The Diabetes Interactive Diary – A Useful Tool for Diabetes Management?

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Abstract

Adoption of a flexible diet and insulin therapy for people with type 1 diabetes reduces the daily burden of the disease. In particular, carbohydrate counting and insulin dose adjustment at each meal promote dietary freedom, quality of life and glycaemic control, without worsening severe hypoglycaemia or cardiovascular risk. To overcome the complex education required to adopt this method, the Diabetes Interactive Diary (DID) represents an automatic carbohydrate/insulin bolus calculator in a mobile phone. It also works as a telemedicine system based on communication between patient and physician via text messages. To avoid methodological flaws found in previous studies on similar devices, DID is undergoing a process of evaluation similar to that usually adopted for pharmacological products: first, its feasibility, acceptability and safety were documented in a phase I study; second, its effectiveness on metabolic control, weight loss and quality of life were preliminarily highlighted in a phase II randomised study; and third, a confirmatory phase III randomised trial is currently under way to investigate the DID's impact on glycaemic variability. If the DID's effectiveness is confirmed, it will increase the proportion of patients who may benefit from flexible diabetes management.

Keywords

Type 1 diabetes, carbohydrate counting, insulin therapy, telemedicine system, metabolic control, quality of life

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Advantages of a Flexible Lifestyle in Type 1 Diabetes

Nutritional management is recognised as one of the cornerstones of diabetes care.[1] Medical nutrition therapy in diabetes aims to provide sufficient and appropriate energy intake, encourage healthy lifelong eating habits and achieve and maintain the best possible glycaemic control and ideal bodyweight.[2] A correct nutritional regimen translates into the prevention of both acute complications (such as hypoglycaemia or hyperglycaemia) and micro- and macro-vascular complications.[3] In this context, carbohydrate counting is an important component of nutritional education. It is usually based on estimating the grammes of carbohydrate in the foods being eaten. Insulin bolus is then adjusted to match the dietary carbohydrate at each meal.[4] Without patients being constrained to eat a specific amount of carbohydrate at each meal, carbohydrate counting represents an effective strategy to promote dietary freedom, quality of life and glycaemic control without worsening severe hypoglycaemia or cardiovascular risk.[5–7]

Nevertheless, the widespread use of carbohydrate counting is limited by the complexity of the educational approach. In fact, patients need to be taught about different aspects of nutrition with increasing levels of complexity: level 1, or basic, introduces patients to the concept of carbohydrate counting and focuses on carbohydrate consistency; level 2, or intermediate, focuses on the relationships among food, diabetes medication, physical activity and blood glucose level and introduces the step needed to manage these variables based on patterns of blood glucose levels; and level 3, or advanced, is designed to teach patients who are using multiple daily injections or insulin infusion pumps how to match short-acting insulin to carbohydrate using carbohydrate-to-insulin ratios. Other issues to be learned are portion control, food exchange and glycaemic index.[4,8]

Telemedicine Systems

For at least two decades a number of forces have been focused on the feasibility, acceptability and cost-effectiveness of different diabetes telemedicine applications developed to support education, decision-making, communication and many other aspects of diabetes care.[9] Recent reviews have emphasised the potential benefits of computerised management of diabetes and highlighted the advantages of monitoring and communicating with patients at a distance. Telemedicine solutions for diabetes care are feasible and acceptable, but their effectiveness in improving glycated haemoglobin (HbA_{1c}) levels, reducing costs while maintaining HbA_{1c} levels or improving other aspects of diabetes management is still not strong. This is mainly due to the availability of a large majority of studies with small sample sizes, not randomised design and a short follow-up.[10,11]

Table 1: Description of the Diabetes Interactive Diary System Installed on the Mobile Phone

Glycaemic diary + Bolus calculator + Telemedicine via text message	
Diabetes diary	To record the blood glucose values, time and dose of insulin injections and daily events
Carbohydrate counting	To quantify the total calories and carbohydrates consumed during a meal, selecting the specific food and the amount ingested from a list of pictures
Food exchange	To exchange food included in the patient diet with another one containing the same amount of carbohydrate
Insulin dose calculation	To suggest the most appropriate bolus insulin in relation to the patient carbohydrate-to-insulin ratio, the factor of insulin sensitivity and the blood glucose goal
Physical activity diary	To manage diet and insulin doses, taking into consideration the level of pysical activity
Prevention of complications	To remind of the dates scheduled for the control of diabetes complications
Telemedicine	To send the data filed in the mobile phone as short text messages to the physician

Nevertheless, in the area of carbohydrate counting education and insulin therapy management, new technologies can represent valid support for patients to overcome difficulties linked to the complexity of the education and the chronic burden of the disease on daily life.

The Diabetes Interactive Diary

The Diabetes Interactive Diary (DID), developed by MeTeDa srl, is a new tool incorporating different functions. It is a carbohydrate/insulin bolus calculator, an information technology and a telemedicine system based on communication between healthcare professional (physician or dietician) and patient by text messages.

To avoid the methodological flaws found in previous studies on devices, DID is undergoing a process of evaluation not dissimilar to that usually adopted for pharmacological products: first, its feasibility, acceptability and safety were investigated in a pilot study involving 50 patients (phase I evaluation); second, its effectiveness on metabolic control, weight loss and quality of life was preliminary tested in the context of a randomised study (phase II evaluation); and third, a confirmatory phase III randomised trial is currently under way to investigate the impact of DID on glycaemic variability.

Description of the Diabetes Interactive Diary System

DID is a software that is installed in a mobile telephone and enables it to be used as a small computer to record the blood glucose values and dose of insulin injections in realtime. In addition, the system is able to suggest daily carbohydrate intake, summing the amount of carbohydrate consumed progressively (see *Table 1*). The patient can decide what to eat during each meal, choosing between all the foods listed in the software. The quantification of the total calories and carbohydrate consumed is facilitated by a list of pictures showing the specific food and the amount ingested.

The carbohydrate-to-insulin ratio and the glycaemic correction factor identified and prescribed by the healthcare professional, together with other information already filled out in the DID (e.g. physical activity, glycaemic target, insulin dose and specific events), allow the DID to automatically calculate and suggest any modifications to the insulin dose. In addition, it also includes an algorithm for the calculation of basal insulin dose based on the value of fasting blood glucose and the presence of hypoglycaemic episodes.

In addition to the collection of data on blood glucose measurements, carbohydrate intake and insulin doses, the use of DID is associated with regular feedback for the patient. In fact, data stored in the mobile phone are periodically sent as short text messages and reviewed on the personal computer of the physician. Any new therapeutic and behavioural prescriptions can be sent from the computer to the mobile phone, thereby improving communication between patients and physicians.

Results of the Phase I Study

In the first study on the DID system,[12] 50 patients with type 1 diabetes were involved in a survey with questionnaires administered before and 12 weeks after the start of using a DID. Patients had a mean (standard deviation [±SD]) age of 33.2±8.9 years and a mean diabetes duration of 13.9±9.5 years. Fifty-seven per cent of the patients were treated with multiple injections of insulin and 43% with continuous subcutaneous insulin infusion. Mean levels of HbA_{1c} were 7.2±0.8%. Most of the patients (91.7%) had had at least 13 years of school education (college degree).

The DID system was judged as 'excellent' or 'good' by 94% of the patients, 'extremely useful' or 'very useful' by 65% of them and 'very easy' or 'somewhat easy' to use by 90%. Patients were also asked to rank the different functions of the DID from the most useful to the least useful. The function considered the most useful was carbohydrate counting (mean rank 1.7±1.0), followed by insulin bolus calculation (mean rank 2.3±1.5), food diary (mean rank 2.7±1.1), physical activity diary (mean rank 3.7±1.3) and food exchange (mean rank 3.7±1.4).

Over 63% of the patients declared that the DID had changed their eating habits as a result of a greater knowledge of the relationship between food, blood glucose and insulin dose. During the study the DID system was regularly used by the participants. More detailed information on carbohydrate content of meals was requested, on average, 3.1±1.5 times a day, blood glucose values were recorded 4.8±2.3 times a day and advice on insulin dose was obtained 3.2±1.3 times a day. Communication with the doctor by text was rated as 'extremely effective' or 'very effective' by 85.5% of the patients.

The main limitations of the system pointed out by some of the patients were the slowness of the software and the lack of some foods in the list and pictures.

As for clinical aspects, no significant variations were shown between baseline and end-of-study data in respect of HbA_{1c} (from 7.2±0.8 to 7.2±0.9%) and body mass index (from 23.4±3.2 to 23.6±3.4kg/m^2). No patients reported serious hypoglycaemic episodes requiring medical intervention during the study. In conclusion, DIDs can represent a useful, safe and easy-to-use tool to help diabetes patients enjoy dietary freedom.

Results of the Phase II Randomised Trial

Starting from the findings of the pilot study, an open-label, international, multicentre, randomised (1:1), parallel-group study was designed to evaluate whether the use of the DID could improve

Table 2: Between-group Differences in Clinical Parameters at Visits Two and Three in Respect of Baseline Values

	DID Group (n=67)			Standard Group (n=63)			Between-group Comparison	
	Baseline	3 months*	6 months*	Baseline	3 months*	6 months*	p** (3 vs 0)	p** (6 vs 0)
HbA_{1c} (%)	8.2±0.8	-0.5±0.8	-0.4±0.9	8.4±0.7	-0.4±0.6	-0.5±1	0.95	0.68
FBG (mg/dl)	182.8±85.6	-1.7±105	-22±99.8	176.9±68.4	3.8±94.7	15.5±90.8	0.83	0.13
SBP (mmHg)	121.5±12.8	-1.8±13.7	-0.8±8.6	119.2±11.5	0.4±11	0.7±11.5	0.19	0.71
DBP (mmHg)	74.4±7.5	-2.4±7.9	-1.3±6.5	74.1±7.6	-2.3±6.8	-1.1±7.6	0.83	0.89
Total cholesterol (mg/dl)	179.5±29.9	-3.8±29.1	-3.6±32.3	184.3±34	3.1±26.6	2.7±28.9	0.15	0.33
HDL cholesterol (mg/dl)	57.6±15.3	0.9±9.4	1.6±8.5	61.1±16.4	-1.7±9.8	4.8±10.3	0.49	0.14
LDL cholesterol (mg/dl)	101.9±28	-0.8±26.4	-3.4±29.1	105.8±27.4	5.7±23.3	0.3±27.6	0.26	0.79
Triglycerides (mg/dl)	94.5±54.9	-10.7±48.8	-10.7±56.1	79.9±54	1.9±43.7	8.2±43.4	0.06	0.04
Weight (kg)	69.9±11.8	-0.1±3.8	0.7±3.6	69.4±11.9	0.7±1.9	1.5±2.3	0.15	0.22

*DBP = diastolic blood pressure; DID = Diabetes Interactive Diary; FBG = fasting blood glucose; HbA_{1c} = glycated haemoglobin; HDL = high-density lipoprotein; LDL = low-density lipoprotein; SBP = systolic blood pressure. *Mean variation at visit 2 and visit 3 in respect of baseline values; **p-values refer to Mann-Whitney test.*

Table 3: Between-group Differences in Quality of Life Scores at Visits Two and Three in Respect of Baseline Values

	DID Group (n=67)			Standard Group (n=63)			Between-group Comparison	
	Baseline	3 months*	6 months*	Baseline	3 months*	6 months*	p** (3 vs 0)	p** (6 vs 0)
DTSQ								
Score	26.7±4.4	1.8±3.63	3.39±4.21	27.5±4.8	0.64±3.85	1.03±4	0.2	0.04
Hyper	3.6±1.6	-1±1.36	-0.42±1.7	3.1±1.3	-0.32±1.65	0.2±1.8	0.05	0.19
Hypos	2.3±1.1	0.37±1.34	0.53±1.66	2.5±1.5	-0.2±1.58	-0.1±1.74	0.08	0.16
SF-36								
Physical functioning	90±13.3	-3.27±16.75	4.28±12.3	94.1±8.3	-0.67±11.78	0.19±7.25	0.95	0.22
Role physical	72.5±36.2	8.62±37.95	7.14±42.95	85.8±27.6	-12.06±38.16	0±28.34	0.05	0.27
Bodily pain	78.4±21.5	3.93±18.32	-2.17±23.87	71.2±19.2	-2.51±21.43	10±25.47	0.35	0.09
General health	56±23.3	4.75±8.91	6.47±16.82	61.4±16.4	-2.77±13.1	-4.61±14.69	0.02	0.02
Vitality	57.8±15.8	4.31±10.49	8.21±17.9	66.7±15.7	-5.05±13.88	0.27±14.09	0.02	0.1
Social functioning	73.3±17.3	0.86±15.99	4.46±23.12	76.3±20.3	4.31±19.84	3.33±22.24	0.53	0.8
Role emotional	60±36.5	14.94±40.42	17.85±52.49	83.9±27.8	-4.02±22.56	-4.02±35.53	0.02	0.05
Mental health	68.7±16.3	-0.34±10.92	4±19.22	70.8±14.9	-1.37±12.1	-0.8±12.79	0.67	0.23
Physical component score	50.3±8.9	1.32±6.57	0.61±7.33	50.6±4.9	-1.7±7.03	1.03±4.86	0.09	0.77
Mental component score	43.5±10.63	2.23±8.08	4.23±12.48	48.1±8.1	-0.29±6.77	-0.76±10.18	0.18	0.14

*DID = Diabetes Interactive Diary; DTSQ = Diabetes Treatment Satisfaction Questionnaire; SF-36 = Short-Form 36. *Mean variation at visit 2 and visit 3 in respect of baseline values; **p-values refer to Mann-Whitney test.*

glycaemic control (HbA_{1c}) in a shorter time period and more easily than the carbohydrate counting standard educational approach.[13] Secondary end-points were changes in fasting blood glucose (FBG) levels, bodyweight, lipid profile (serum total cholesterol, high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol and triglycerides) and blood pressure. In addition, some safety issues (frequency of hypoglycaemic episodes and hospitalisations) and resource consumption (differences in time dedicated to educational activities and extra visits and average cost of text messages) were taken into consideration. Finally, changes in health-related quality of life were evaluated in the subgroup of Italian patients using generic (SF-36 Health Survey and World Health Organization [WHO] Well Being Questionnaire) and diabetes-specific (WHO Diabetes Treatment Satisfaction Questionnaire [DTSQ]) measures.

The study involved seven diabetes outpatient clinics: three in Italy, two in England and two in Spain. All of the centres habitually adopted carbohydrate counting education and used electronic databases. Every centre enrolled 20 patients ≥18 years of age with type 1 diabetes who had not previously been educated in carbohydrate counting but had been treated with multiple daily injections of short-acting and long-acting insulin analogues or with continuous subcutaneous insulin infusion. The patients practised self-monitoring of blood glucose at least three times a day.

Eligible patients were randomised to start the standard carbohydrate counting educational programme or the DID approach. Randomisation was performed through a telephone call to the co-ordinating centre. Random lists were stratified by centre. To ensure equal allocation rates within centres, permuted block randomisation was used. Patients randomised to the experimental group attended a course on the use of the DID lasting up to two weeks. The course was provided as an outpatient programme of three encounters with a physician and/or dietician. Patients randomised to the control group received the standard educational approach lasting up to three months. Every centre used its own usual standard educational approach. Overall, nine patients withdrew from the study, of whom two were in the standard group and seven in the DID group. Clinical changes after three and six months are shown in *Table 2*.

A significant reduction in HbA_{1c} levels of about 0.5% was documented in both groups after three months and maintained to

the end of study. This improvement in metabolic control was obtained by devoting to carbohydrate counting education a median of six (two to 15) hours in the DID group and of 12 (2.5–25) hours in the standard group (p=0.07). In addition, after six months FBG decreased in the DID group (from 182.8±85.6 to 162.9±67.0mg/dl) and it increased in the standard group (from 176.9±68.4 to 186.3±79.1mg/dl; p=0.13). Increases in bodyweight were lower in the DID group (+0.7±3.6kg) than in the standard group (+1.5±2.3kg; p=0.22), probably as a consequence of lower doses of insulin required. In fact, although we found no differences in mean daily doses of short-acting insulin between the two groups (DID group: 20.6±8.2UI/die; standard group: 20.1±7.8UI/die; p=0.92), mean daily doses of long-acting insulin were lower in the DID group than in the standard group (DID group: 17.4±7.4UI/die; standard group: 21.4±10.0UI/die; p=0.12). As for the other clinical parameters investigated, the DID group showed a significant decrease in triglyceride levels in comparison with the standard group. No other between-group changes were documented.

Within-group changes were also considered. The DID group generally showed a tendency towards a small, not significant improvement in all of the measures considered, whereas in the standard group all parameters, except diastolic blood pressure and HDL cholesterol, tended to slightly increase at the end of the study. No patients in either group were admitted to hospital during the study, and none reported any severe hypoglycaemic episodes requiring assistance. In each group, two patients reported episodes of mild hypoglycaemia (p=0.93). The median number of outpatient visits during six months was four (two to six) for the DID groups and three (zero to four) for the standard group (p=0.01).

The median (range) number of text messages sent by each patient during the study was 52 (six to 75), and the median number of text messages sent by the physician was 39 (22–70). In other words, patients sent about two text messages per week to their physician, and the physician regularly replied to confirm the therapeutic scheme or to modify the parameters set in the DID (carbohydrate-to-insulin ratio, insulin sensitivity factor and/or blood glucose goal). In terms of costs for the patient, assuming a cost of 10–15 cents per message and considering that, on average, each patient sent 52 text messages, the overall cost sustained did not exceed eight euros.

Results of the quality of life evaluation performed on the subsample of 60 patients enrolled in the Italian centres are shown in *Table 3*. A statistically significant difference in favour of the DID group was documented for treatment satisfaction, as expressed by the DTSQ score. Similarly, the score testing the perceived frequency of hyperglycaemic episodes significantly decreased after three months in the DID group but not in the control group. Several SF-36 subscales (role physical, general health, vitality and role emotional) also showed significantly higher improvements in the DID group than in the standard group.

Conclusions

These results suggest that the use of DID is at least as effective as the traditional educational approach to carbohydrate counting, but it allows avoidance of the complexities of carbohydrate counting, thus increasing dietary freedom for a larger proportion of individuals with type 1 diabetes. The use of DID is also associated with lower weight gain, probably due to the requirement of lower doses of long-acting insulin. In addition, it is associated with a halving in the time dedicated to education and does not increase the risk of severe hypoglycaemic episodes. Finally, the use of DID significantly improved several quality of life dimensions.

A new confirmatory, open-label, national, multicentre, randomised (1:1), parallel-group study involving 13 Italian centres and 130 patients is currently ongoing. The new study aims to compare the impact of DID education versus usual practice on HbA_{1c} levels, glycaemic variability and all the parameters already included in the previous trial in patients treated with the same insulin regimen (insulin glargine and prandial insulin glulisine). In addition, the DID system has been further improved based on previous experience, and the DID educational intervention has been standardised carefully. The sample has been estimated to allow the detection of a difference of 0.5% in HbA_{1c} levels between groups, with a statistical power of 80%.

The trial will allow the achievement of definite conclusions on the effectiveness of the system. If its effectiveness is confirmed when introduced into the market, it will be able to increase the proportion of patients who can obtain benefits from carbohydrate counting and insulin adjustment. ■

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