MOBILE PHONE TELEMEDICINE FOR THE SELF-MANAGEMENT OF TYPE 1 DIABETES: CLINICAL EVALUATION AND MEASURES OF CONTROL USING BLOOD GLUCOSE FORECASTING

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Abstract: A mobile phone-based telemedicine system has been developed to assist patients in the self-management of Type 1 diabetes. Blood glucose test results and patient diary information are transmitted in real time to a secure server. Graphical feedback is shown to each patient on their phone screen, and to patients and clinicians via individual web pages. This system has been studied in a clinical randomized controlled trial, which demonstrated improvements in blood glucose control, as measured by the blood glucose results and by the clinical haemoglobin A_{1c} (HbA_{1c}) measurements. Nurse support was an important element of the telemedicine system: sustained compliance and improved blood glucose control were found in the nurse-supported group of patients. The data set obtained during the trial is being used to develop algorithms to assess blood glucose control by predicting HbA_{1c} values based on the patients' recorded data.

Introduction

Type 1 diabetes mellitus is caused by the destruction of insulin-producing beta cells in the pancreas. Patients inject insulin to control blood glucose levels, adjusting the insulin dose to take account of diet, exercise, and their current blood glucose level, measured using an electronic meter. High blood glucose levels can cause short-term problems such as diabetic ketoacidosis, and long-term complications including retinopathy and neuropathy. The injected doses of insulin must be carefully chosen to avoid low blood glucose (hypoglycaemia) which can also be dangerous.

People with Type 1 diabetes are conventionally treated with an intensive therapy of typically four insulin injections per day. This therapy has been shown to delay and reduce long-term complications caused by excessively high blood glucose levels [1]. In conventional diabetes care, patients discuss their blood glucose control at three-monthly clinics without access to computer-based blood glucose data or visualisations. Average blood glucose control during recent months is also usually assessed at clinics by measuring the proportion of haemoglobin A_{1c} (HbA_{1c}) in the blood. A lower HbA1c value (measured as a percentage of red blood cells) indicates better overall control of blood glucose in recent months.

Materials and Methods

A telemedicine system for diabetes self-management, using a Motorola T720i mobile phone interfaced to a LifeScan One Touch Ultra blood glucose meter, has been previously described [2]. The patient equipment for the system is shown in Figure 1. Custom Java software runs on the phone and downloads blood glucose measurements from the meter directly via a purpose-built interface cable. The phone software then asks the patient a short series of questions about diet, exercise and other factors affecting blood glucose levels. Patients also enter the dosage of insulin which they are planning to inject. This information is immediately transmitted to a server using the General Packet Radio Service (GPRS), an "always-on" mobile connection to the Internet. The phone software displays graphs of recent blood glucose data, with the patient's target blood glucose range superimposed. A secure web server allows the data to be viewed with a web browser (Figure 2), including plots highlighting the relationship between each insulin dose and the next blood glucose measurement. In comparison to previous diabetes telemedicine systems in the literature [3], this system provides immediate transmission of data and graphical feedback to the patient. The system is based on standard, readily-available components (a mobile phone and blood glucose meter), is portable and can be easily integrated into a patient's daily routine.

A nine-month randomized controlled trial investigated the use of the system by young adults (aged 18-30 years) who had sub-optimal blood glucose control at recruitment (HbA_{1c}values of 8% - 11%). Ninety-three patients from the Paediatric Transition Clinic or the Young Adult Diabetes Clinic in Oxford were randomized into two groups; both groups used the phone and meter as described above, but the intervention group received additional graphical feedback, both on the phone screen (Figure 3) and on their web pages, and proactive telephone support from diabetes specialist nurses. The nurses checked the incoming data fortnightly or more often, and could contact patients in the intervention group by telephone or text message.

Results

During the trial, the system performed reasonably well: over 51,000 blood glucose readings were transmitted. However, some technical problems were reported, such as temporary absences of GPRS connectivity. (In such cases, data were stored in the phone memory for later transmission.) Problems were also experienced with reliability of the interface cable, which sometimes required replacement.

Clinical measurements of HbA_{1c} were the primary outcome measure of blood glucose control in the trial. After nine months a reduction in HbA_{1c} (indicating blood glucose levels closer to non-diabetic levels) was found in both groups. The mean HbA_{1c} in the nurse-supported group changed from 9.2% to 8.5% (p=0.001), and in the control group from 9.3% to 8.9% (p=0.04). The difference in reductions between the groups is not statistically significant (p=0.3).

An HbA_{1c} result of 8% or more is often regarded as representing sub-optimal control. During the trial the proportion of patients with HbA_{1c} <= 8% increased in the nurse-supported group from 10.6% to 46.8% but in the control group only from 19.6% to 23.9%, a between-group difference which is statistically significant (p<0.0001).

Patients' control can also be assessed by the raw blood glucose data. The medians of the blood glucose measurements during the trial for the two groups were 8.9 mmol/l (IQR 5.4 to 13.5) for the nurse-supported group and 10.3 mmol/l (IQR 6.5 to 14.4) for the control group. This difference is statistically significant (p < 0.001). Figure 4 shows the distributions of blood glucose readings from the two groups. A greater proportion of readings from the intervention (nurse-supported) group lie in the "non-diabetic" range of approximately 4-7 mmol/l.

The compliance of patients was assessed from the number of blood glucose readings transmitted in each week of their participation in the trial. Figure 5 shows that the number of readings received per patient was sustained in the nurse-supported group but declined during the trial in the control group. The mean number of weeks in which no blood glucose measurement was received was significantly different (p<0.0001) between the nurse-supported group (3.9 weeks) and control group (11.4 weeks). Clearly, therefore, nurse support was important to maintain compliance levels and guide improvements but the nurse time required was not excessive: 1.5 phone calls were logged per patient per month, each lasting, on average, 7 minutes 9 seconds.

Figure 1: The mobile phone, blood glucose meter and interface cable

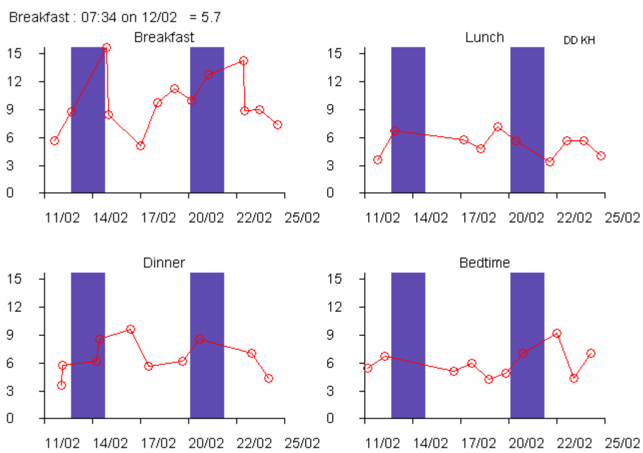

Figure 2: Web page display of blood glucose readings, with weekends (when different patterns of behaviour might be found) marked in blue.

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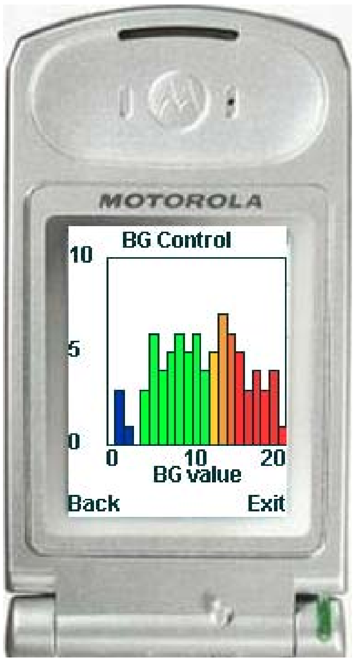

Figure 3: Graphical feedback screen displayed by the mobile phone, showing a histogram of recent blood glucose readings

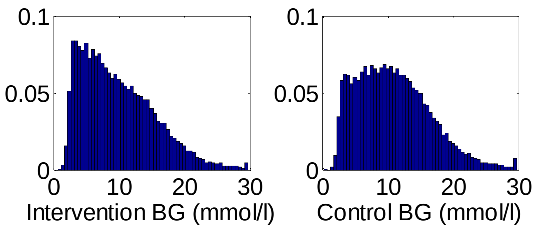

Figure 4: Histograms of blood glucose readings received during the trial from each group of patients, with areas normalized

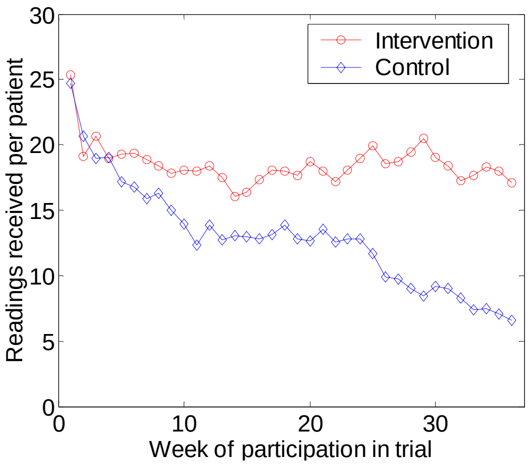

Figure 5: Mean number of readings received from patients in the intervention (nurse-supported) group and control group, during each week of the patients' participation in the trial

HbA_{1c} prediction from blood glucose data

The relationship between blood glucose measurements and clinical HbA_{1c} results was studied for the data gathered during this trial. The fraction of HbA_{1c} is known to be related, by a two-stage reversible process [4], to blood glucose levels in the previous 90-120 days. The HbA1c value is weighted towards the most recent 2-3 weeks of blood glucose levels, due to the red blood cell lifetime.

An algorithm to predict HbA_{1c} results has been investigated, using a weighting function applied to the blood glucose measurements prior to the prediction time, and a linear model to map this weighted average to the subsequent HbA_{1c} level. All patients in the trial were randomly assigned to the training or test set. Predictions were only attempted for HbA_{1c} results preceded by at least 30 readings during the previous 6 weeks, to avoid problems with lack of data and to exclude the HbA_{1c} measurements made on entry to the trial. A step function was used to weight the blood glucose measurements, with the time of the step change optimised within the range 1 to 120 days prior to the HbA_{1c} prediction time, to minimise the normalised root mean squared error of the predictions in the training set. The optimal timing of the step change was 90 days (+/- 1 day) before the HbA_{1c} result. The linear model fitted using the training set had gradient 0.457 and intercept 3.58. Figure 6 shows the predictions made using this model on the training set. The predictions were deemed to be "good" if they fell in the range +/- 1 unit of HbA_{1c} compared to the actual clinical HbA1c result (the +/- 1 unit limits are shown by red lines in the figure). This method of classifying the predictions has been used previously to assess HbA_{1c} prediction algorithms [5] since it corresponds to standards of accuracy required for laboratory measurement of HbA_{1c}. Figure 7 shows the results for the test set in the same way. It can be seen that although most of the predictions are within or close to the +/- 1 unit limits, the algorithm performs poorly in some cases, especially for high values of HbA_{1c}.

This algorithm will be developed using methods to account for sampling bias in the blood glucose measurements, more sophisticated functions to weight the blood glucose data through time, and produce measures of confidence in each prediction.

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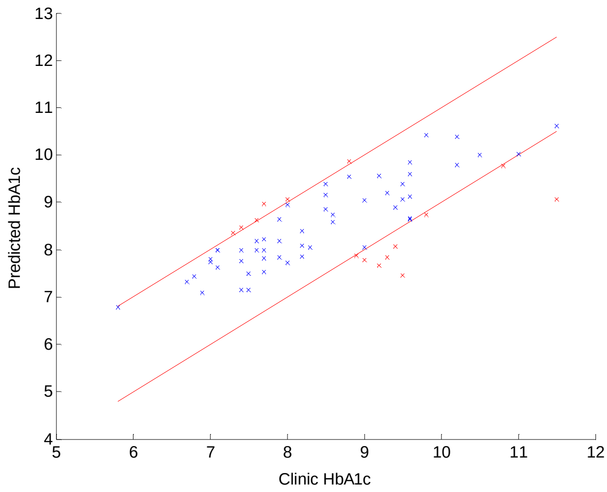

Figure 6: Predictions of HbA_{1c} results for the training set. The predictions which were within one HbA_{1c} unit of the clinical result are in blue.

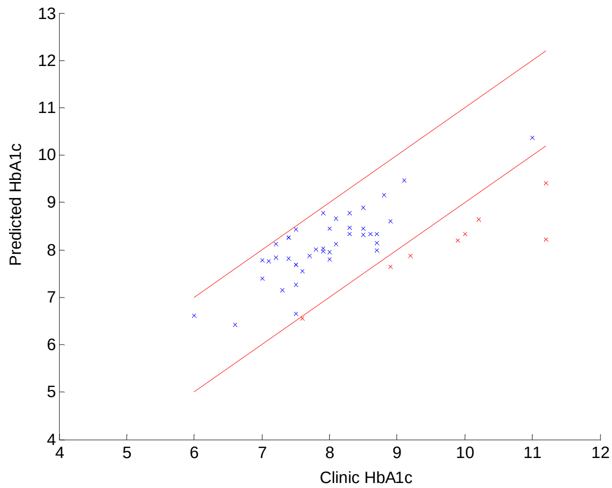

Figure 7: Predictions of HbA_{1c} results for the test set. The weighting of blood glucose values used, and the linear model used to predict HbA_{1c} from weighted blood glucose, had previously been optimised using the data in Figure 6.

Discussion

The clinical trial described above demonstrated that a telemedicine system can be used to transmit blood glucose test results and related diary data in real time. Blood glucose control improved in both groups of patients using the system, and the improvement was greater in the group which also received proactive nurse feedback. Nurse feedback was also essential to maintain compliance, but the nurse time required was not excessive.

The technical problems reported during the trial have been addressed in subsequent versions of the telemedicine system. The interface cable, which was vulnerable to damage, has been replaced by a wireless Bluetooth link between the blood glucose meter and phone.

Since HbA_{1c} is a widely-used measure of blood glucose control, an algorithm to predict HbA_{1c} using blood glucose measurements would be a useful addition to a telemedicine system for diabetes self-management. Patients could then track their HbA_{1c} between clinical HbA_{1c} measurements.

Conclusions

The mobile phone telemedicine system was evaluated in a clinical setting and led to improvements in diabetes self-management. The addition of remote nurse support maintained compliance and further improved blood glucose control. Automatic algorithms to generate measures of control, such as a prediction of the clinical HbA_{1c} value, could prove valuable to patients and result in better targeting of nurse support to improve outcomes without substantial increases in resources.

Acknowledgements

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