ORIGINAL RESEARCH

Efficacy of A1C Reduction Using Internet Intervention in Patients with Type 2 Diabetes Treated with Insulin

Hugh D. Tildesley[1,2] MD, Adel B. Mazanderani[2] BSc, Jeremy H.M. Chan[3] BA, Stuart A. Ross[4] MD

[1]Department of Endocrinology and Metabolism, St. Paul's Hospital, Vancouver, British Columbia, Canada
[2]University of British Columbia, Vancouver, British Columbia, Canada
[3]Endocrine Research Society, Vancouver, British Columbia, Canada
[4]University of Calgary, Calgary, Alberta, Canada

ABSTRACT

OBJECTIVE: To assess the effect of an Internet-based glucose monitoring system (IBGMS) on glycated hemoglobin (A1C) levels in patients with type 2 diabetes mellitus treated with insulin.

METHODS: Fifty patients were randomly assigned to receive conventional care alone (control) or additional follow-up via IBGMS for 6 months. Patients randomized to the IBGMS group uploaded blood glucose readings to a secure website every 2 weeks to receive feedback from their endocrinologist. After 6 months, all patients returned to conventional care. A1C and laboratory test results were collected at 0, 3, 6 and 12 months.

RESULTS: Baseline parameters were not significantly different. After a 6-month follow-up, A1C dropped from 8.8% to 7.6% (p<0.001) in the IBGMS group vs. the control group, which showed no significant change (8.5% to 8.4%, p=0.51). Both groups then returned to conventional care, and after 12 months, the A1C differences in the IBGMS and control groups were not sustained (8.2% vs. 8.5%, p=0.35).

CONCLUSION: IBGMS significantly improved A1C levels in patients with type 2 diabetes treated with insulin, but this effect was lost with cessation of the intervention.

KEYWORDS: Internet-based blood glucose monitoring, remote monitoring, type 2 diabetes

RÉSUMÉ

OBJECTIF : Évaluer l'effet d'un système de surveillance de la glycémie par Internet (SSGPI) sur les taux d'hémoglobine glycosylée (HbA_{1c}) chez des patients insulinotraités atteints de diabète de type 2.

MÉTHODES : Cinquante patients ont été répartis au hasard pour recevoir les soins classiques seuls (groupe témoin) ou en association au SSGPI pendant six mois. Les patients du groupe SSGPI ont téléchargé leurs glycémies vers un site Web sécurisé toutes les deux semaines et reçu des commentaires de leur endocrinologue. Après six mois, les patients de ce groupe ont cessé d'utiliser le SSGPI. Les taux d'HbA1c et d'autres paramètres de laboratoire ont été déterminés au départ et après trois, six et douze mois.

RÉSULTATS : Il n'y avait pas de différences significatives entre les groupes pour ce qui est des paramètres initiaux. Après six mois, le taux d'HbA_{1c} avait baissé : il était de 7,6 % (par rapport à 8,8 % au départ; p < 0,001) dans le groupe SSGPI et de 8,4 % (par rapport à 8,5 % au départ; p = 0,51) dans le groupe témoin. L'utilisation du SSGPI a été abandonnée et, après douze mois, il n'y avait plus de différence entre le groupe SSGPI et le groupe témoin pour ce qui est du taux d'HbA_{1c} (8,2 % et 8,5 %; p = 0,35).

CONCLUSION : Le SSGPI a significativement amélioré les taux d'HbA_{1c} chez les patients insulinotraités atteints de diabète de type 2, mais cet effet a disparu après la fin de l'intervention.

MOTS CLÉS : surveillance de la glycémie par Internet, surveillance à distance, diabète de type 2

INTRODUCTION

In the management of diabetes mellitus, self-monitoring of blood glucose (SMBG) is performed as an adjunct to glycated hemoglobin (A1C) measurements in order to assess and modify treatment (1-3); however, it often requires healthcare professionals to help interpret these results to refine treatment (4-6). The Internet provides a readily accessible platform for communication and remote health monitoring (7). In this study, we evaluated whether the use of an Internet-based glucose monitoring system (IBGMS)

Address for correspondence: *Hugh D. Tildesley, Room 416, 1033 Davie Street Vancouver, British Columbia, Canada V6E 1M7. E-mail: hught@istar.ca*

would improve the outcome of care for patients with type 2 diabetes compared to conventional care alone.

METHODS

We enrolled 50 patients with type 2 diabetes treated with insulin, either alone or in combination with oral antihyperglycemic agents. Inclusion criteria included a recent A1C >7.0%, Internet access and prior training in SMBG. Patients were randomly assigned to IBGMS or a control group for 6 months using a computer random number generator. All patients were provided with a blood glucose meter and test strips for testing at least 3-times daily, and were asked to perform a laboratory blood test and visit their endocrinologist at 3 and 6 months. All patients met with the same endocrinologist and were provided with standard office-based care.

Patients randomized to the control group were asked to keep a diary of SMBG to bring to their endocrinologist. Patients randomized to the IBGMS group were asked to upload their SMBG readings every 2 weeks to a secure, commercially available website (ALR Technologies Inc, Atlanta, Georgia). The preliminary results of this intervention are documented elsewhere (8), and more details of the web-based care can be found at www.alrt.com. Data were presented in table and graph formats according to time of day, and automatic calculations were done to show the mean, standard deviation and range for specific time periods. The system allowed patients to input medications, set alarms, view summaries of readings and contact their endocrinologist, who viewed the readings and sent feedback through the ALR messaging system. Patients randomized to the control group were given the option of calling the endocrinologist when they needed assistance. Neither group was taught how to interpret SMBG results, although as part of the inclusion criteria, all patients had completed prior training in SMBG. The endocrinologist's recommendations included changes in insulin dosage, suggestions on testing frequency or giving compliments. A1C values were measured in both groups at 0, 3, 6 and 12 months.

Baseline demographic data were collected from patient charts. A1C values were measured using the ADVIA Centaur Immunoassay System (Siemens, Tarrytown, New York). Data were analyzed using a computer database (Excel, Microsoft Inc., Redmond, Washington) and SAS statistical software (SAS Institute Inc., Cary, North Carolina). Paired sample and independent Student's t-tests were used to compare within- and between-group changes, respectively. The primary outcome was difference in A1C between the IBGMS and control groups at 12 months. Differences between A1C levels were evaluated by performing analysis of covariance that tested between-group changes from the start to the end of the study while adjusting for baseline values. Analysis of variance was performed to see whether changes in A1C correlated with upload compliance on the IBGMS. For all analyses, statistical significance was established at $p<0.05$.

RESULTS

Key demographic and baseline clinical characteristics are summarized in Table 1. Four patients (2 from each group) were excluded because they were nonadherent. Differences between the 2 groups at 6 months post-intervention was statistically significant only for A1C (8).

The IBGMS group showed a statistically significant decrease in A1C from baseline (8.8±1.3%) to 3 months (8.2±0.9%, p=0.053) and 6 months (7.6±0.8%, $p<0.001$). The control group, on the other hand, had A1C levels that were statistically equivalent (Table 2). The baseline A1C-adjusted differences in 6 month A1C were –1.3% and –0.1% for the IBGMS and control groups, respectively ($p<0.05$). However, 6 months after both groups had returned to conventional care (12 months from baseline), A1C in the IBGMS group returned to baseline levels

Table 1. Demographic and baseline clinical characteristics of the study population

Characteristic	*IBGMS (n=23)**	*Control (n=23)**	*p value*
Age, y	57±10	62±7.2	0.097
Male/female, n	14/9	15/8	
Duration of diabetes, y	19.1±9.4	18.8±6.4	0.898
BMI, kg/m^2	33.6±6.5	33.1±6.0	0.799
A1C, %	8.8±1.3	8.5±1.2	0.420

Unless otherwise indicated, data are shown as mean±SD
*Two subjects in the control and IBGMS groups did not follow protocol and were excluded

A1C = glycated hemoglobin
BMI = body mass index
IBGMS = Internet-based glucose monitoring system

Table 2. Changes in A1C for control vs. IBGMS groups

	IBGMS A1C, % (n=23)	*Control A1C, % (n=23)*	*p value*
Start	8.8±1.3	8.5±1.2	0.42
3 months	8.2±0.9	8.3±1.1	0.60
6 months	7.6±0.8†	8.4±1.4	<0.05*
12 months	8.2±1.0‡	8.5±1.3	0.35

Unless otherwise indicated, data are shown as mean±SD
*Statistically significant, IBGMS vs. control; analysis adjusted for baseline A1C
†Statistically significant vs. A1C at start and 3 months ($p<0.001$)
‡Statistically significant vs. A1C at 6 months ($p<0.05$), but not vs. start (p=0.055)

A1C = glycated hemoglobin
IBGMS = Internet-based glucose monitoring system
NA = not applicable

(8.2±1.0%, p=0.055) and were no different from those of the control group (8.5±1.3%, p=0.35).

The IBGMS group had the option to upload their data 12-times within the 6-month period. On average, patients in the IBGMS group uploaded 71.9% (range 28%–94%) of the time, with an average of 9.4 uploads. The percentage of uploads on the IBGMS was not correlated with change in A1C (p=0.51) after 6 months. Two patients from the IBGMS group were excluded from the above analyses because they were nonadherent.

DISCUSSION

Patients with diabetes treated with insulin are often concerned about the risk of hypoglycemia and/or hyperglycemia. To avoid these situations, frequent SMBG testing is required. However, a significant number of patients require communication with their physician to interpret these results and modify insulin dosage to achieve glucose targets. We used and tested an IBGMS to test whether communication over the Internet was sufficient enough to improve glycemic control.

In our study, patients randomized to the IBGMS group had significant A1C improvement after 6 months. Both study groups were provided with resources for testing blood glucose levels and met with an endocrinologist at 3 and 6 months. The only difference was that the IBGMS group was asked to upload their blood glucose levels onto an Internet platform. Almost all study patients in the IBGMS group, except 2 who were nonadherent and excluded from analysis, uploaded their data regularly, as they were frequently reminded to test and upload their data through the ALR messaging system. This ongoing communication allowed the endocrinologist to recommend changes in insulin dosage and regimen, and/or patterns of testing as needed to direct redistribution of the insulin regimen. At 12 months, both groups returned to pre-study A1C levels after resuming conventional care for 6 months. Our results demonstrate that the improvement during the study was not sustained after discontinuation of the IBGMS intervention, indicating that constant communication is required for optimal care. It should be noted that all patients attend a comprehensive 4-day education course when diagnosed with diabetes. As such, they have already been taught blood glucose goals and insulin adjustment. Despite this standardized education, further improvement was seen in the IBGMS group. This improvement reversed to baseline when the intervention was withdrawn.

There are several limitations to this study. We monitored only glycemic control, and thus some factors that were not measured may have confounded the results. In the 6 months of conventional care following IBGMS, we did not monitor the number of blood glucose tests being used and did not supply patients with test strips. Therefore, changes in A1C levels could result from a lower number of SMBG tests performed by the IBGMS group. However, the control group did not have access to these resources either, and their A1C levels stayed the same. Furthermore, all patients were testing regularly, because they were administering insulin and were seen by an endocrinologist within 3 to 6 months. The period of conventional care also mimics the real world, where patients are seen every 3 or 6 months, with no recurrent follow-ups in between.

The advantages of using an IBGMS include automatic uploading, eliminating the need for patients to keep a written diary. In addition, the uploaded data can be analyzed and displayed in table and graph formats, giving a sense of glucose trends and monitoring frequency. This can save time for the physician and increase the accuracy of data interpretation (9). Limitations of the system include patient's unwillingness or lack of desire to use the Internet and the absence of a payment model to reimburse out-of-office consultations.

Previously published studies have also shown improvements in A1C levels in patients with type 2 diabetes who used an IBGMS system compared to controls (10-12). However, these studies involved nurses, dietitians or an electronic medical records system, while our study was limited to the patient's endocrinologist monitoring and making recommendations based on an IBGMS. While this was not a substitute for the patient–physician interaction in a clinical setting; however, it significantly improved A1C and, over time, we observed better glycemic control and patient satisfaction. This method of follow-up can reduce the inconvenience of booking appointments solely for giving recommendations on changes in insulin dosage and may be a more cost-effective method of follow-up, especially for rural patients where access to a diabetes specialist is limited. In summary, the continuous use of an IBGMS is an effective method of improving glucose control compared to standard care.

AUTHOR DISCLOSURES

This work was supported by Endocrine Research Society (Vancouver, British Columbia), which received funding from ALR Technologies Inc. We extend our appreciation to Abbott Diabetes Care Inc. for their generous gifts of glucose meters and test strips.

AUTHOR CONTRIBUTIONS

HT designed the study; developed the protocol; collected and interpreted data; and wrote, reviewed and edited the manuscript. AM contributed to protocol development; collected, analyzed and interpreted data; and wrote, reviewed and edited the manuscript. JC analyzed and interpreted

data; and wrote, reviewed and edited the manuscript. SR contributed to the study design and protocol development; interpreted data; and reviewed and edited the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Dailey G. Assessing glycemic control with self-monitoring of blood glucose and hemoglobin A(1c) measurements. *Mayo Clin Proc.* 2007;82:229-236.
2. Austin MM, Haas L, Johnson T, et al. Self-monitoring of blood glucose: benefits and utilization. *Diabetes Educ.* 2006;32:835-847.
3. Nielsen JK, Christiansen JS. Self-monitoring of blood glucose—epidemiological and practical aspects. *Diabetes Technol Ther.* 2008;10:S35-S42.
4. American Diabetes Association. Standards of medical care in diabetes—2008. *Diabetes Care.* 2008;31(suppl 1):S12-S54.
5. Klonoff DC, Bergenstal R, Blonde L, et al. Consensus report of the coalition for clinical research—self-monitoring of blood glucose. *J Diabetes Sci Technol.* 2008;2:1030-1053.
6. Hirsch IB, Bode BW, Childs BP, et al. Self-monitoring of blood glucose (SMBG) in insulin- and non-insulin-using adults with diabetes: consensus recommendations for improving SMBG accuracy, utilization, and research. *Diabetes Technol Ther.* 2008;10:419-439.
7. Meystre S. The current state of telemonitoring: a comment on the literature. *Telemed J E Health.* 2005;11:63-69.
8. Tildesley HD, Mazanderani AB, Ross SA. Effect of Internet therapeutic intervention on A1C levels in patients with type 2 diabetes treated with insulin. *Diabetes Care.* 2010;33:1738-1740.
9. Azar M, Gabbay R. Web-based management of diabetes through glucose uploads: has the time come for telemedicine? *Diabetes Res Clin Pract.* 2009;83:9-17.
10. Kwon HS, Cho JH, Kim HS, et al. Establishment of blood glucose monitoring system using the Internet. *Diabetes Care.* 2004;27:478-483.
11. Cho JH, Chang SA, Kwon HS, et al. Long-term effect of the Internet-based glucose monitoring system on HbA1c reduction and glucose stability: a 30-month follow-up study for diabetes management with a ubiquitous medical care system. *Diabetes Care.* 2006;29:2625-2631.
12. Ralston JD, Hirsch IB, Hoath J, et al. Web-based collaborative care for type 2 diabetes: a pilot randomized trial. *Diabetes Care.* 2009;32:234-239.