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A Telemedicine System That Includes a Personal Assistant Improves Glycemic Control in Pump-Treated Patients with Type 1 Diabetes

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Abstract

Background:
The DIABTel system, a Web-based telemedicine application, integrates a whole communication system (glucometer, insulin pump, wireless hand-held assistant) for medical remote advice. We sought to evaluate, in terms of glycemic control, the DIABTel system in a randomized crossover clinical study.

Methods:
Ten patients with type 1 diabetes [5 women, age 40.6 (21–62) years, diabetes duration 14.7 (3–52) years] were included. During the 4-week active phase, data sent by patients were analyzed by the physician and modifications of the basal rate and bolus were advised in the following 24 hours. During the control phase, patients sent glucose data without any feedback from the medical center.

Results:
The mean numbers of daily glucose values and bolus sent by patients during the active period were 4.46 ± 0.91 and 4.58 ± 0.89, respectively. The personal digital assistant functionalities used more frequently by patients were (times per week) data visualization (8.1 ± 6.8), data download from the insulin pump (6.8 ± 3.3), and synchronization with the telemedicine server (8.5 ± 4.9). After the experimental phase, serum fructosamine decreased significantly (393 ± 32 vs 366 ± 25 μmol/liter; $p < 0.05$) and hemoglobin A1c (HbA1c) tended to decrease (8.0 ± 0.6 vs 7.78 ± 0.6; $p = 0.073$), whereas no changes were observed during the control phase. The number of treatment modifications proposed and performed by the patients correlated with the change observed in HbA1c during the active phase ($r = -0.729$, $p = 0.017$).

Conclusions:
The DIABTel system, a telemedicine system that includes a wireless personal assistant for remote treatment advising, allows better glycemic control in pump-treated patients with type 1 diabetes. To our knowledge, this is the first study that demonstrates improved glycemic control with the use of a telemedicine system that incorporates insulin delivery data.

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Abbreviations: (HbA1c) hemoglobin A1c, (PDA) personal digital assistant, (SA) Smart Assistant

Keywords: telemedicine, insulin pump, personal assistant

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Introduction

The demanding level of care needed to prevent or delay microvascular complications in type 1 diabetes is difficult to achieve and maintain in everyday clinical practice. The latest advances in communication technologies can be used by patients for ongoing advice from health professionals and may reduce the burden of disease management.[1,2] Nevertheless, the impact of telemedicine on glycemic control has not been well established. The DIABTel system[3] provides telemedicine services for diabetes care, emphasizing the provision to physicians and patients of 24-hour telemonitoring and telecare services based on a multiaccess telemedicine server [Web, personal digital assistant (PDA), mobile phone].[4] The system supports the treatment prescription, generates clinical report and email services, and manages monitoring data: blood glucose, insulin basal rate and bolus/boluses, exercise, hypoglycemia symptoms, and others. The majority of monitoring data was retrieved directly from the glucometer and insulin pump and was integrated into a wireless PDA-based Smart Assistant (SA). The aim of the study was to evaluate the impact of use of the DIABTel system and the SA in terms of glycemic control in a group of patients with type 1 diabetes treated with an insulin pump.

Research Design and Methods

Patients were randomized to begin the study in the intervention or in the control group, and the crossover to the alternate arm occurred after 4 weeks. During the intervention phase, patients were assisted using telemedicine, whereas conventional care was provided during the control phase.

Ten patients with type 1 diabetes (five men) with negative c-peptide, a body mass index less than 25 kg/m^2, and hemoglobin A1c (HbA1c) less than 10% were included. All the patients had been treated with an insulin pump for more than a year and wore the same device (D-tron plus, Disetronic infusion system, Burgdorf, Switzerland) for at least the previous 6 weeks. During a run-in period of 2 weeks, patients were instructed in the use of the DIABTel Web service, management of the SA, and data transmission from the glucometer (Accutrend and Acculink modem, Roche Diagnostics, Basel, Switzerland). The DIABTel Web service supports all the functionalities and tools of the telemedicine service (**Figure 1**) and can be accessed from any internet connection. The INCA SA communicates with the patient devices through a personal wireless network (local loop) and additionally through a mobile Wide Area Network for providing telemonitoring, telecare, and remote information services (**Figure 2**). The user terminal supporting the SA is a commercial PDA (iPAQ HP2210 pocket PC, Palo Alto, CA) provided with wireless communication facilities, such as infrared, Bluetooth, and GPRS. The SA can work as a stand-alone system, supported on its own local application and database, providing the patient with an "electronic logbook" and implementing a virtual interface to the medical devices operating in the personal wireless network.

Patients were required to send glucose and insulin data at least twice a week. The system notified doctors with predefined alarm messages whenever recurrent out-of-range glucose values occurred. Data sent by patients were analyzed by health care professionals, and modifications of the basal rate and boluses were advised in the following 24 hours when necessary. Patients and the physician were allowed to use the email service freely, and all messages exchanged were automatically registered by the DIABTel system.

Patients in the intervention phase used the whole communication system (pump, PDA, glucometer, Web application) and received advice feedback from the hospital, whereas patients in the control phase only used the glucometer plus modem for sending glucose data but without any feedback from the diabetes care center. Confidentiality of the transferred information was completely guaranteed through data encryption before transmission using the Secure Socket Layer secure protocol. Additionally, patients' names were never transmitted and were coded when interacting with the Web site.

Evaluations were performed at the beginning and after each treatment period. At every visit, physical examinations, including body weight and blood pressure, were performed, as well as whole blood taken for serum fructosamine (EDTA) and HbA1c (EDTA) assays. HbA1c was measured using ion-exchange high-pressure liquid chromatography (Bio-Rad VARIANT™ II, Bio-Rad Laboratories, München, Germany), with a reference range of 4.2 to 5.7%. Fructosamine was measured by a colorimetric assay system (nitroblue tetrazolium method)[5] provided by BioSystems (Barcelona, Spain). The reference range was 205 to 285 μmol/liter. The interassay coefficient of variation was 3% at 281 μmol/liter and 4% at 531 μmol/liter. In the last 3 days of each period continuous subcutaneous glucose monitoring was also performed (CGMS, MiniMed Medtronic, Northridge, CA) and a group of variables were compared (mean glucose, standard deviation, percentage

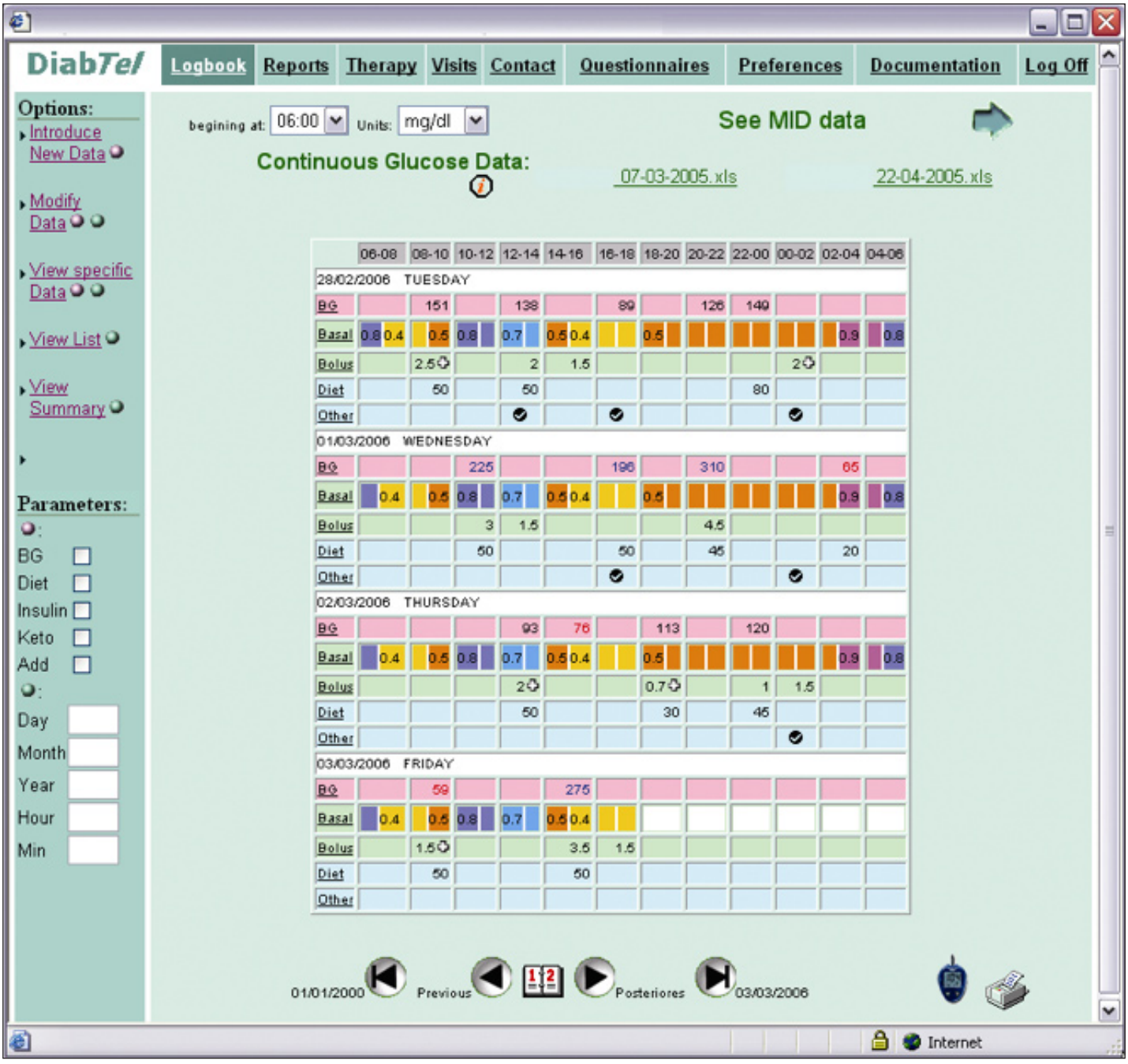

Figure 1. User interface of the DIABTel Web application for patients.

of time above 180 mg/dl, and area under the curve above 180 mg/dl) using data provided by the software CGM Sensor 3.0 (MiniMed Medtronic).

Analysis was performed using the SPSS 14 statistical package for Windows (SPSS, Chicago, IL). Comparison between groups was performed using Student's *t* test (Gaussian distribution) and Mann–Whitney's *U* test (non-Gaussian distribution) for quantitative data and χ^2 for qualitative variables. Comparisons within a group were made using Student's *t* for paired data or Wilcoxon's test. Bivariate correlations were performed between continuous data (Spearman's ρ).

The study had approval from the local ethical committee and patients signed the informed consent.

Results

All the patients completed the study. The main clinical characteristics were as follow: age 40.6 ± 12 years, weight 64.4 ± 2 kg, diabetes duration 14.7 (3–52) years, previous pump

Figure 2. User interface of the Wireless personal assistant.

treatment duration 3.4 (1–7) years, baseline HbA1c 8.0 ± 0.6%, and baseline serum fructosamine 393 ± 32 μmol/liter. Two patients had mild retinopathy and one had macroalbuminuria.

Use of the System

All the patients used the SA and additionally five of them used PC Web access (8.8 ± 3.7 times weekly). Patients used the Acculink modem 3.5 ± 1.2 times per week on average, being the mean number of daily blood glucose values sent during the active period (4.5 ± 0.9). The most frequently used SA functionalities were the electronic logbook (8.1 ± 6.8 times per week), data download from the insulin pump (6.8 ± 3.3 times per week), and synchronization with the remote telemedicine server (8.5 ± 4.6 times per week). The doctor checked monitoring data sent by the patients 10.8 ± 7.3 times per week, with each session lasting a mean of 26 minutes 58 seconds, and advised 44 therapy changes (**Table 1**). Nevertheless, retrospective analyses of pump data showed that only 24 of them were finally followed by the patients. Patients sent a total of 39 text messages and 47 were written on the doctor's side. Throughout the whole trial the system generated 62 alarm notifications, most of them because of hyperglycemia (above 300 mg/dl) in two consecutive values (56%), without differences in both study periods.

Glycemic Control

Changes in serum fructosamine are shown in **Figure 3**. In brief, during the active phase, fructosamine decreased significantly (393 ± 32 vs 366 ± 25 μmol/liter; $p < 0.05$), whereas no change was observed during the control phase. Furthermore, HbA1c tended to decrease after the active phase (baseline 8.0 ± 0.6 vs telecare 7.78 ± 0.6; $p = 0.073$) but did not change during the control phase. The number of treatment modifications prescribed by the physician (M. Rigla) and carried out by the patients correlated with the change observed in HbA1c during the telecare phase ($r = -0.729$, $p = 0.017$). Eight out of 10 patients reduced the percentage of home blood glucose values above 180 mg/dl during the intervention phase, with the total group mean reduction being 16.6%. Furthermore, the percentage of glycemic values below 65 mg/dl was reduced in 29.6%. No significant differences were obtained between both periods in the CGMS predefined variables.

Table 1.
Number and Type of Therapy Changes Advised during Intervention Phase

	Therapy changes (N/%)	Increased dose advised (%)	Decreased dose advised (%)	Average increased dose	Average decreased dose
Basal and bolus	16/35.5	56.2	43.7	0.92	-1.03
Basal dose	40/89	57.5	42.5	0.48	-0.72
Bolus dose	21/67	57.1	42.8	0.80	-1.16
Breakfast bolus	8/18	62.5	37.5	0.80	-1.00
Lunch bolus	12/27	50	50	0.86	-1.12
Dinner bolus	8/18	37.5	62.5	0.67	-0.44

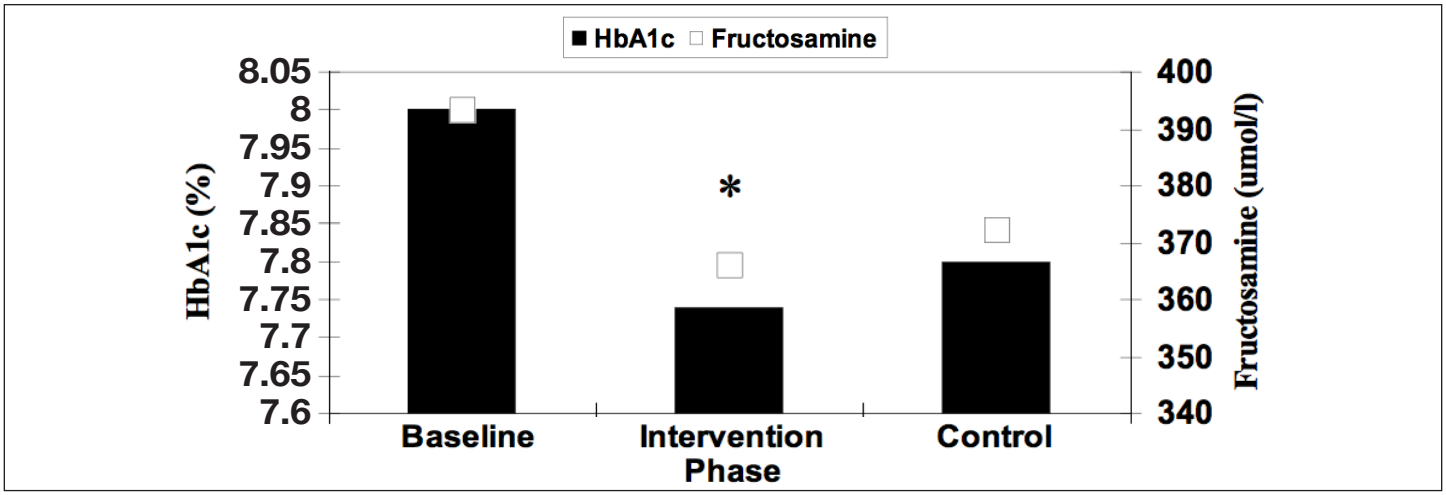

Figure 3. Changes in HbA1c and fructosamine observed at baseline and after each study phase. Fructosamine was lower after the intervention phase in comparison with baseline levels (*$p < 0.05$).

Conclusions

Our study demonstrated that the 4-week use of a telemedicine system for remote advice achieved a reduction in serum fructosamine levels in a small group of patients with type 1 diabetes treated with insulin pumps. Fructosamine was an indicator of overall glycemic control for the previous 3 weeks, whereas HbA1c reflected the previous 8 to 10 weeks.[6] Because each period studied was 4 weeks, it is plausible to consider that changes in serum fructosamine reflected the impact of the intervention on the glycemic control better than changes in HbA1c.

To our knowledge, this is the first study that demonstrated the benefit, in terms of glycemic control, of a telemedicine system that incorporates insulin delivery data in patients treated with pumps and allows making fine-tune adjustments. Unexpectedly, patients did not follow all the changes in the prescribed treatment, even though their doctor would realize patients' noncompliance in the following days. However, the doctor's advice played a role in glycemic control improvement because the decrease in HbA1c significantly correlated with the number of treatment changes finally carried out by patients.

According to the results of some metanalyses,[7,8] the effect of telemedicine in glycemic control has been described as very scarce and, in general, no higher than conventional care with face-to-face visits. Nevertheless, regarding the term "telemedicine," a wide spectrum of interventions have been included, so it is not appropriate to reach common conclusions from previously published studies. Regarding studies that focused on glycemic control using a Web-based system, all of them were designed as a randomized trial with parallel groups and most of them found significant improvements in glycemic control.[9–11] One study[9] demonstrated a benefit of using a mobile phone to download glucose self-monitoring results directly from the glucometer and to send them to a remote server, but in this case insulin doses were introduced manually and feedback from nurses was made by telephone calls. Another group published a controlled randomized trial about long-time Web-based care management, obtaining higher improvements in HbA1c in comparison with patients under usual care. Patients also downloaded glycemic values from glucometers, and the communication system was based on an internal messaging system and telephone calls.[10] Our system is the first one that allowed doctors to advise therapy changes based on actual data provided directly from glucometers and pumps. This is of particular interest, as monitoring data could neither be omitted nor modified by patients and were obtained without any extra effort from users. The Medtronic sensor augmented pump allows patients to transfer glucose monitoring data into the pump,[12] but the effect of this system on glycemic control has not been demonstrated yet.

Although previous work described the utility of a bolus calculator running in a hand-held device,[13] our results explored for the first time the use of a wireless personal assistant for remote advice in patients wearing insulin pumps. This device is able to generate a large amount of data that are difficult to record in a traditional logbook. Furthermore, the personal assistant provides all the relevant data available anywhere and anytime, including access to their medical records and any new changes in insulin therapy advised by their doctor. This kind of "autonomous supervision" through a SA

could be implemented in routine diabetes care in some situations where patients need very intensive care, as in pregestational preparation.

In conclusion, the DIABTel system, a telemedicine platform that includes a wireless personal assistant for remote treatment advising, allows better glycemic control in pump-treated patients with type 1 diabetes.

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