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Self-Monitoring of Blood Glucose in Type 1 Diabetes Patients with Insufficient Metabolic Control: Focused Self-Monitoring of Blood Glucose Intervention Can Lower Glycated Hemoglobin A1C

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Abstract

Objective:

Little attention has been given and few studies have been published focusing on how to optimize self-monitoring of blood glucose (SMBG) use to monitor daily therapy for persons with type 1 diabetes mellitus. This study was designed to evaluate the effect on glycated hemoglobin (A1C) of a structured intervention focused on SMBG in type 1 diabetes patients with insufficient metabolic control (A1C ≥ 8%) using a randomized clinical trial design.

Method:

One hundred fifty-nine outpatients with type 1 diabetes on multiple injection therapy with insulin and A1C ≥8% were recruited and randomized to one group receiving a focused, structured 9-month SMBG intervention (n = 59) and another group receiving regular care based on guidelines (n = 64).

Results:

Glycated hemoglobin values (mean % ± standard deviation) at study start was similar: 8.65 ± 0.10 in the intervention group and 8.61 ± 0.09 in the control group. The two groups were comparable (age, gender, body mass index, complication rate, and treatment modality) at study start and had mean diabetes duration and SMBG experience of 19 and 20 years, respectively. At study end, there was decrease in A1C in the intervention group ($p < .05$), and the A1C was 0.6% lower compared with the control group ($p < .05$). No increase in the number of minor or major hypoglycemia episodes was observed in the intervention group during the study period.

Conclusions:

A simple, structured, focused SMBG intervention improved metabolic control in patients with longstanding diabetes type 1 and A1C ≥ 8%. The intervention was based on general recommendations, realistic in format, and can be applied in a regular outpatient setting.

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Abbreviations: (A1C) glycated hemoglobin (ADA) American Diabetes Association, (BG) blood glucose, (CSII) continuous subcutaneous insulin infusion, (CV) coefficient of variance, (SD) standard deviation, (SMBG) self-monitoring of blood glucose, (WHO) World Health Organization

Keywords: A1C, glycemic control, self-monitoring of blood glucose, type 1 diabetes

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Introduction

Patients with type 1 diabetes started using instruments for self-monitoring of blood glucose (SMBG) in the early 1980s. This quickly became the cornerstone in daily blood glucose (BG) management in type 1 diabetes, making patients better able to adjust their insulin doses and monitor for hypoglycemia. Early studies showed promising benefits from SMBG, although some questioned a possible risk of increased hypoglycemia related to insulin overdosing.[1–4] In type 2 diabetes, its value has been questioned.[5,6] Randomized clinical studies of insulin treatment in diabetes have SMBG as an integrated part of their intervention, although the main study focus remained the treatment itself.[7–10] A common yet not thoroughly evaluated clinical recommendation for type 1 patients is to perform SMBG 3–4 times/day, although clinical recommendations should be individualized.[11,12]

Virtually all patients with type 1 diabetes in Norway perform SMBG, a practice that has been unchanged since the 1980s. The analytical quality of instruments and the potential benefit of SMBG have improved considerably during this period, resulting in reduced risk of miscalculating insulin doses.[13] Several reports question whether the daily frequency of SMBG is less than what is needed to monitor type 1 diabetes patients properly,[11,14] and although SMBG has been available for a long time, little attention has been given on how to optimize SMBG use to monitor daily diabetes therapy.[15] The role of SMBG in diabetes care has been widely discussed, including monitoring frequency and more effective ways to take actions based on the SMBG results.[11,12,16,17] A consensus conference has made recommendations on SMBG, an integral but underutilized part of disease management.[11] Many diabetes clinics will have a therapeutic challenge with a group of patients with long diabetes duration and SMBG experience where the metabolic control is still insufficient. This group of patients may have different barriers to improve BG control, and they perform SMBG but without reaching recommended treatment targets. Can the SMBG tool that every type 1 diabetes patient already uses be applied in a better way? We designed the "MEASURE" (Metabolic Effects of Accurate Blood Sugar Results and Education in Type 1 Diabetes) trial to evaluate the effect of a simple, structured, realistic SMBG intervention on the metabolic control in patients with type 1 diabetes and longstanding experience in performing SMBG.

Patients and Methods

The study was performed between September 2004 and September 2006 at the diabetes outpatient clinic at Stavanger University Hospital, Stavanger, Norway. The clinic serves an urban and nonurban population of approximately 310,000 people, and no other clinic in the area provides a similar specialized service. Most type 1 patients in the catchment area received their routine care at this clinic. When the patients attended regular diabetes visits with an endocrinologist, a diabetes nurse, or a podiatrist, they were recruited and randomized consecutively. The general design of the intervention was based on our own clinical experience and current SMBG recommendations by the American Diabetes Association (ADA)[18] and the World Health Organization (WHO).[19] The ADA states that SMBG should be an integrated part of diabetes care, be included in the management plan, and include evaluation of SMBG performance and technique to enable patients to use the data for therapy adjustment. The WHO recommends building up BG profiles by performing SMBG at specific times of the day/night. In Norway, an unlimited number of strips for SMBG are reimbursed, and patients can perform SMBG without financial costs.

Only type 1 diabetes patients were eligible for the 9-month study. Inclusion criteria were most recent measured glycated hemoglobin (A1C) ≥ 8%, treatment with multiple insulin injections or continuous subcutaneous insulin infusion pump (CSII), 18–70 years of age, and a SMBG user. Exclusion criteria were unstable condition with more than 5 kg weight variation or more than 1.5% variation in A1C within past 12 months, hypoglycemia unawareness, mental instability, or any condition limiting the patients ability to follow the study protocol. All patients had received comparable care and follow-up before inclusion in the study. Educational levels and social class were not assessed specifically. No survey for depression or general well-being was performed. Patients would have a set of reasons for insufficient metabolic control and complex explanations. All patients with elevated A1C received special attention on this issue to reach treatment targets. We included 134 patients: 69 randomized to the intervention and 65 to the control group. The patients in the intervention group were immediately scheduled for their first study visit after signing the informed consent form. The patients in the

control group received regular diabetes care according to guidelines and were asked for participation and signed the consent form when returning for a regular visit approximately 9 months after randomization time. This design was carefully chosen to avoid disclosing the randomization code to the caregivers and their possible influence from the caregivers on study results. This was based on the fact that patients were included in a study focusing on the tools and targets already used in daily practice. We found this approach to be an advantage when performing the randomization in only one clinic involving relatively few professionals. Ten patients in the intervention group refused to participate for personal reasons and due to time limits or were excluded during the study due to mental disease and instability. One patient in the control group refused to participate.

The control group continued to receive regular diabetes care according to Norwegian guidelines. Norwegian guidelines recommend daily SMBG performance, weekly eight-point SMBG profiles, and an A1C goal of <7.0–7.5%.[20] All patients performed a number of additional measurements for monitoring hypoglycemia. For consultations, patients usually brought their written BG results or their instrument where BG values are available in the instrument memory function. For a patient with insufficient metabolic control, all areas of possible intervention were assessed. A regular visit usually lasted approximately 30 min. The patients would normally attend a minimum of one clinical visit at the outpatient clinic in the period between randomization and the final 9-month study visit. **Figure 1** outlines the overall study design.

Intervention patients were scheduled for six visits (including inclusion and final visit) over the 9-month study period. At the first study visit, the intervention group was introduced to HemoCue Monitor (HemoCue AB, Ängelholm, Sweden), a new, accurate glucose instrument for daily SMBG performance (coefficient of variance [CV] 2.3% and bias of 2.4%, compared to a standardized comparison method). The consultation performed by a diabetes nurse and a biomedical laboratory scientist was strictly focused on correct SMBG performance, on knowledge about individual variations in BG values in daily life, and on actions to be taken based on the results. The patient SMBG performance with the instrument was assessed and reinforced at every visit. To make patients enhance their focus on BG self-management, the patients received and brought a BG diary for BG profiles at every visit, a "fasting BG map," and a hypoglycemia registration. The 10-point BG profile (for three different

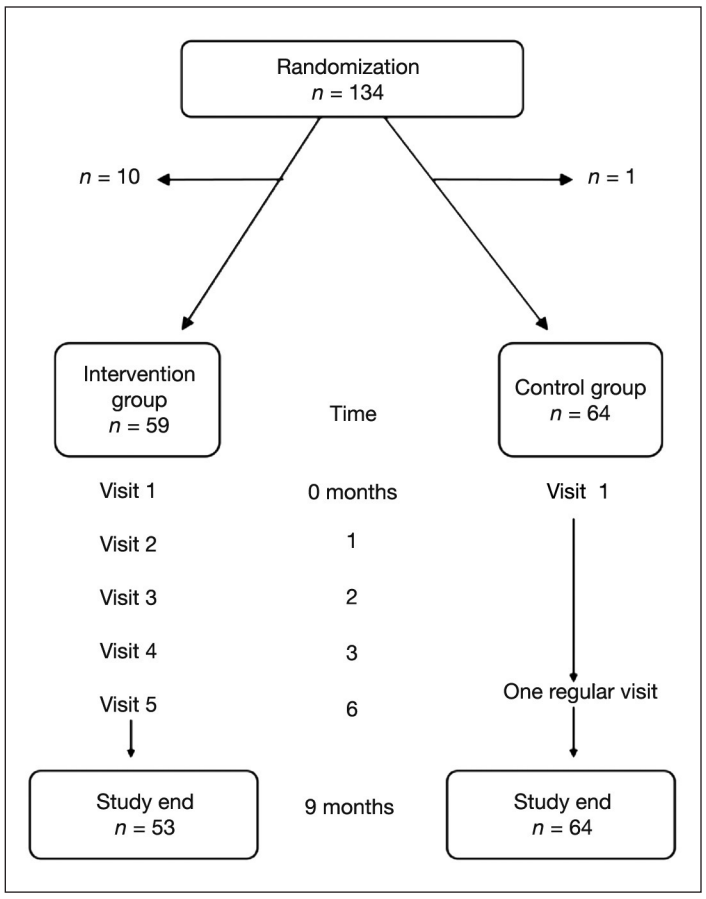

Figure 1. Study overview and design.

days) included measurements before and after (1.5 h) every meal (usually four meals) and one 3:00 AM value for each visit and also included corresponding insulin doses. The patients provided daily fasting BG values at every visit, marked and visualized on a "BG map" included in the BG diary. The diary also included registration of major (requiring assistance) and minor hypoglycemias (symptomatic or plasma glucose below 45 mg/dl [2.5 mmol/liter]). Meters were downloaded, but no comparison was done with logbooks, and the intervention was based on written logbooks, although some patients would use meter memory to add SMBG information and number of measurements to the discussion with the study nurse. At every visit, patterns of SMBG and BG values were discussed in depth in order for patients to make changes in insulin doses and profiles or in lifestyle to improve BG control. Algorithms were applied for changing both bolus and basal insulin dosing according to SMBG results. Application of the dosing algorithm was individualized in the discussion with the patients, taking individual differences into account. Target fasting BG and postprandial values were 72–108 mg/dl (4–6 mmol/liter), and deviations from this resulted in a focused therapy improvement discussion.

Each visit would last up to 30 min, including all aspects described. The clinical research location and the study nurse were different and physically separated from the outpatient clinic with the outpatient clinic personnel caring for the control group and regular patients otherwise.

Regular A1C analysis at every visit was performed locally, and the patients in both study groups were informed about results consecutively as in regular clinical practice. In addition, a capillary blood sample for analyzing A1C on the study method was obtained at every visit and stored at -80 °C. At study end, A1C was then analyzed at the Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway, using High-Performance Liquid Chromatography Variant II, (Biorad Laboratories, Diagnostic Group, USA). Due to the inclusion procedure for the control group in which the patients were included in the study 9 months after randomization time, some of the initial samples were missed for this group. For these patients, we had to use the locally obtained A1C results. However, to be able to compare these results with results obtained using the frozen samples, we established an equation (based on local results compared with the results from the study method) to ensure correct estimates of results. The study method for A1C analysis was certified by the National Glycohemoglobin Standardization Program and was traceable to the Diabetes Control and Complications Trial reference method.[21] The instrument showed good analytical quality with a CV of 1.2% and a bias of 2%.

Prestudy power calculations for the number of patients to be included in the study showed a need of 60 patients in each group in order to obtain a statistically significant result (95% confidence) with an absolute difference in A1C between groups at 9 months of 0.5%. The analysis was done based on the intention-to-treat principle. Chi-square test and Student's *t*-test were used for comparisons between groups. The statistical analysis was performed using Statistical Package for the Social Sciences software package (Version 15.0). A p-value < .05 was considered significant. The study design, informed consent form, and conduct were approved by the Regional Committee for Medical Research Ethics, Bergen, Norway.

Results

The randomization resulted in comparable study groups with no major differences (**Table 1**). In the control group, two additional patients started pump therapy during the study period. All patients had a long-standing experience

Table 1.
Baseline Clinical Characteristics of the Control and Intervention Groups[a]

	Control	Intervention
Age (years)	38 ± 9	39 ± 12
Diabetes duration (years)	19 ± 12	20 ± 11
Body mass index (kg/m^2)	26 ± 5	25 ± 3
Women (%)	52.4	57.4
Retinopathy (%)	42	43.5
Nephropathy (%)	20	19
Neuropathy (%)	11	13
Daily smokers (%)	15.4	16
CSII users (%)	22.5	20.4
Mean A1C at inclusion (%)	8.61 ± 0.09	8.65 ± 0.10

[a] Data are means ± SD unless otherwise indicated

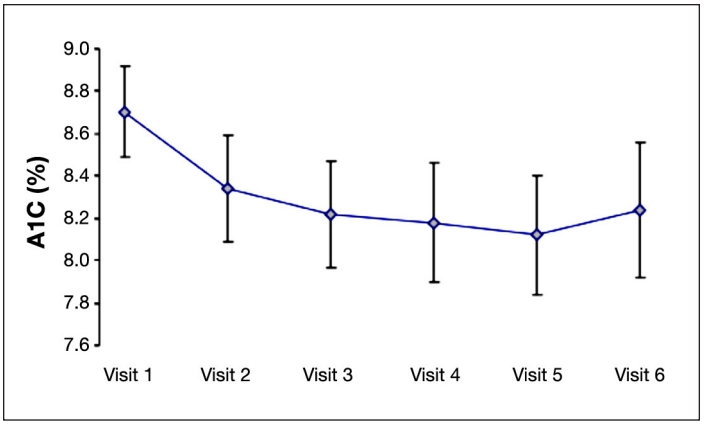

Figure 2. Mean A1C for patients in the intervention group. Error bars indicate 95% confidence interval.

in performing SMBG. Mean A1C results were similar at study start: 8.61% (standard deviation [SD] = 0.09) for the control group and 8.65% (SD = 0.1) for the intervention group. We observed a continuous decrease in A1C in the intervention group for the first 6 months to 8.2% and a minor increase during the last 3 months (**Figure 2**). The control group was stable, with comparable A1C values at study start and study end, 8.61 versus 8.84% (p = .12). At study end, 10% of intervention patients had reached a guideline goal of A1C < 7.0%, 24% had A1C < 7.5%, and 39% had A1C < 8.0%. In the control group, no patient obtained A1C < 7.5%, and 13% of patients had A1C < 8.0% at 9 months. When comparing the two groups at study end at 9 months, A1C was approximately 0.6 % lower in the intervention group (**Figure 3**). Patients in the intervention group attended

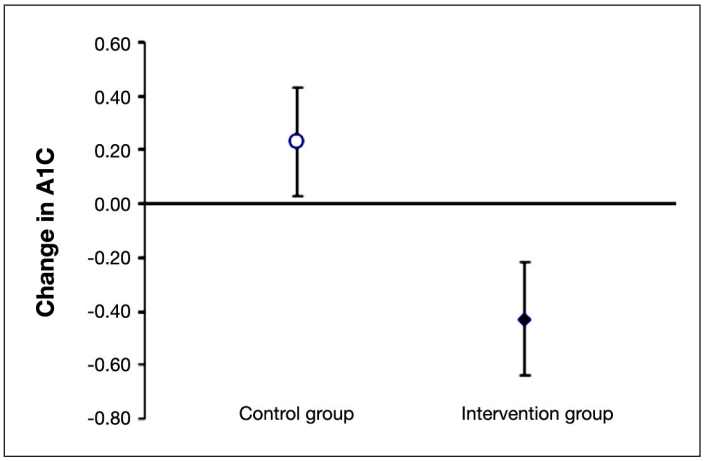

Figure 3. Mean change in A1C from baseline to study end (9 months) for the two study groups. Error bars indicate 95% confidence interval.

89% of scheduled study visits, and no difference in A1C was observed between patients attending all or less than all study visits. Twelve percent did not complete the intervention, and 25% skipped at least one study visit. Intervention patients had the same mode of insulin treatment at study start and end. In the control group, 22.5% of patients were insulin pump users at study start, 25% at study end. We observed no increase in major or minor hypoglycemia in the intervention or control group patients during the study period.

Discussion

The failure to achieve metabolic goals in large groups of patients with diabetes type 1 is associated with long-term complications and clinical consequences.[22] We found a 0.6% decrease in A1C in the SMBG intervention group compared to the control group after 9 months. Newer or comparable randomized clinical studies on SMBG in adult type 1 diabetes patients are unavailable, although the need for more knowledge and research in the field has been underlined and discussed.[11,12,14,17,23] In a systematic review by Coster *et al.*,[24] eight randomized controlled trials evaluating the effect of SMBG use on A1C in type 1 diabetes patients were found. These studies are old, partially done in children, and several compared SMBG with urine glucose testing. In a study by Schiffrin *et al.*,[16] a higher frequency of SMBG was shown to improve A1C, but the population studied was small (n = 21), highly motivated, and different from the study population of the present study. Coster *et al.* as well as evidence-based guidelines for point-of-care testing[15] conclude that further studies should be done and that evidence for an effect of SMBG, even in type 1 patients, is partly lacking. It is virtually impossible to design a study limiting an intervention to SMBG only, since diabetes and BG regulation is complex and always involves many aspects. Two older studies, however, showed that knowledge and education about diabetes without use of SMBG were not enough to lower A1C.[25,26]

Based on the general recommendations by the ADA and the WHO, we designed the present study to evaluate if it was possible to improve the current use of the SMBG tool in poorly controlled but very experienced type 1 diabetes patients. Compared with older studies, our study included only outpatient visits and had a stronger, more specific focus on SMBG performance and consequences and less on general education and treatment modality.[24–26] On the other hand, the patients in the intervention group were seen more frequently than the control patients, resulting in a stronger focus on their diabetes in general. The awareness of the intervention group being included in a study could also contribute to the study effect (Hawthorne effect). The patients received a new and accurate instrument, but instruments and strips were distributed at no cost to patients, and we do not think this fact contributed substantially to the intervention effect. The total effect of the intervention can be contributed to all aspects of the intervention, including the strong SMBG focus. The two main reasons that 12 % did not complete the intervention was tight time schedules or lack of motivation for the intervention. Some patients completing the intervention were also not compliant with the SMBG intervention at every visit, possibly weakening the effect of the intervention. This may have reduced the potential metabolic benefit in these specific patients, since more compliant patients are likely to benefit more from the intervention. We did not change the basic modes of insulin therapy, and the consultations were strongly focused on SMBG and its consequences for treatment. In the control group, the number of insulin pump users was higher at study end, and more patients changed treatment modality, possibly indicating an active attitude to improve metabolic control even in this group. The intervention group showed a decrease in A1C for 6 months and a minor increase for the last 3 months. This could be due to long, strong focus becoming tiring for some patients, as well as the increasing interval between study visits. Since the control group was seen less frequently than the intervention group, this could have possibly reduced the chance of improvement in their A1C values. Since one of the study intentions was to be compared with current practice, we chose not to include a control group with increased frequency of visits, representing another possible intervention. The frequency of hypoglycemia in the intervention group did not change during the study period, as could have been expected with decreased A1C. One explanation for this

might be that A1C was still relatively high and therefore not resulting in a measurable increase in hypoglycemia frequency.

The interventional approach was applied for patients with type 1 diabetes having rather poor metabolic control with A1C ≥ 8.0%. The study shows an overall decrease in A1C for the intervention group receiving a simple, realistic intervention with a strong focus on SMBG and more frequent visits compared with the control group receiving standard care based on guidelines and current practice. The study intervention appears to be safe with no measurable increase in minor or major hypoglycemias.

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