The dilemma of self-monitoring of blood glucose

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Published online: 18 January 2007

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Keywords Blood glucose · Self monitoring of blood glucose · Type 2 diabetes

Abbreviations

ROSSO Retrolective Study ‘Self-monitoring of Blood Glucose and Outcome in Patients with Type 2 Diabetes’

SMBG self-monitoring of blood glucose

In a paper published in *Diabetologia* last year, Martin et al. [1] reported that self-monitoring of blood glucose (SMBG) in the observational retrospective cohort Retrolective Study ‘Self-monitoring of Blood Glucose and Outcome in Patients with Type 2 Diabetes’ (ROSSO) was associated with significantly decreased diabetes-related morbidity and all-cause mortality even after adjusting for age, sex, comorbidities at diagnosis of diabetes (hypertension, CHD and history of stroke), fasting plasma glucose concentrations, triacylglycerol levels and treatment. These findings remained true for patients not taking insulin. In contrast, in the present issue of *Diabetologia*, Davis et al. [2] report that, in the observational, prospective Fremantle study, SMBG was not associated with improved outcomes of diabetes-related morbidity, cardiac death or all-cause mortality after adjustment for confounders. The confound-

ers adjusted for in the Fremantle study were age, sex, duration of diabetes, prior CHD, prior peripheral arterial disease, neuropathy, retinopathy, microalbuminuria, systolic blood pressure, total serum cholesterol and current smoking. Surprisingly, there was a significant 79% increased risk of cardiovascular mortality in those patients who were not taking insulin but were performing SMBG.

How can the disparate results of these two large studies be explained and what lessons can we learn from them? First, there are many factors that might impinge on the outcomes, especially the macrovascular ones, and taking all the appropriate confounders into account may be problematic. Second, there may be a self-selection process for physicians in terms of who is recommended for, and patients who perform, SMBG. Evidence for the former is the finding that those who perform SMBG have higher glycaemia than those who do not [1, 3]. Evidence for the latter was supplied by a large observational retrospective health plan study in which patients who performed SMBG more frequently had lower HbA_{1c} levels [4]. However, a self-administered questionnaire or a computer-assisted telephone interview administered to plan members (83% of whom responded) revealed that self-care practices and healthy lifestyle behaviours were significantly more common in patients who performed SMBG more frequently.

By definition, an observational study is not an experimental one, i.e. interventions are chosen rather than randomly assigned. This leads to the possibility of selection bias which, in turn, means that outcomes may not be caused by the intervention under study [5]. Although identifiable differences can be taken into account when the data are analysed, one cannot be certain that these adjustments are adequate because all of the relevant differences may not be

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known [5]. The differences in the confounders considered in the ROSSO [1] and Fremantle [2] studies may have contributed to their contradictory conclusions. Randomised trials circumvent this problem and provide reliable estimates of the effect of the intervention.

Randomised trials studying the effect of SMBG in insulin-requiring patients would not be ethical, as a number of observational trials have shown that HbA_{1c} levels are inversely related to the frequency of SMBG measurements [4, 6–11]. However, SMBG values must be acted on for improved control (a point that I will return to later). In one study, lower HbA_{1c} levels were seen in those insulin-requiring type 2 diabetic patients who self-adjusted their insulin doses, but not in those who did not [12]. With few exceptions, observational studies evaluating the frequency of SMBG and changes in HbA_{1c} levels in patients not taking insulin have shown no effect [13].

Nine allegedly randomised controlled trials evaluating the effect of SMBG on HbA_{1c} levels in type 2 diabetic patients not taking insulin have been identified in two recent reviews [14, 15]. Five of these showed no effect [2, 16–19]. One of these perhaps deserves special mention because although it was a small study, it was a truly blinded, randomised trial, with clinical decisions being made by a single provider who was unaware of the SMBG status of the patients [19]. The provider was a nurse who followed detailed treatment algorithms. All patients were seen an equal number of times over 6 months by a dietitian. Patients in the SMBG group were instructed to measure before and after different meals, 6 days/week (45% compliance), and the values were utilised in the nutritional counselling. There was a similar fall in HbA_{1c} levels (% $\pm$ SD) from baseline between the control group (-0.6 ± 1.6) and the SMBG group (-0.8 ± 2.1).

The four ‘positive’ studies had flaws that raise serious questions about the conclusion that SMBG per se led to significantly lower HbA_{1c} levels. In three of them, the SMBG group received either more intensive counselling [20] or more intensive treatment along with the increased counselling [21, 22] compared with the control group. Furthermore, in one of these three studies, not only were patients taking insulin or oral agents alone combined, but those in the intervention group (who received counselling over the internet) who failed to provide SMBG values for >3 weeks were dropped from the study [22]. In the fourth study, there was a huge dropout rate: 40% in the control group and 48% in the SMBG group [23]. If the SMBG dropout subgroup was enriched with those patients who were showing the least response, the results could be due to self-selection.

It seems fair to say that, at present, SMBG has not been shown to be beneficial in diabetic patients not taking insulin. However, theoretically, SMBG could (1) educate

patients; (2) motivate them; (3) document hyperglycaemia so that action could be taken to reduce it acutely; (4) be used by physicians to adjust oral glucose-lowering drugs; and (5) document hypoglycaemia. Regarding education, few patients receive meaningful feedback from their health-care providers regarding their SMBG results. In addition, postprandial glucose values (or better yet, the difference between pre- and postprandial values) would serve to educate patients regarding which foods (and how much) cause the greatest postprandial increase. However, few patients are instructed to measure at these times. Most simply measure before breakfast, and some also measure before supper. Thus, the educational potential of SMBG is lost. Regarding motivation, preprandial values are lower than postprandial ones and are therefore not such good motivators.

Insulin-taking patients who have elevated (or decreased) preprandial SMBG values can adjust their short-acting insulin dose, or change the timing or content of the meal to acutely react to the measured value. Patients on pills have fewer options. Changing the content of the meal could be helpful, but unless they are taking a glinide or an α -glucosidase inhibitor, medication adjustments will not help. Although there are no data on how often physicians adjust oral doses based on SMBG values instead of laboratory tests, this is probably not very common. Finally, since hypoglycaemia is unusual and sporadic in patients not taking insulin, SMBG for this purpose alone would not seem warranted.

The cost of this unproven modality in diabetic patients not taking insulin is enormous, at least in the USA [13]. Medicare B is an insurance programme provided by the government for patients aged ≥ 65 years who agree to pay the premiums. The cost for SMBG (strips, meters, lancets, calibration solutions and batteries) in 2002 for diabetic patients not taking insulin enrolled in the Medicare B program was US\$465,000,000! The total cost of SMBG in those not taking insulin in the USA, which includes other patients aged ≥ 65 years who were not enrolled in the Medicare B program, as well as all younger patients, is obviously much higher.

Many observational studies, some very large, have failed to show a benefit for SMBG in diabetic patients not taking insulin. One can postulate that an even larger one, or perhaps a better designed one, might finally give us a definitive answer. This seems unlikely for the reasons given above. Furthermore, to date, the randomised clinical trials available have either not shown a beneficial effect in these patients or had serious design flaws invalidating their conclusions. Thus, the dilemma of SMBG for diabetic patients not taking insulin; it is an expensive and popular procedure without an evidence base. We are left with the need to pursue the answer to this question with properly

designed, randomised clinical trials. Given the available evidence, we are spending a tremendous amount of money on an unproven clinical methodology. Those resources might be better spent in other areas of diabetes care.

Acknowledgements M. B. Davidson was supported by NIH grant no. U54-RR014616.

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