Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes: systematic review and meta-analysis

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CRD summary
Continuous glucose monitoring, particularly its real-time system, had a favourable effect on glycaemic control in patients with type 1 diabetes, compared with self monitoring of blood glucose. This was a well conducted systematic review and despite the limited quality of some of the included trials, the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the efficacy and safety of continuous glucose monitoring systems compared with self-monitoring of blood glucose in patients with type 1 diabetes.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CRD databases, and Trip Database were searched to June 2011; some search terms were reported. In addition, clinical trial registers, medical product approval agencies, conference abstracts presented at two international diabetic meetings and the reference lists of retrieved articles were searched for additional relevant studies. Only studies published in full were eligible for inclusion.

Study selection
Randomised controlled trials (RCTs) of at least 12 weeks duration that compared continuous glucose monitoring with self-monitoring of blood glucose were eligible for inclusion. Participants had to be patients with type 1 diabetes on an intensive insulin regimen (with continuous subcutaneous insulin infusion or multiple daily injections). Trials were excluded if patients were pregnant, had new-onset type 1 diabetes, were being treated in an intensive care unit, if insulin was administered intraperitoneally or if only noninvasive systems of glucose monitoring were assessed. Outcomes of interest were HbA1c change from baseline, HbA1c at the end of the study, proportion of patients that achieved target HbA1c, number and duration of hypo- and hyperglycaemic episodes and safety (risk of severe hypoglycaemic events, ketoacidosis, adverse reactions at the sensor implantation site and continuous glucose monitoring system errors).

The mean age of participants in the included trials ranged from nine to 52 years; some studies only included children and adolescents, some only included adults and some included both. The mean duration of diabetes ranged from six to 28 years, where reported. Mean baseline HbA1c values ranged from 6.4% to 11.5%. Some studies used continuous glucose monitoring systems in an ongoing manner (device used continuously at least six days per week) and some used continuous glucose monitoring systems in an intermediate manner (device was used less frequently; ranging from one 72-hour reading to a sequence of six readings per month corresponding to up to 18 days of measurement per month). Most studies offered real-time glucose readings, while some provided retrospective readings.

Two reviewers independently assessed studies for inclusion; disagreements were resolved by consensus or involvement of a third reviewer.

Assessment of study quality
Study quality was assessed using the Jadad scale. The authors did not state how many reviewers undertook quality assessment procedures.

Data extraction
For dichotomous outcomes, odds ratios (OR) and risk ratios (RR) were calculated with 95% confidence intervals (CI). For continuous outcomes, mean differences (MD) with 95% confidence intervals, were calculated.

Data extraction was undertaken independently by two reviewers, disagreements were resolved by consensus or involvement of a third reviewer.
Methods of synthesis
Data were pooled using the inverse variance or Mantel-Haenszel method in the absence of significant statistical heterogeneity and presented as the pooled odds ratio, pooled risk ratios, or weighted mean difference (WMD) with 95% confidence intervals. In the presence of significant heterogeneity the DerSimonian and Laird random-effects model was used.

For dichotomous outcomes, if differences between trial groups reached statistical significance, the number-needed-to-treat or number-needed-to-harm was also calculated.

Subgroup analyses were conducted according to patient age, level of glycaemic control at baseline, type of device and frequency of use. Heterogeneity was assessed using the Cochrane Q-test. Publication bias was assessed using the Egger test.

Results of the review
Fourteen RCTs were included in the review (1,268 participants, range nine to 322). Study duration ranged from three to six months. Seven RCTs scored one or two out of five on the Jadad scale, seven scored three out of five.

Patients using continuous glucose monitoring systems had a significantly greater decrease in HbA1c from baseline compared with self monitoring of blood glucose (WMD -0.26, 95% CI -0.34 to -0.19; 14 RCTs). There was no evidence of statistical heterogeneity (I²=0%).

Devices that offered real-time glucose readings for continuous glucose monitoring had a significantly greater decrease in HbA1c from baseline compared with self monitoring of blood glucose (WMD -0.27, 95% CI -0.34 to -0.19; eight RCTs), but the difference was not statistically significant for devices that provided retrospective readings. Results of other subgroup analyses were similar to those of the main analysis. Results were similar for studies of children and adolescents and studies of adults.

Similar results were reported for end of trial HbA1c levels, but there was significant heterogeneity associated with these results. A significantly higher proportion of patients using continuous glucose monitoring systems achieved target HbA1c levels compared with patients using self monitoring of blood glucose (OR 2.14, 95% CI 1.41 to 3.26; numbers-needed-to-treat 7.40, 95% CI 4.70 to 17.43; four RCTs).

There was a significant reduction in hypoglycaemic events in the continuous glucose monitoring group compared with the self monitoring of blood glucose group (SMD -0.32,95% CI -0.52 to -0.13; four RCTs), but there was no significant difference in the frequency of severe hypoglycaemic episodes.

Only a few trials reported adverse events; the most common was mild reactions at the sensor implantation site in the continuous glucose monitoring group. Only a small number of patients reported experiencing more severe reactions (painful itching, severe pain during sensor implantation, skin abscess formation or cellulitis). The risk of ketoacidosis episodes was rare and not significantly different between groups. Three studies reported technical problems related to the use of continuous glucose monitoring systems.

There was no evidence of significant publication bias.

Authors' conclusions
Continuous glucose monitoring, particularly its real-time system, had a favourable effect on glycaemic control and decreased the incidence of hypoglycaemic episodes in both adult and paediatric type 1 diabetic patients, compared with self monitoring of blood glucose.

CRD commentary
The review question and inclusion criteria were clearly reported. A number of relevant sources were searched for eligible trials, but only trials published in full were eligible for inclusion. Publication bias was assessed and there was no evidence of significant publication bias. Study selection and data extraction were undertaken in duplicate, which reduced the potential for reviewer bias and error.

The quality of the included trials was assessed using a validated tool. Half of the trials were poor quality (scoring 1 or 2
out of 5 on the Jadad scale), in addition, many trials only included a small number of participants. Study duration was only three to six months. Appropriate methods were used to pool the included studies, heterogeneity was assessed and subgroup analyses were undertaken. Despite the inclusion of some small, limited quality studies, the results of the individual studies consistently favoured continuous glucose monitoring in terms of glycaemic control. However, the results related to the incidence of hypoglycaemic episodes were less consistent.

Overall, this was a well conducted systematic review and the authors’ conclusions are likely to be reliable.

**Implications of the review for practice and research**
The authors did not state any implications for practice and further research.

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