Comparison of minimally invasive glucose monitoring devices with conventional monitoring in MITRE

A randomised controlled trial to compare minimally invasive glucose monitoring devices with conventional monitoring in the management of insulin-treated diabetes mellitus (MITRE)

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Executive summary

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Executive summary

Background

Diabetes is associated with significant morbidity, which has been shown to be reduced by improved glycaemic control. Although subject to much debate, self-monitoring of blood glucose is seen as a key element in implementing intensive therapy as it provides real-time feedback on the effects of diet, exercise and stress on the actual blood glucose, thus allowing patients to determine blood glucose values and identify hypo- or hyperglycaemia. Patients are, however, reluctant to test their blood glucose because of the pain, inconvenience and discomfort experienced, as well as any perceived stigma associated with the procedure. Even if performed more frequently, this form of blood glucose monitoring only provides a snapshot and may miss debilitating episodes of hypo- and hyperglycaemia. To address these limitations, minimally invasive continuous glucose monitoring devices have been developed to provide more detailed information along with analyses of trends of blood glucose. It has been assumed that this additional information will lead to more appropriately targeted advice and improved glycaemic control.

Objectives

The objective of this study was to evaluate whether the additional information provided by two minimally invasive glucose monitors resulted in improved glycaemic control in people with poorly controlled insulin-requiring diabetes in both the long and medium term. In addition, the acceptability and health economic impact of the devices was assessed.

Methods

Design

This was a four-arm randomised controlled trial. Two groups (groups 1 and 2) received minimally invasive glucose monitoring devices. Group 1 received the GlucoWatch Biographer device and group 2 the MiniMed Continuous Glucose Monitoring System (CGMS). These groups were compared with group 3, an attention control group that received standard treatment but with nurse feedback sessions at the same frequency as those in the groups receiving the devices, and group 4, a standard control group that reflected common practice in the clinical management of diabetes in the UK.

Setting

Participants were recruited from secondary care diabetes clinics in four hospitals. Two sites were inner-city locations, the third was an urban, relatively affluent area with a high proportion of retired people and the fourth was a socioeconomically deprived area. Assessment visits took place in diabetes outpatient clinics.

Participants

Participants were eligible if they were aged over 18 years, had insulin-treated diabetes mellitus (type 1 or type 2) and were receiving two or more injections of insulin daily. They also had to have been diagnosed with diabetes for at least 6 months and to have had two glycosylated haemoglobin (HbA1c) values greater than or equal to 7.5% in the last 15 months.

In total, 100 participants were recruited and randomised to receive the GlucoWatch (group 1), 102 were recruited to receive the CGMS (group 2), 100 were recruited to the attention control group and 102 were recruited to the standard care control group. At baseline HbA1c ranged from 7.0% to 15.5% with group means ranging from 8.9% to 9.4%.

Intervention

The intervention was divided into two phases.

- Phase 1 (0–3 months for participants in groups 1–3). Participants in the device groups were provided with the GlucoWatch Biographer or CGMS monitors. Those in the GlucoWatch group were trained and asked to use the device a minimum of four times per month and a maximum attempted use of four times per week. The information provided by the

GlucoWatch was downloaded at the nurse feedback sessions. Participants in the CGMS group were requested to be fitted with the device at baseline and at 6 and 12 weeks and received nurse feedback sessions 72 hours later. Participants in groups 1–3 also attended three nurse feedback sessions in this phase.

- Phase 2 (3–18 months for each participant). During this phase participants in group 1 used the GlucoWatch Biographer as desired and participants in group 2 were fitted with the CGMS at 6, 12 and 18 months. Participants in groups 1–3 also attended nurse feedback sessions at 6, 12 and 18 months.

All participants were provided with the same self-monitoring glucose meter and trained in its use at the baseline clinic visit.

Main outcomes

Change in HbA1c from baseline to 18 months was the primary indicator of long-term efficacy in this study. Change in HbA1c from baseline to 3 and 6 months evaluated short-term efficacy, and change from baseline to 12 months assessed efficacy in the medium term. Perceived acceptability of the GlucoWatch and CGMS was assessed by use and a self-report questionnaire, developed for the purpose of this study, at 3, 6, 12 and 18 months. A health economic analysis of the trial was also performed.

Results

At 18 months all groups demonstrated a decline in their HbA1c levels from baseline. Mean percentage changes in HbA1c were –1.4 for the GlucoWatch group, –4.2 for the CGMS group, –5.1 for the attention control group and –4.9 for the standard care control group. At 18 months the relative percentage reduction in HbA1c in each of the intervention arms was less than that in the standard care control group. In the intention to treat analysis the difference in the relative percentage reduction between the GlucoWatch and standard care control groups was 3.7% [95% confidence interval (CI) –1.1 to 8.5], for the CGMS 0.9% (95% CI –3.8 to 5.7) and for the attention control group 0.1% (–4.3 to 5.4). No significant differences were found between any of the groups at any of the assessment times. The findings indicated no advantage of having the additional information provided by a continuous glucose monitoring device on change in HbA1c in unselected individuals with poorly controlled insulin-requiring diabetes.

There was also no evidence that the additional information provided by the minimally invasive glucose devices resulted in any change in the number or nature of treatment recommendations offered by the nurses.

The health economics analysis indicated no advantage in the groups who received the continuous blood glucose monitoring devices. Using the health economic tools a lower cost and higher benefit was found for the attention control arm in the trial period.

A comparison between the devices in terms of use and acceptability indicated a decline in use of both devices but this was most marked in the GlucoWatch group, as opposed to the CGMS group, by 18 months (20% still using the GlucoWatch device versus 57% still using the CGMS). The participants using the GlucoWatch device reported more side effects, greater interference with daily activities and more difficulty in using the device than those using the CGMS.

Conclusions

The outcomes indicate that continuous glucose monitors as assessed in this study do not lead to improved clinical outcomes in unselected individuals with poorly controlled insulin-requiring diabetes.

In addition, the data suggest that the additional information provided by the two continuous glucose monitoring devices in this study (CGMS and GlucoWatch) is not cost-effective for improving HbA1c in an unselected population with poorly controlled type 1 or type 2 diabetes.

The findings also indicate that the two devices were accepted differently by participants. The GlucoWatch device was associated with a large number of side effects and its acceptability to participants was particularly low with only 20% of participants continuing to use the device at 18 months. On acceptability grounds alone the data suggest that the GlucoWatch technology assessed in this study will not be frequently used by individuals with diabetes. The findings emphasise the importance of examining acceptability, as devices may demonstrate clinical value, but if potential users find them unacceptable or choose

not to use them then it is unlikely that they could be introduced into routine care.

Future studies of continuous glucose monitoring devices should target specific subgroups for study such as poorly controlled type 1 patients with hypoglycaemia unawareness. The acceptability of these devices to participants and health-care professionals is an area that needs further research and should be included in studies of their potential clinical benefit.

Trial registration

This trial is registered as ISRCTN33678610.

Publication

Newman SP, Cooke D, Casbard A, Walker S, Meredith S, Nunn A, *et al*. A randomised controlled trial to compare minimally invasive glucose monitoring devices with conventional monitoring in the management of insulin-treated diabetes mellitus (MITRE). *Health Technol Assess* 2009;**13**(28).

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The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 01/13/03. The contractual start date was in December 2002. The draft report began editorial review in April 2007 and was accepted for publication in October 2008. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

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