CHAPTER 4

EFFECTS OF SELF-MONITORING OF GLUCOSE IN BLOOD OR URINE ON HbA1c IN NON-INSULIN TREATED TYPE 2 DIABETES PATIENTS

Submitted

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Abstract

Objective To investigate the effects of self-monitoring of blood glucose and urine glucose on HbA1c among non-insulin treated patients with type 2 diabetes.

Methods 181 patients with non-insulin treated type 2 diabetes were randomly assigned to blood glucose self-monitoring (SMBG), urine glucose self-monitoring (SMUG) or control group. Hba1c was measured at baseline, 4 and 12 months.

Results After 4 months no between group differences in changes in HbA1c were found (p=0.47; Mean adjusted difference (MD) between SMBG and control group = -0.15%, (95% CI -0.44 to 0.15) and between SMUG and control group MD = 0.04% (95% CI -0.28 to 0.35). Mean adjusted differences over 12 months time between SMBG and control group was 0.03% (95% CI -0.19 to 0.24) and between SMUG and control group 0.00% (95% CI -0.23 to 0.23).

Conclusions Evidence for a short or long-term glycaemic effect of self-monitoring of glucose levels in blood or urine with pre-set instructions compared to control was not found.
Introduction
Self-monitoring of glucose is widely used by patients with type 2 diabetes, however, evidence for the value of self-monitoring in achieving glycaemic control is conflicting in patients who do not require insulin\(^1\);\(^2\). Self-monitoring is often used by diabetes educators as a tool to explain daily variation in blood glucose levels to help patients reach glycaemic control. We investigated the short-term and long-term effects of self-monitoring of blood glucose and urine glucose on glycaemic control in non-insulin treated patients with type 2 diabetes.

Research design and Methods
The IN CONTROL-trial was a 3-armed randomized clinical trial performed in The Netherlands. The aim of the trial was to assess the effects of i) self-monitoring of blood glucose (SMBG) and ii) self-monitoring of urine glucose (SMUG) compared to iii) control (i.e. standardized diabetes care according to the most recent standard of the Dutch college of General Practitioners\(^3\) on diabetes specific emotional distress, self-efficacy and glycaemic control in non-insulin-treated type 2 diabetes patients. Details of the trial design and conduct are reported elsewhere\(^4\).

Patients (diabetes duration $\geq$ 1 year, age $45 \geq 75$ years, HbA1c $\geq 7.0\%$, no insulin use, self-reported self-monitoring frequency of maximum 3 times in the previous year) were recruited from three regional diabetes care systems and were randomized. Patients in the SMBG and SMUG group were trained in performing and interpreting SMBG or SMUG by trained research assistants and were provided with a flowchart with instructions when to perform and how to interpret self-monitoring results and what actions to take. Patients in the SMBG group were all provided with a glucose meter (LifeScan OneTouch\(^\circledR\) Ultra\(^\circledR\)\(^2\)) and were asked to perform three pre-prandial and three post-prandial measurements a day on two separate days each week. Patients in the SMUG group were asked to test their urine (Urispec\(^\text{TM}\) plus) on two separate days each week after dinner. All patients were allowed to adjust self-monitoring frequency ‘ad libitum’ eight weeks after baseline. Compliance was measured from glucose diaries and downloaded glucose meter readings.
Pre-designated outcome was between group changes in HbA1c at 4 months and mean group differences over a 12 month course. Secondary outcome was changes in prescribed glucose lowering medication after 4 and 12 months. Blood samples were taken at or shortly before baseline, 4 and the 12-months follow-up visit and measured with DCCT aligned assays. Intention-to-treat analysis was performed using data of all randomized patients in their allocated groups with baseline and at least one follow-up HbA1c measurement\textsuperscript{5,6}. When follow-up data for the 12-month measurement was not available we imputed the data by carrying the 4 months measurement forward. First, analysis of variance, adjusted for baseline HbA1c values (ANCOVA) was used to explore differences between the three groups in effect of self-monitoring after 4 months. When a statistically significant difference (\(p\leq 0.05\)) was detected, independent pair wise-group comparisons (linear regression) was performed. Subsequently, linear mixed models (LMM) were used, controlled for baseline levels as fixed effects and subject as random effects to explore mean differences (MD) between group means of HbA1c over a 12-months course. Changes in prescribed medications between groups were compared with a \(\chi^2\)-test. Finally, effect modification by treatment (sulfonyl-urea or non sulfonyl-urea) was explored with a test for interaction (critical significant value \(p<0.10\)).

**Results**

Between July 2008 and December 2009, 181 patients with non-insulin treated type 2 diabetes were randomized to one of three groups: SMBG (n=60); SMUG (n=59); control (n=62). After 4 months, 50 SMBG, 41 SMUG, and 52 control group patients responded to the invitation for a follow-up measurement. At the end of the trial, 13 patients were found lost-to-follow-up, 25 patients stopped monitoring (SMBG=8; SMUG=17), 6 patients discontinued the trial (control=6)) and 2 patients died (control=2) (Figure 1). Hence, 143 patients were included in the 4 months analysis and 174 patients (SMBG=57; SMUG=57; control=60) in the 12 months LMM analysis. Explanatory analyses of non-completers vs. completers showed no differences in baseline characteristics.
Figure 1. Flow of patients
Patient characteristics at baseline, including prescribed glucose lowering medications, were not different between the three groups, although there was a higher proportion of patients with HbA1c > 10.0% in the SMUG group (3.4%; 2 patients), compared to SMBG (0%; 0 patients) and control group (1.6%; 1 patient), respectively. No between group differences in changes in HbA1c after 4 months, corrected for baseline values (ANCOVA) were found (p=0.47; SMBG vs. control: MD = -0.15%, 95% CI -0.44 to 0.15; SMUG vs. control: MD = 0.04%, 95% CI -0.28 to 0.35) (Figure 2). Mean differences between groups over 12 months time, corrected for baseline values (LMM) showed similar results (SMBG vs. control, MD = 0.03% 95% CI -0.19 to 0.24; SMUG vs. control, MD = 0.00% 95% CI -0.23 to 0.23) (Figure 2). Changes in prescribed diabetes medication were not different between groups after 4 months (p=0.07) and 12 months (p=0.36). Insulin was prescribed to 3% of included patients (SMBG=2 patients; SMUG=2 patients; control=1 patient) after 4 months and to 7.5% of included patients (SMBG=3 patients; SMUG=6 patients; control=4 patients) after 12 months. Furthermore, effect modification by treatment (SU or non-SU) was not present (p for interaction=0.9).

![Figure 2](image)

**Figure 2.** Changes in mean (SD) HbA1c adjusted for baseline value over 12 months in patients with non-insulin treated type 2 diabetes, by randomisation group.
During the first eight weeks compliance to the recommended minimal frequency was 55% (median (q1, q3) 93 (65, 108)) in the SMBG and 53% (16 (14, 16)) in the SMUG group, respectively. The following eight weeks compliance marginally changed to 52% (161 (126, 205)) in the SMBG group and remained the same with 53% (30 (28, 31)) in the SMUG group.

**Conclusion**

This randomised controlled study showed that self-monitoring of glucose levels in blood or urine did not improve HbA1c compared to usual care over a short-term (4 months) and a long-term period (12 months). Furthermore, changes in glucose lowering agents as prescribed by a general practitioner were not different between groups over 12 months.

Self-monitoring of glucose was investigated within structured care systems providing identical diabetes education to all patients. Patients in the intervention groups received training in SMBG or SMUG from trained research assistants and received flowcharts how to interpret and react to the values on their glucose meter. Patients were individually randomized with concealed allocation and were analysed as intent to treat with á priori decided outcomes.

The present study was sufficiently powered to detect a clinical relevant decrease in HbA1c of 0.5% between SMBG and control. However, at 4 months a non-significant difference in HbA1c of -0.15% between SMBG and control was found. Similar results have been found at short-term in newly diagnosed patients ⁷ and at long-term for patients with a diabetes duration over one year ⁸.

The decrease in HbA1c observed in all groups is evenly distributed and may be subscribed to regression to the mean. The additional decrease observed in the SMBG and the SMUG group may be explained by the attention and education patients randomised in one of the intervention groups received. We did not find any differences in changes in prescribed glucose lowering medications over time. This finding may suggest that in this study patients and caregivers minimally used self-monitoring results as a source for treatment intensification.
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References


