Original article

Telemedicine and type 1 diabetes: Is technology per se sufficient to improve glycaemic control?

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Abstract

Aim. – In the TELEDIAB-1 study, the Diabeo system (a smartphone coupled to a website) improved HbA1c by 0.9% vs controls in patients with chronic, poorly controlled type 1 diabetes. The system provided two main functions: automated advice on the insulin doses required; and remote monitoring by teleconsultation. The question is: how much did each function contribute to the improvement in HbA1c?

Methods. – Each patient received a smartphone with an insulin dose advisor (IDA) and with (G3 group) or without (G2 group) the telemonitoring/teleconsultation function. Patients were classified as “high users” if the proportion of “informed” meals using the IDA exceeded 67% (median) and as “low users” if not. Also analyzed was the respective impact of the IDA function and teleconsultations on the final HbA1c levels.

Results. – Among the high users, the proportion of informed meals remained stable from baseline to the end of the study 6 months later (from 78.1 ± 21.5% to 73.8 ± 25.1%; P = 0.107), but decreased in the low users (from 36.6 ± 29.4% to 26.7 ± 28.4%; P = 0.005). As expected, HbA1c improved in high users from 8.7% [range: 8.3–9.2%] to 8.2% [range: 7.8–8.7%] in patients with (n = 26) vs without (n = 30) the benefit of telemonitoring/teleconsultation (−0.49 ± 0.60% vs −0.52 ± 0.73%, respectively; P = 0.879). However, although HbA1c also improved in low users from 9.0% [8.5–10.1] to 8.5% [7.9–9.6], those receiving support via teleconsultation tended to show greater improvement than the others (−0.93 ± 0.97 vs −0.46 ± 1.05, respectively; P = 0.084).

Abbreviations: BG, Blood glucose; CSII, Continuous subcutaneous insulin infusion; FBG, Fasting blood glucose; MII, Multiple insulin injections; PPBG, Post-prandial blood glucose.

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Conclusion. – The Diabeo system improved glycaemic control in both high and low users who avidly used the IDA function, while the greatest improvement was seen in the low users who had the motivational support of teleconsultations.
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Keywords: Telemedicine; Telemonitoring; Decision support software; Type 1 diabetes

1. Introduction

The Diabeo system, comprising a smartphone coupled to an Internet to provide individualized insulin dose adjustment and telemedical support, has been shown to significantly improve HbA1c levels in patients with poorly controlled type 1 diabetes. The two components of the system—the basal and prandial insulin dose advisor (IDA), and the teletransmission of these data to a caregiver, offering brief but helpful telephone consultations every 2 weeks—may both be contributing to HbA1c improvements. In the 6 month open-label, parallel-group, multicentre TELEDIAB-1 study [1], the patients randomized to have access to the full system (as described above; group G3) achieved a 0.9% reduction in HbA1c compared to those randomized to receive only the standard quarterly follow-up (group G1). Intermediate results were obtained in patients randomized to group G2 (given a smartphone with the IDA, but with quarterly visits to their caregiver instead of teleconsultations), who had a 0.7% reduction in HbA1c. In the two groups using the smartphone (G2 and G3), the IDA function undeniably led to a substantial overall improvement in HbA1c. However, its use varied among patients, with some using it regularly at each meal and others less frequently. Based on the actual rate of IDA use by each patient, the aim of our study was, first, to assess the extent to which effective use of the function contributed to improvement in glycaemic control and, second, to build profiles for patients deriving the most benefit from the IDA part of the Diabeo system, and for those who benefited from the telemonitoring and phone consultations providing motivational support.

2. Patients and methods

2.1. Patients

The current work was a post-hoc analytical substudy of TELEDIAB-1, a 6 month, open-label, parallel-group, multicentre study of 180 adult patients with type 1 diabetes (>1 year), using a basal–bolus insulin regimen (>6 months) and having an HbA1c value ≥8% [1]. The patients were randomized to three groups:

- those receiving the standard quarterly follow-up (group G1);
- those with home use of a smartphone with an IDA function as well as quarterly caregiver visits (group G2);
- those given a smartphone with an IDA and access to short teleconsultations every 2 weeks, but no caregiver visits until the end of the study (group G3).

For each patient in groups G2 and G3, the actual rate of use of the IDA function, derived from the proportion of “informed” meals taken, was determined. An informed meal was defined as a meal for which the system proposed an insulin dose based on pre-prandial blood glucose (BG) or fasting blood glucose (FBG) values, physical activity, if any, and the amount of carbohydrates to be consumed, assessed either roughly (“as usual”, “more than usual”, “less than usual”) or precisely (by carbohydrate counting), depending on the carbohydrate assessment method used by the given patient.

All these data were retrievable via the Medpassport database. The median percentage of informed meals was used to determine system high users (whose rates were greater than the median) and low users (whose rates were lower than the median). Clinical characteristics of the high vs low users of the IDA function were also compared.

2.2. Methods

The Diabeo software uploaded into the smartphone has been described elsewhere by Charpentier et al. [1]. It includes a prandial IDA using validated algorithms that take into account pre-prandial self-monitored BG levels; carbohydrate counts and planned physical activity. A basal IDA is also integrated into the system, allowing for adjustment of basal insulin doses or of basal rates when continuous subcutaneous insulin infusion (CSII) is being used. In the event of BG values outside the prefixed target levels, the system suggests adjustments for the carbohydrate-to-insulin ratio, long-acting insulin analogue dose or pump basal rates, all of which can lead to improvements in both prandial and basal algorithms over time.

In addition, all of the data collected by the smartphone could be transmitted to the computers of medical staff via general packet radio service (GPRS) to secure websites, thus, allowing easy telemonitoring and teleconsultation. The Diabeo system was designed by the Centre d’études et de recherches sur l’intensification du traitement du diabète (CERITD; Center for Studies and Research on the Development of Diabetes Treatment) and produced by Voluntis (Paris, France).

No structured face-to-face consultation or teleconsultation plan was required by the protocol, and both types of consultation focused on adapting insulin treatment according to patient data provided by either the patients themselves or via a paper diary (group G1), or the smartphone system (groups G2 and G3). There was no specific educational programme for each type of consultation, although telephone consultations were specifically designed to ensure motivational support by means of regular and frequent contact.

2.3. Statistical analysis

Data were summarized by size and frequency for categorical parameters, and by means and standard deviation for continuous
parameters, as well as by medians and 25th and 75th percentiles where necessary.

Baseline characteristics were compared using Student’s t-test for continuous parameters, and the Mann–Whitney test for non-Gaussian distributions. Independence between qualitative parameters was assessed using the chi-square test. Wilcoxon tests for paired samples were used to compare the percentages of informed meals taken between baseline (the first month of the study) and 6 months later (m6) in each patient group.

Repeated measures analysis of variance (ANOVA) was carried out on monthly intervals between baseline and m6 to compare the relative proportions of informed meals taken in the low users vs high users. Also, as the assumption of sphericity was not satisfied, the Greenhouse–Geisser adjustment was applied. Univariate analyses were carried out using logistic regression models to assess predictors of low or high usage, and the results of this analysis are presented as odds ratios (ORs) with 95% confidence intervals (CIs). A P value <0.05 was considered statistically significant. All statistical analyses were performed using STATA release 12 software for PCs (StataCorp, College Station, TX, USA).

3. Results

3.1. Baseline characteristics of high vs low users

The median percentage of meals with an insulin dose proposed by the Diabeo system was 67% for all patients assigned a smartphone with the IDA function (groups G2 and G3), indicating good compliance. High users (\(n = 56\)) had a median rate of informed meals of 90% [25th–75th percentiles: 77.2–96.1] vs 28.6% [6.2–50.2] in low users (\(n = 57\); \(P \leq 0.001\)). Comparisons between these two groups showed that high users had lower HbA1c values at baseline (\(P = 0.008\)) and were more familiar with carbohydrate counting (\(P \leq 0.001\)). They also tended to be older, to have diabetes of longer duration, and to be more often involved in managerial activities, although these differences were not statistically significant (Table 1).

Univariate analysis revealed that for each additional percentage point of HbA1c at baseline, the probability of being a high user decreased by 40% (OR: 0.58 [0.39–0.87]; \(P = 0.009\)). The probability tended to increase in patients involved in managerial work (OR: 2.71 [0.96–7.67]; \(P = 0.06\)), and was 5.5-fold higher (OR: 5.54 [2.46–12.52]; \(P \leq 0.001\)) in those who used carbohydrate counting.

3.2. Glycaemic control

Both smartphone groups showed significant decreases in HbA1c levels from m0 to m6: from 8.7% [8.3–9.2] to 8.2% [7.8–8.7], \(\Delta = -0.5\% \) [−0.8 to −1.5], in high users; and from 9.0% [8.5–10.1] to 8.5% [7.9–9.6], \(\Delta = -0.8\% \) [−1.5 to −0.10], in low users (Fig. 1). Among low users, the percentage of patients with a >1% reduction in HbA1c was 42.1% (\(n = 24\)) vs only 16.1% (\(n = 9\)) among high users (\(P = 0.002\)). Among high users of the system, the proportion of informed meals was similar (91.2% [74–95.2] in G3 vs 88.7% [78.6–96.1] in G2; \(P = 0.805\)) whether patients had the benefit of teleconsultations (G3: \(n = 26\)) or not (G2: \(n = 30\)). There was also no significant difference in HbA1c at m6 between these two groups: −0.49 ± 0.60 vs −0.52 ± 0.73, respectively (\(P = 0.879\)).

Among low users of the system in G2 (\(n = 26\)) and G3 (\(n = 31\)), the proportion of informed meals was around 30% in both groups (28.4% [6.2–48.9] vs 34.5% [6.1–61.6], respectively; \(P = 0.537\)). However, the reduction in HbA1c was higher for low users in the G3 group who had access to teleconsultation compared with those in the G2 group who had no such access (−0.93 ± 0.97 vs −0.46 ± 1.05), although there was only a trend towards significance (\(P = 0.084\)).

3.3. Follow-up

Among high users (\(n = 56\)), six patients stopped using the system before the end of the study, although their percentages of informed meals were >67% throughout their study involvement. For those who continued with the system (\(n = 50\)), the rate of informed meals remained stable (73.8 ± 25.1% of informed meals at m6 vs 78.1 ± 21.5% at baseline; \(P = 0.107\)).

Of the low users (\(n = 57\)), twice as many stopped using the system vs high users (\(n = 14\) vs \(n = 6\), respectively; \(P = 0.054\)), with one patient not using it at all. Of the low users who continued using the system throughout the study, they had logged details of 25% fewer meals at m6 than at baseline (26.7 ± 28.4 vs 36.6 ± 29.4%, respectively; \(P = 0.005\)).

The average consultation time during follow-up was 66.9 ± 27.1 min for low users in group G2 and 68.2 ± 29.3 min.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>High users ((n = 56))</th>
<th>Low users ((n = 57))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HbA1c (%)</td>
<td>8.7 [8.3–9.2]</td>
<td>9.0 [8.5–10.1]</td>
<td>0.008&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Male patients [(n)%]</td>
<td>19 (33.9)</td>
<td>23 (40.4)</td>
<td>0.480&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age (years)</td>
<td>33 [23–44.5]</td>
<td>25 [21–36]</td>
<td>0.086&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>17 [9–23]</td>
<td>14 [9–19]</td>
<td>0.083&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Managerial activities [(n)%]</td>
<td>13 (23.2)</td>
<td>7 (12.3)</td>
<td>0.128&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Proportion of informed meals (%)</td>
<td>90 [77.2–96.1]</td>
<td>28.6 [6.2–50.2]</td>
<td>(\leq 0.001)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Carbohydrate counting [(n)%]</td>
<td>42 (75)</td>
<td>20 (35.1)</td>
<td>(\leq 0.001)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Data are presented as medians [25th–75th percentiles] unless otherwise stated.

<sup>a</sup> Mann–Whitney test.

<sup>b</sup> Chi-square test.
for low users in group G3 (teleconsultation only). There was also no significant difference between the two groups ($P = 0.866$) in total consultation time whether face-to-face or by telephone. Patients in G2 had only two face-to-face consultations, whereas the mean number of teleconsultations was 9.2 ± 2.4 for low users in G3.

4. Discussion

At a time when a number of meta-analyses have questioned the value of telemedicine in chronic diseases, in general [2,3], and in diabetes, in particular [4], it seemed of major importance to highlight the technical systems that have proved effective for glycaemic control and to identify the subgroups of patients for whom such systems would be most suitable in the long term.

The efficacy of a system embedded in a smartphone and having a dual component has now been demonstrated for the first time in type 1 diabetes patients, involving:

- an automated (real-time) advisor for basal and prandial insulin doses (the IDA);
- a system that transmits data to a medical team, thereby, allowing teleconsultation.

The use of the full Diabeo system with the IDA function plus teleconsultations led to a marked decrease in HbA1c of 0.9% compared to a control population of patients with type 1 diabetes and poor glycaemic control in spite of optimized insulin regimens (multiple insulin injections or insulin pumps) [1]. Intermediate results were obtained for those with access to the IDA function alone (−0.7% in HbA1c values).

Although these mean HbA1c reductions are significant in comparison, recent clinical studies and meta-analyses have shown a maximum reduction of 0.5% for continuous glucose monitoring systems in similar patient populations [5,6] – they do not reflect the diverse patient populations in our G2 and G3 groups, whose interest in the technology is likely to have varied widely from one patient to another. However, as the IDA represented the common component of the Diabeo system in both our G2 and G3 groups, it was our focus in terms of percentages of informed meals according to the databases of patients in both groups and was also used to define our two populations of high and low users.

High IDA users tended to be older, to have longer-standing diabetes and to be more involved in managerial activities; they also displayed statistically significantly greater familiarity with carbohydrate counting. In fact, these patients generally appeared to have less difficulty in coping with their diabetes, as evidenced by less impaired glucose control at baseline. It may also be assumed that their main limitation was the continued use of carbohydrate counting over time. Thus, these patients benefited from the assistance of the IDA function to accurately adjust their basal and prandial insulin doses throughout the study, and they maintained a high level of IDA use regardless of the frequency of teleconsultations. Indeed, it might even be said that HbA1c improvement among high IDA users was to be expected.

In contrast, low IDA users were younger and may have had greater difficulties in both accepting their diabetes and adhering to treatments, as they tended to have poorer glycaemic control at baseline. In these patients, the rate of IDA use was 36% during the first month of the study and continued in a downward trend thereafter.

But what can account for the fact that these low IDA users nevertheless achieved improvements in HbA1c levels? Although a fortuitous reduction (regression to the mean) cannot be excluded, the technological tool represented by the IDA function was not sufficient on its own to explain the improvement in glycaemic control. This suggests that the improvement, if not accidental, could be attributed to the second component of the Diabeo system – the facilitated communication with caregivers.

Within the classifications of high and low users, the impact of the two functions of the Diabeo system was explored by differential analysis of the G2 and G3 groups. Among low IDA users, those in the G3 group had regular contact with caregivers (on average, nine teleconsultations over the 6-month study period), whereas those in the G2 group had only two visits, although the total patient time spent with physician monitoring was similar in both groups. The telephone consultations were primarily intended to provide regular support to patients and
to ensure that they used the system regularly. In fact, it appears
that simply increasing the frequency of even brief consultations,
without necessarily providing any structured motivational
intervention, led to improvement in glycaemic control. These
results suggest that the frequency of consultations had a
major impact on glycaemic control in this patient population.
Thanks to regular interactions between physicians and patients,
improved glycaemic control was achieved by even low users in
G3, independent of their use of the IDA.

Regular contact between caregivers and patients has already
proved effective in reducing HbA1c in patients with diabetes.
In the intensive-therapy group of the Diabetes Control and
Complications Trial (DCCT) [7], patients optimized their insulin
therapy and visited their study centre each month, and were also
contacted more frequently by telephone to review and adjust
their regimens. Although the impact of telephone consultations
per se on HbA1c values could not be determined individually,
it was clear that the telephone consultations contributed to the
significant improvement in metabolic control observed in the
intensive-therapy vs these control groups (HbA1c: 7.3% vs 9.1%,
respectively; mean follow-up: 6.5 years). In addition, it has
already been shown that in type 2 diabetes patients starting basal
insulin therapy, reductions in HbA1c were strongly correlated
with the frequency of both clinical and telephone contacts, and
both constituted independent predictors of HbA1c improvement
[8]. In insulin-dependent diabetic patients with poor glycaemic
control, an intervention consisting of three 15 min calls per week
from a nurse specializing in diabetes to make insulin dose adjust-
ments for 6 months led to a major reduction in HbA1c in the
intervention group compared to the standard treatment group
(−1.8% vs −0.5%, respectively; P < 0.01) [9]. However, albeit
effective [9,10], such phone consultations were time-consuming
[9] and could not be contemplated on a large scale, whereas the
DiaSys system, which allows frequent contact with caregivers,
has been shown here to not increase the amount of time spent by
caregivers on consultations. As the system proposes automatic
adjustments to insulin doses based on predetermined algorithms
established by the attending physician, the latter is no longer bur-
dened with having to deal with daily insulin dose adjustments,
especially in cases of carbohydrate counting. As long as the
patient uses the system, the physicians can focus their attention
on their priority task, which is to ensure their patients’ commit-
tment to improving their glycaemic control and managing their
diabetes more effectively.

The main limitation of the present work is that it was a post-
hoc analysis of the TELEDIAB-1 study, thereby, precluding any
firm conclusions from being drawn. Moreover, as the analyses
were conducted in small subgroups of patients, statistical
significance was not always attained. Finally, although HbA1c
reductions were significant in both our smartphone groups,
the possibility that some of these reductions (particularly, in
low users) may have been fortuitous (regression to the mean)
cannot be ruled out. Nevertheless and despite these limitations,
the present study, which also aimed to build patient profiles,
has addressed a major issue that has been largely ignored until
now, especially in type 1 diabetes patients. Profiling patients
as either “technophiles” (those who find the system appealing)
or “technophobes” (those for whom the system has no great
appeal) may help to identify those patients most likely to benefit
from this technology-based system [11].

In the present analysis, the more marked improvement in
HbA1c among low users in group G3 suggests that while tech-
nology can be helpful for one subset of patients, it may not
necessarily be enough for those who require regular contact with
a caregiver even when provided via such a tool. This point is of
paramount importance for those seeking to further develop these
tools. Is the technology in itself sufficient? It appears that for a
number of patients, most likely those who have the greatest
difficulty in coping with diabetes and its constraints—the primary
benefit of the device was to facilitate interaction with a
caregiver. This aspect is essential to ensure that the tool is not
viewed by patients as simply a gadget, but as a valid means of
providing proper medical support.

Based on our present findings, two critical functions need to
be integrated into the system: a function that allows automatic
data analysis, and generates alerts notifying caregivers if BG
values fall outside the target range or if the system is not
being used enough; and a function dedicated to the delegation
of diabetologist tasks to nurses specialized in diabetes and
telemedicine. Both functions should increase the responsiveness
of the system, allowing caregivers to intervene as soon as a
problem is identified without increasing their workload, as
part of their work has been effectively delegated. This means
that caregivers are then able to focus their interventional work
on those patients who have greater difficulties in coping with
their diabetes and who, in general, tend to require more regular
contact and support from caregivers. Such task delegation and
reorganization of care is especially critical in the current context
of a shortage of diabetologists.

All that remains is to demonstrate that the Diabeo system
equipped with these additional functions can improve metabolic
control in the wider patient population and over a longer period
of time. Another major challenge is to show that the system can
lower treatment costs and be an effective instrument for optimiz-
ing healthcare. These issues are to be addressed in the forthcom-
ing Telesage study, involving 700 patients from around 100 dia-
betes centers for a period of 2 years. Confirmation of these points
will be critical for obtaining reimbursable status for the Diabeo
system from the French National Health Insurance system.

Disclosure of interest

S. Franc and G. Charpentier are members of the Expert Board
of Sanofi-Aventis for the Telesage study. G. Charpentier is the
president of CERITD; S. Franc and D. Dardari have worked
for CERITD for several years. CERITD is the non-profit clinical
translational research centre in Corbeil (Corbeil-Essonnes,
France) that developed the Diabeo system in collaboration with
Voluntis.

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**Appendix A. Supplementary data**

Supplementary data associated with this article can be found, in the online version, at [http://dx.doi.org/10.1016/j.diabet.2013.09.001](http://dx.doi.org/10.1016/j.diabet.2013.09.001).

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