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Impact of long-term use of eHealth systems in adolescents with type 1 diabetes treated with sensor-augmented pump therapy

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Abstract

Telemedicine in diabetes includes telemonitoring and transmission of important data (self monitoring of blood glucose data, insulin therapy, pump setting, etc.) from the patient s home to the diabetic unit, with a real-time health feedback. Moreover, an eHealth approach is thought to facilitate diabetes management and to improve compliance to CSII/SAP treatment in adolescents, but to date, limited literature related to this topic is available and long-term studies are still lacking. The main aim of this study was to compare the long-term effect on glycometabolic control of eHealth intervention and traditional care in T1DM SAP-treated adolescents. In our study we demonstrated a favorable impact of monthly teleassistance on treatment compliance. Adolescents receiving frequent feedback provided by the medicalmultidisciplinary team, due to the telemonitoring, resulted more compliant in self-management of diabetes. In particular, the medical team feedback resulted in interventions on behavioral errors and insulin therapy adjustments, leading to an improved glycometabolic control.

Keywords

Telecare, telemedicine, telehealth, teleconsulting, eHealth

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Background

Type 1 diabetes (T1DM), more frequent in young adults and children, accounts for between 5–10% of all cases of diabetes.[1] The ideal intensive insulin scheme (basal-bolus with insulin analogues, or with human regular insulin, or pump therapy) for children and especially for adolescents with diabetes is controversial. Several treatments have been proposed and numerous meta-analyses of randomized controlled trials showed that mean glycated hemoglobin A1c (HbA1c) levels and hypoglycemic episodes benefit from continuous subcutaneous insulin infusion (CSII) as compared with multiple daily insulin injections (MDIs), both in children and young adults.[2] Mean HbA1c differed between treatments of 0.3–0.6%, with an even greater reduction in patients treated with sensor-augmented pump (SAP) therapy,[3] especially in very young children.[4]

Moreover, pump therapy apparently seems a more practical treatment to fit in patient's daily activities with a direct benefit in terms of quality of life, patient's satisfaction and perceived clinical efficacy.[5] It is well known that particularly in adolescence, when the therapeutic management moves from the parents to the teenagers, acceptance of treatment is one of the major problems in all chronic patients. Typically, during this age period, diabetic patients, although treated with CSII and SAP therapy, show a progressive and temporary deterioration of glucose control due to poor bolus compliance.[6]

Telemedicine (eHealth as mHealth) in diabetes, defined as the use of telecommunications to deliver healthcare services, includes telemonitoring and transmission of important data (self monitoring of blood glucose data, insulin therapy, pump setting, etc.) from the patient's home to the diabetic unit, with real-time health feedback. Especially for diabetic patients who live in remote rural areas with difficult access to health care facilities, tTelemedicine seemed to improve diabetes-related outcomes.[7] Moreover, an eHealth approach is thought to facilitate diabetes management and to improve compliance with CSII/SAP treatment in adolescents.[8] Recently, an online

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website on web-based intervention for adolescents with T1DM demonstrated in fact that the eHealth approach seems to be a promising tool for better disease management.[9] Unfortunately, to date, limited literature related to telemedicine in adolescents with T1DM is available and long-term studies are still lacking. According to the impact of telemedicine on diabetes control, a recent review confirmed discordant results between studies, and results are difficult to compare due to different sample sizes, methodology, and duration of interventions.[10] Larger studies over longer periods of time are needed to determine the lasting effects of telemedical approach.

Objectives

The main aim of this study was to compare the long-term (five years) effect on glycometabolic control of eHealth intervention and traditional care in T1DM SAP-treated adolescents.

Methods

A total of 29 consecutive T1DM, SAP-treated adolescents, followed at Bambino Gesù Children's Hospital, Unit of Endocrinology and Diabetes, were randomly (randomization 1:1) assigned to a telemedical intervention (Group 1), or to a traditional care (Group 2) (in-hospital periodic visits at three-month intervals). The telemedical intervention guaranteed monthly tele-assistance and tele-interaction between the medical team and the patients/families. All the enrolled patients were monitored and followed for a study-period of $\geqslant 5$ years. Patients with a Tanner Stage <IV (pre-pubertal) were excluded from this study. The Tanner System describes the sequence of changes in secondary sexual characteristics and is the staging system utilized most frequently in children and adolescents. Moreover, in order to exclude a potential effect of duration of disease on diabetes compliance and management capacities, patients with diabetes duration <1 year were excluded from the randomization. Furthermore, mean HbA1c level in the year before randomization was evaluated for each study group.

Standard protocol

During the whole study all patients received a regular and standardized protocol of education about correct diabetes control provided by a multidisciplinary team (diabetologist, nurse, dietician, and psychologist). All the patients and their families were given instruction in carbohydrate-counting procedures and were recommended to follow a balanced nutritional program with a calorie intake regularly distributed between carbohydrate (55%), protein (15%) and lipids (30%). Moreover, all of the enrolled subjects followed a similar and regular aerobic physical activity program for a total commitment of three hours per week.

Patients in the telemedicine group were also asked to download monthly glucose and pump parameters on a personal profile of the online website in order to receive regular feedback provided by the medical team during the virtual sessions at one-month intervals. They were also educated and periodically (at 24-month intervals) re-trained to use one of two commercial web-based systems, the Diasend System (Diasend AB Datavägen 14A SE-436 32 Askim, Sweden) or the Interactive Medtronic Platform, Carelink (Medtronic, Northridge, California, USA), in relation to the type of pump used. These two web-based platforms are both freely accessible for patients treated with SAP therapy; both patients and members of the health care team are allowed entry to the website, each with his own user ID and password. The platforms are able to analyze data, assembled in the form of graphs and

Table 1. Study procedures.

	n	Standard protocol	Training for web-based platforms (24-month intervals)	Data download (monthly intervals)	Blood sampling for HbA1c (six-month intervals)	Virtual visit (monthly intervals)	In-hospital visit (three-month intervals)	Data summary (six-month intervals)
Group 1	15	x	x	x	x	x		x
Group 2	14	x			x		x	x

HbA1c: hemoglobin A1c.

Table 2. Study population.

	n	M/F	Age at DM onset, years	DM duration, years	Age at SAP start, years	Mean HbA1c (%)
Group 1	15	5/10	6.7 (0.6)	4.1 (0.7)	12.8 (0.9)	8.1 (0.3)
Group 2	14	6/8	7.1 (0.8)	4.6 (0.8)	13.2 (0.8)	8.2 (0.4)
p		NS	NS	NS	NS	NS

DM: diabetes mellitus; F: female; HbA1c: hemoglobin A1c; M: male; NS: not significant; SAP: sensor-augmented pump.
Data are expressed as mean (standard deviation (SD)) unless otherwise stated.

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Table 3. Complete data for the study.

	n	Age at SAP start (years)	HbA1c 0 (%)	HbA1c 6 (%)	HbA1c 12 (%)	HbA1c 18 (%)	HbA1c 24 (%)	HbA1c 30 (%)	HbA1c 36 (%)	HbA1c 42 (%)	HbA1c 48 (%)	HbA1c 60 (%)	Mean sensor use (day/month)	Mean boluses/day (N°/day)	Mean SMBG/day (N°/day)	Mean follow-up HbA1c (%)
Group 1	15	12.8 (0.9)	8.02 (0.6)	7.2 (0.3)	7.2 (0.4)	7.9 (0.9)	7.8 (1)	7.8 (1)	7.8 (0.8)	7.6 (0.8)	7.3 (0.5)	7.2 (0.6)	14 (6.5)	4.2 (1)	5.5 (0.7)	7.5 (0.3)
Group 2	14	13.2 (0.8)	8.1 (0.7)	7.5 (0.7)	7.6 (0.7)	7.8 (1)	7.9 (1)	7.9 (1.1)	8.1 (1.4)	7.9 (0.8)	8 (0.6)	7.9 (0.7)	9.2 (5.3)	3.3 (1)	3.8 (0.7)	7.8 (0.2)
p		NS	NS	NS	0.04	NS	NS	NS	NS	0.05	0.009	0.001	0.05	0.03	0.001	0.03

HbA1c: hemoglobin A1c; NS: not significant; SAP: sensor-augmented pump; SMBG: self-monitoring of blood glucose.
Data are expressed as mean (±standard deviation (SD)); mean HbA1c for each group is expressed at six-month intervals.

tables, for simple use of both the patients and the health care team.

All patients were evaluated at six-month intervals for HbA1c values. They were also asked to keep a daily home record of frequency of sensor use, insulin boluses per day, self-monitoring of blood glucose (SMBG) tests per day and severe hypoglycemic episodes and all this information was summarized by the health care team at six-month intervals.

Patients in the control group were asked to store their glucose data in a diary (traditional care protocol) to be reviewed by the same medical team only during the ambulatory visits (in-hospital periodic visits at three-month intervals).

Table 1 reports the protocol procedures for each group. The study design conformed to the ethical guidelines of the Declaration of Helsinki (1975), and the Ethics Committee of Bambino Gesù Children's Hospital and Research Institute approved it.

Statistical analysis

In order to determine the optimal number of patients to be consecutively enrolled in the study, when planning the present clinical trial, the calculation of the sample size was performed together with the statisticians. A minimum of 25 participants was considered adequate for this study aiming at obtaining a statistically significant effect of the main variable evaluated (eHealth approach). This means that at least 13 patients were needed in each group in the study.

The recorded outcomes were analyzed using GrafPad software. Differences between the mean values of the two groups were statistically analyzed by student's *t*-test for HbA1c, number of boluses per day and number of SMBG tests per day. When the p-value was <0.05, it was considered as statistically significant. When the p-value was <0.01, it was considered as highly statistically significant.

Results

The study population is described in Table 2. Our results showed that both groups were homogeneous for sociodemographic characteristics. Mean follow-up duration for each group was more than 60 months. Two out of the 29 enrolled patients left the study during the last year of observation because of moving to another diabetes clinic and the described effect and results during the fifth year of follow-up referred to patients continuing the study for all of the observational period. Complete data are reported in Table 3.

In the telemedicine group the frequency of downloading pump/glucometer data was kept constant (a monthly download was requested at the beginning of the study and maintained during the whole follow-up period) and the Diabetes Team regularly reviewed insulin therapy and behavioral adjustments.

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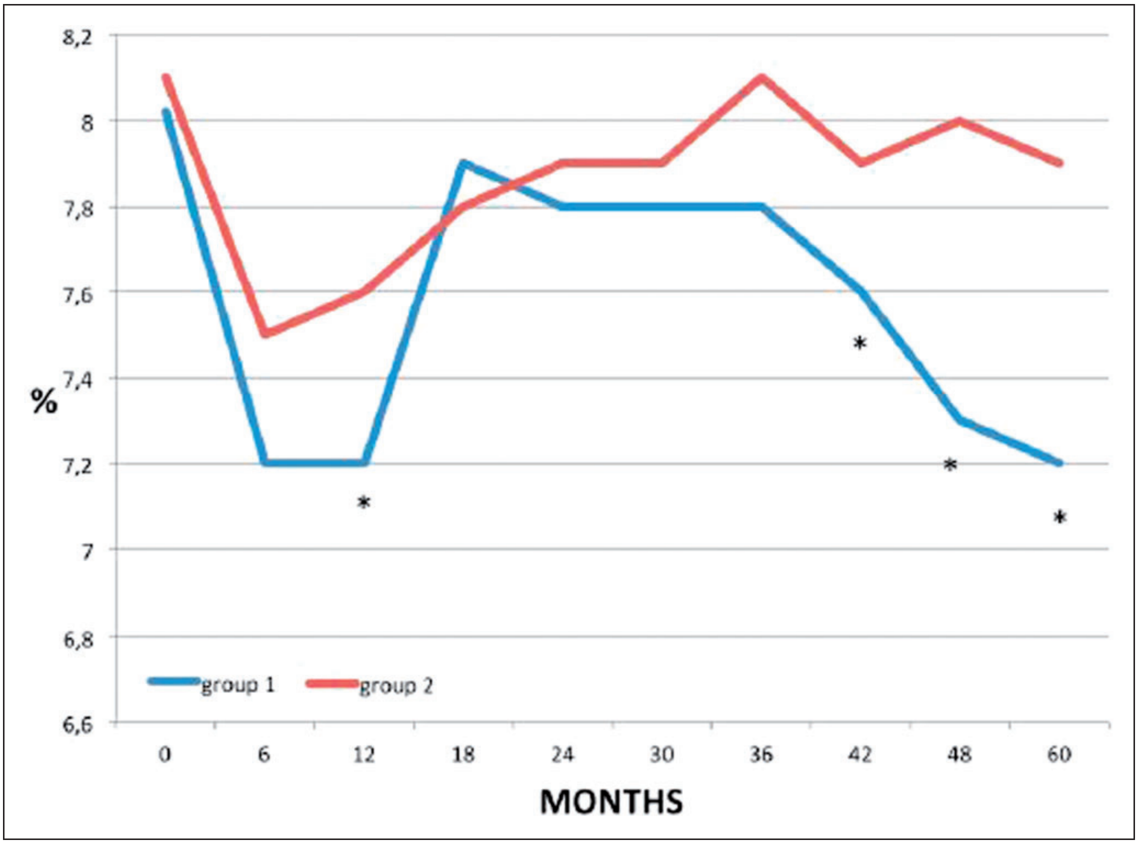

Figure 1. Hemoglobin A1c (HbA1c) (%) levels during the follow-up period (months); * for $p < 0.05$.

Mean HbA1c values during the whole follow-up period were significantly ($p = 0.03$) lower in the telemedicine group (7.5 ± 0.3 %) as compared to the control group (7.8 ± 0.2%). In particular, HbA1c values significantly decreased in the telemedicine group during the first year of therapy as compared to HbA1c in the control group in the same period. Surprisingly, this result was lost up to the third year of follow-up and it was observed again in the last two years of observation, only in the group treated with the eHealth approach. At the end of the study we recorded a value of 7.2% (standard deviation (SD) 0.6), significantly ($p = 0.001$) lower compared to 7.9 % (SD 0.7) of the control group (Figure 1).

As reported in Table 3, the observed HbA1c decrease in the telemedicine group was associated with better treatment compliance in terms of frequency of sensor use, number of SMBG tests and number of insulin boluses. Moreover, a significant difference was found for mean sensor use per month (14 ± 6.5 vs 9.2 ± 5, three days per month; $p < 0.05$), mean SMBG tests per day (5.5 ± 0.7 vs 3.8 ± 0.7; $p = 0.001$) and mean insulin boluses per day (4.2 ± 1 vs 3.3 ± 1; $p = 0.03$) (Table 3) between groups.

Patients monitored without telemedicine (control group) showed HbA1c values between 8–12% and individual patients tended to have higher mean levels of HbA1c equal to 8% or even surpassing this threshold. On the contrary, patients monitored with eHealth systems presented HbA1c levels between 6–10% and individual patients tended to have mean levels of HbA1c lower than 8%.

Discussion

Although SAP therapy is still considered the gold standard of insulin therapy in T1DM, frequently SAP-treated adolescents fail to reach recommended values of HbA1c aimed at prevention of long-term diabetes complications.[11] The eHealth approach is thought to improve compliance in treatment especially in this age group of patients, even though literature is scarce, improvement in primary outcomes such as HbA1c is controversial and possible complications are not well described.[12] In a recent paper, Frøisland and Årsand demonstrated that mobile applications based on visualization seem to be an important way to support young people with diabetes, especially in order to empower them to adjust their treatment schemes.[13] At the same time, another study[14] demonstrated a beneficial effect of telemedical intervention, especially on glycometabolic control. Conversely, other authors[10,15] have suggested that long-lasting studies are needed in order to determine the real effect of telemedicine on glucose control. In our study we compared two groups of SAP-treated T1DM adolescents with a long-term follow-up (five years). The first group was followed with telemedicine, while the second control group was followed

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in a traditional care setting, with periodic in-hospital visits and consultations. The two groups were similar in terms of gender, age at onset of diabetes, duration of diabetes, duration of CSII therapy and mean HbA1c during the year before randomization, with no statistical differences for the aforementioned parameters (see Table 2).

We demonstrated a favorable impact of monthly tele-assistance on treatment compliance. Patients receiving frequent feedback provided by the medical/multidisciplinary team, thanks to the telemonitoring, were more compliant in self-management of diabetes. In particular, the medical team feedback resulted in interventions on behavioral errors and insulin therapy adjustments. Furthermore, given that the two groups did not differ in terms of diabetes duration and mean HbA1c values in the previous year before randomization, the eHealth approach seems to be the distinct, independent variable able to favorably affect glycometabolic control.

In the telemedicine group, the frequency of sensor use, as well as SMBG tests and consequently frequency of insulin boluses, was significantly higher as compared to the control group. Both the improved compliance and the consequent benefit on the overall management of the disease have a direct effect on glycometabolic control. The results of our study, in fact, demonstrated a better level of HbA1c even after a long-term follow-up.

All the enrolled patients presented a Tanner Stage at the beginning of the study between IV–V, therefore the initial improvement in HbA1c, followed by a temporary worsening and then a final improvement, does not seem to be related to the effect of puberty. The initial improvement in both groups could indeed reflect the beneficial effect of new technology when implemented.

In the near future we are planning to develop a new website, also available as an mHealth version. The innovation of this new network is the potential development of a 'Triage App' in order to better manage patients and give them quick and specific feedback. At the same time the new 'Triage App' will be helpful for physicians to have a priority list of answers or patients needs.

In conclusion, our study demonstrated that new technology (telemedicine) added to SAP therapy significantly improves T1DM adolescents' compliance in disease self-management. More and larger studies are needed in order to confirm this interesting data and to better define the most appropriate patient populations for the eHealth approach.

Declaration of Conflicting Interests

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