Evaluation of Self Monitoring of Blood Glucose in Non-Insulin-Treated Diabetic Patients by Randomized Controlled Trials: Little Bang for the Buck

Mayer B. Davidson*

Charles Drew University, Los Angeles, California, USA

Abstract: Although self monitoring of blood glucose is accepted to be effective in lowering Hb A1c levels in insulin-treated diabetic patients, any benefit in non-insulin-treated patients remains controversial. Observational studies cannot answer this question because of either patient self selection (individuals with healthier life styles chose to perform more SMBG) or physician self selection (patients in poorer control are asked to perform SMBG). Only randomized controlled trials (RCTs) can provide the answer. Of the 14 published bona fide RCTs, nine show no benefit in lowering Hb A1c levels. In four of the five positive ones, the SMBG group received more intensive education and/or treatment than the control group. In the one in which patients in both groups were followed similarly, over 500 patients were required to produce a statistically significant difference of 0.2% favoring SMBG, the clinical significance of which is debatable. Thus, there is scant evidence that very expensive SMBG in non-insulin-treated patients is effective in lowering Hb A1c levels. This lack of benefit argues for redirecting these resources into areas of diabetes care where strong evidence exists for improving diabetes outcomes.

Key Words: Self monitoring of blood glucose (SMBG); randomized controlled trials (RCTs); non-insulin-treated patients.

There is little doubt that the self monitoring of blood glucose (SMBG) is beneficial in lowering glycemia in insulin-treated diabetic patients although randomized controlled trials (RCTs) have not evaluated this and at this time it would not seem ethical to carry them out. Whether SMBG is beneficial in lowering glycemia in non-insulin-treated diabetic patients remains controversial. Some observational studies, both retrospective and prospective, suggest that it is while others do not. However, observational studies cannot be used to evaluate this question. For instance, in a large observational retrospective health plan study, non-insulin-treated diabetic patients who performed more SMBG had lower glycated hemoglobin (Hb A1c) levels [1]. However, a self-administered questionnaire or a computer-assisted telephone interview administered to the plan members whose records were reviewed (83% of whom responded) revealed that self-care practices and healthy lifestyle behaviors were significantly more common in patients who carried out SMBG more frequently. This finding casts doubt on whether the lowered Hb A1c levels could be ascribed to SMBG per se and is an example of patient self selection. On the other hand, Fig. (1), relating the number SMBG tests per day and Hb A1c levels in type 2 diabetic patients, demonstrates physician self selection. The upper decreasing curve shows the expected relationship in insulin-treated patients. The lower increasing curve shows the perhaps unexpected relationship in non-insulin-treated patients, probably due to the fact that physicians are more likely to ask uncontrolled patients to perform SMBG and to test more frequently the worse the control. In general, patients who perform SMBG have more hyperglycemia than those who don’t [3,4]. Certainly one cannot infer that performing SMBG leads to higher Hb A1c levels.

Thus, the only way to evaluate the effect of SMBG in non-insulin-treated diabetic patients is by RCTs. I have followed the literature on SMBG in non-insulin treated diabetic patients for many years and have identified 14 RCTs evaluating its effect on Hb A1c levels in this cohort (Table 1) Nine studies showed no difference between patients who performed SMBG compared to those who did not [5-7,9,11,12,15-17]; five of them showed a significant lowering of Hb A1c levels in the SMBG group [8,10,13,14,18]. However, compared to the control group, the SMBG group either received more intense education [13], were treated much...
more intensively at frequent visits by a pharmacist [10] or were referred to their physicians by the practice nurse monthly if the fasting SMBG values exceeded 180 mg/dl [8]. In one study, 48% and 40% of the SMBG and control groups, respectively, dropped out [14] invalidating any conclusions. In the one study in which the SMBG and control groups were treated comparably, Hb A1c levels in the SMBG group fell 0.2% more than in the control group (P <0.01). It required over 500 subjects to demonstrate this statistical difference whose clinical importance is debatable.

Table 2 summarizes six meta-analyses of data obtained from alleged RCTs evaluating the glycemic effect of SMBG in (mostly) non-insulin-treated patients. Towfigh et al. [25]
concluded that the higher the Hb A1c levels were, the less effective SMBG was in lowering them. In contrast, Poolsup et al. [27] concluded that SMBG was only effective if Hb A1c levels were ≥8.0%. Reasons for questioning the validity of four of the studies [8,10,13,14] on the contribution of SMBG per se were discussed above. Three studies included in some of the meta-analyses [19,22,24] were not included as bona fide RCTs in Table 1 for the following reasons. Estey et al. [20] taught SMBG to both the intervention and control groups but during the 10 weeks of the study, only the intervention group was called four times by the nurse and had one home visit to encourage SMBG testing. The intervention group did perform SMBG more frequently than did the control group. Kwon et al. [23] taught their intervention group to use the internet to relay information, questions and SMBG values to the diabetes center during a 12 week period whereas the control group received usual care. Both groups were taught SMBG. The mean number of logon times for each patient in the intervention group was 42.3. Therapy was changed by a physician at the diabetes center if necessary based on SMBG values. Patients in the control group visited the diabetes center two or three times during the study. Frequency of SMBG testing was higher during the study in the intervention group (71.5 vs 38.1 times). Hb A1C levels fell 0.54% (P <0.05) in the intervention group and rose non-significantly by 0.33% in the control group. Brown et al. [26] randomized Mexican-American diabetic patients into an intensively educated group (52 contact hours over 12 months including SMBG instruction) and a wait-list control group. One-quarter of the both groups were receiving insulin. After one year, Hb A1c levels in the intervention group fell significantly (P<0.02) from 11.8% to 10.9% while the change in the control group from 11.8% to 11.6% was not significant. There was no difference in the rates of SMBG in those in the intervention group who reduced their Hb A1c levels and those who did not. There was no mention of SMBG status in the control group.

Scherbaum et al. [28] performed a randomized non-inferiority trial comparing SMBG once a week versus four times a week in non-insulin-treated diabetic patients. After one year, Hb A1c levels in the intervention group fell significantly (P<0.02) from 11.8% to 10.9% while the change in the control group from 11.8% to 11.6% was not significant. There was no difference in the rates of SMBG in those in the intervention group who reduced their Hb A1c levels and those who did not. There was no mention of SMBG status in the control group.

It is relatively straightforward how SMBG could benefit insulin-treated diabetic patients. Patients could respond acutely to high or low pre-prandial values by changing their insulin dose, the timing or carbohydrate (CHO) content of the meal or exercising if the value were high. The long term patterns of SMBG values are necessary for ongoing insulin dose adjustments, either by the patient if instructed appropriately or by the physician. In non-insulin-treated patients, the value of SMBG is less obvious. Certainly, changes in meal timing or CHO content or exercise patterns are possible but acute medication changes are problematic. Only changes in gliptides or α-glucosidase inhibitors (which only have ~1% of the market of oral diabetic medications) might acutely influence the value measured. Laboratory or office glucose con-

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**Table 2. Summary of Meta-Analyses of Randomized Controlled Trials in (Mostly) Non-Insulin-Treated Diabetic Patients**

<table>
<thead>
<tr>
<th>Meta-Analysis</th>
<th>Studies Analyzed</th>
<th>Results*</th>
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<tbody>
<tr>
<td>Coster [19]</td>
<td>Wing [5], Fontbonne [6], Allen [7], Rutten [8], Muchmore [9], Miles [11], Estey [20]</td>
<td>SMBG vs Controls (no SMUG) -0.25% (-0.61 to +0.10) (N = 4) SMBG vs. SMBUG -0.03 (-0.52 to +0.47) (N = 3)</td>
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<tr>
<td>Welchen [21]</td>
<td>Fontbonne [6], Allen [7], Muchmore [9], Schwedes [13], Guerci [14], Davidson [15]</td>
<td>SMBG vs Controls (no SMUG) -0.39 (-0.56 to -0.21) (N = 4) SMBG vs. SMBUG -0.17 (-0.96 to +0.61) (N = 2)</td>
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<tr>
<td>Sarol [22]</td>
<td>Fontbonne [6], Muchmore [9], Jaber [10], Schwedes [13], Guerci [14], Davidson [15], Estey [20], Kwon [23]</td>
<td>SMBG vs Controls (no SMUG) -0.39 (-0.54 to -0.23) (N = 8)</td>
</tr>
<tr>
<td>Jansen* [24]</td>
<td>Wing [5], Fontbonne [6], Allen [7], Muchmore [9], Jaber [10], Miles [11], Schwedes [13], Guerci [14], Davidson [15], Estey [20], Kwon [23], Brown [26]</td>
<td>SMBG vs Controls (no SMUG) -0.39 (-0.78 to -0.09) (N = 10) SMBG vs. SMBUG -0.26 (-0.84 to +0.35)</td>
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<tr>
<td>Towfigh† [25]</td>
<td>Wing [5], Fontbonne [6], Rutten [8], Muchmore [9], Schwedes [13], Guerci [14], Davidson [15], Farmer [16]</td>
<td>SMBG vs Controls (no SMUG) 6 months -0.23 (-0.48 to +0.02) (N = 5) 12 months -0.26 (-1.00 to +0.48) (N = 4)</td>
</tr>
<tr>
<td>Poolsup [27]</td>
<td>Fontbonne [6], Muchmore [9], Jaber [10], Schwedes [13], Guerci [14], Davidson [15], Farmer [16] O’Kane [17], Barnett [18]</td>
<td>SMBG vs Controls (no SMUG) -0.24 (-0.34 to -0.14) (N = 9)</td>
</tr>
</tbody>
</table>

*Mean difference of change in Hb A1c levels (%) in SMBG group minus change in control group (95% CI); †self monitoring of urine glucose; ‡P <0.05; §only non-insulin-treated patients; ‖adjusted for baseline Hb A1c levels.
centrations and Hb A1c levels, rather than the long term pattern of SMBG values, are mostly used to adjust oral diabetes medications. SMBG values in these patients could be useful to educate and motivate these patients but the evidence that they are effective in that regard is minimal (Table 1). A further problem is that physicians usually ask patients to test pre-prandially as opposed to post-prandially where the higher values are more likely to be motivational. Since the most important determinant of post-prandial hyperglycemia is the pre-prandial glucose concentration, pre- and post-prandial values around the same meal provide the best education regarding the effect of the food (both portion size and CHO content) in that meal on glycemia. Unfortunately, SMBG testing before and after the same meal is not often prescribed.

SMBG is expensive. In 2002, the total cost for reagent strips, lancets, lancing devices, meters, batteries and calibration solutions or chips was $465,503,576 in non-insulin-treated diabetic patients enrolled in the Medicare part B fee-for-service program run by the U.S. government [29]. This represented 59% of the total medical costs for this group of patients during that year. This nearly half billion dollar cost did not include the 10% of Medicare beneficiaries enrolled in HMO Managed Medicare, the patients enrolled in Medicare part A only nor all of the non-insulin-treated diabetic patients <65 years old. In the DiGEM study [30], compared to the control group, the per patient yearly costs in the less intensive and more intensive SMBG groups were 92 ($182) and 84 ($166) English pounds, respectively, both significantly higher due entirely to the cost of SMBG as other medical costs were similar. Given the lack of a beneficial effect on Hb A1c levels, the authors concluded the “neither type of self monitoring is likely to be cost effective if added to standardised usual care.” In contrast, using economic models based on the CORE Diabetes Model [31,32] in a Kaiser population of non-insulin-treated diabetic patients [1], it was concluded that SMBG would be cost-effective in both the United Kingdom[33] and in the United States [34] although the latter analysis has been challenged [35]. An analysis utilizing the actual costs updated to 2008 of patients followed in the German ROSSO study [4] also concluded that in the Spanish health care system, SMBG in non-insulin-treated diabetic patients would be cost effective [36]. However, the ROSSO study was an observational one and the possibility of healthier lifestyles of the patients selecting to perform SMBG rather than SMBG itself being responsible for the improved clinical outcomes as discussed above may invalidate this conclusion. Finally, in a Veterans Affairs system of medical care, strips for SMBG in non-insulin-treated diabetic patients were limited to 50 per 90 days [37]. Compared to the year prior, testing during the six months after this change decreased by 35% in diet-controlled patients and by 46% in pill only patients with a savings of $6.37 per patient per month and no change in Hb A1c levels.

In the two studies in which they were evaluated, quality of life [30] was significantly lower and depression [17] was significantly greater in patients who performed SMBG.

The International Diabetes Federation recently published a guideline for SMBG in non-insulin-treated diabetic patients [38]. They concluded that SMBG should be used in these patients under the following conditions: a) only when both the patient or their care givers and their health care providers “have the knowledge, skills and willingness to incorporate SMBG monitoring and therapy adjustment into their diabetes care plan in order to attain agreed treatment goals”; b) at time of diagnosis for educational purposes; c) as part of self-management education; d) individualization of SMBG protocols “to address each individual’s specific educational/behavioural/clinical requirements (to identify/prevent/manage acute hyper- and hypoglycemia) and provider requirements for data on glycaemic patterns and to monitor impact of therapeutic decision making”; d) agreement between the patient and provider concerning purposes/goals and review of SMBG; and e) SMBG should be easy to perform and the results should be accurate. Nice concepts but for over 20 years, RCTs have provided scant evidence that SMBG in these patients has been effective in lowering Hb A1c levels. Currently, SMBG costs are approaching $1.00 per test. We are getting little bang for the buck in patients not treated with insulin. Perhaps it’s time to seriously consider redirecting these resources to other aspects of diabetes care where strong evidence exists for beneficial effects on diabetes outcomes.

REFERENCES

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