Lagarde et al, 2006). *Box 1* gives an example of how CGM data can be used to improve glycaemic control.

Although some people may have an unrealistic expectation of CGM – anticipating that it will improve their glycaemic control instantly – others realise the commitment and work required to sustain significant improvements. Careful patient selection is required as the success of CGM depends on the individual and family understanding and willingness to change behaviour based on the CGM results.

Even small changes in HbA_{1c} levels driven by an increase in patient knowledge and motivation may have long-term benefits. The key to effective use of CGM is interpretation of the data, support from the healthcare team and realistic expectations from the individual and the family, ultimately empowering the child and family to understand their glucose patterns and maximise their diabetes management. ■

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Box 1. Case study.

A girl aged 4 years who had been diagnosed with type 1 diabetes at 18 months and was quite sensitive to rapid-acting insulin had persistent HbA_{1c} levels of approximately 9% (75 mmol/mol). She had frequent periods of hypoglycaemia, usually occurring mid-morning or at lunch time and occasionally during the night. Her initial insulin regimen was premixed insulin twice daily. Various mixtures were tried, but insulin doses were difficult to adjust and her mother agreed to change to a free-mixed, rapid-acting insulin analogue and isophane insulin pre-breakfast with a long-acting insulin analogue in the evening to avoid risk of hypoglycaemia overnight. The results of continuous glucose monitoring revealed that despite earlier problems with hypoglycaemia on the premixed insulin, blood glucose levels were now mainly high after teatime and persisting overnight. Discussion of the graph allowed her mother to see that the HbA_{1c} level was high because of long periods of hyperglycaemia overnight. The results prompted the introduction of a small dose of the rapid-acting insulin analogue pre-teatime. Her blood glucose levels improved and overall HbA_{1c} level was reduced to 8.5% (69 mmol/mol).

"The key to effective use of continuous glucose monitoring is interpretation of the data, support from the healthcare team and realistic expectations from the individual and the family, ultimately empowering the child and family to understand their glucose patterns and maximise their diabetes management."

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