

## Self-monitoring of blood glucose – problems with progress

People with newly diagnosed diabetes are faced with an overwhelming amount of information about their condition, new skills to learn and adaptation to a new lifestyle.

There is little debate regarding the value of self-monitoring of blood glucose (SMBG) in subjects with type 1 diabetes and a number of studies have shown that SMBG is effective both in reducing HbA<sub>1c</sub> as well as overall costs of disease management.<sup>1,2</sup> A recent study of 19 491 subjects with type 1 diabetes in Germany and Austria reported an overall benefit of -0.26% HbA<sub>1c</sub> per SMBG per day. These subjects performed an average of 4.4 tests per day. Furthermore, the benefit was higher in subjects treated intensively ( $\geq 4$  injections per day or CSII): -0.32% HbA<sub>1c</sub> per SMBG per day, compared to -0.16% HbA<sub>1c</sub> per SMBG per day in subjects on  $< 4$  injections per day.<sup>3</sup>

As for type 1 diabetes, benefit has been shown in persons with insulin treated type 2 diabetes performing regular SMBG.<sup>4,5</sup> In the Kaiser Permanente Study, HbA<sub>1c</sub> was significantly lower in insulin-treated subjects with type 2 diabetes who performed SMBG at least once daily ( $8.2 \pm 1.7\%$  vs  $8.9 \pm 2.2\%$ ,  $p < 0.0001$ ).<sup>5</sup>

The debate of efficacy of SMBG really revolves around the use of this technology in subjects with type 2 diabetes who are not on insulin therapy. A Cochrane systematic review, in 2005 reviewed six trials and found improvement in HbA<sub>1c</sub> associated with SMBG in two.<sup>6</sup> The authors concluded that SMBG may be effective in this group of subjects with type 2 diabetes.

The largest study was undertaken in the United Kingdom (the DiGEM Study) and included 453 subjects with type 2 diabetes, mean age 65.7 years, median duration of diagnosed diabetes three years and mean baseline HbA<sub>1c</sub> 7.5%.<sup>7</sup> The subjects were randomly assigned to one of three arms: usual treatment with 3-monthly HbA<sub>1c</sub> (N = 152); usual care plus SMBG and facility to consult a health professional in interpretation of the results (N = 150) and usual care plus SMBG as well as training in the interpretation and implementation of changes depending on results (N = 151). At 12 months, the primary outcome ( $\Delta$  HbA<sub>1c</sub>) was no different between the 3 groups (-0.14%; -0.35%; -0.17% for each group,  $p = 0.12$ ).<sup>7</sup> More recently an assessment of the economic benefit of SMBG in the DiGEM study was undertaken and concluded that higher costs were associated with SMBG, with no benefit in terms of metabolic improvement.<sup>8</sup> Furthermore, the same publication reported that subjects performing SMBG in the DiGEM trial had lower quality of life as measured by the EuroQol EQ-5D questionnaire.<sup>8</sup>

A meta-analysis of studies on SMBG in non-insulin treated subjects with type 2 diabetes found nine studies (including the DiGEM study) suitable for inclusion.<sup>9</sup> Five out of six trials in which SMBG was performed for at least six months found a significant overall reduction in HbA<sub>1c</sub> (pooled estimate -0.21% HbA<sub>1c</sub>, 95% confidence intervals -0.38 to -0.04). No benefit was seen in studies reporting results at 12 months.

Therefore there is probable benefit in SMBG in subjects with type 2 diabetes not on insulin therapy, although the effect is small.

There are many other issues to consider in SMBG, including affordability, availability, use of the information and technical performances of the devices.

In the current issue of JEMDSA, Essack and colleagues raise awareness of the technical performance of five different meters tested both in a laboratory and a tertiary clinic setting in Cape Town.<sup>10</sup> Of some concern is the conclusion that none of the glucose meters satisfied the American Diabetes Association guidelines for meter performance and only three of the meters satisfied the International Standardization Organisation criteria. This is clearly worrying in the context of patients striving for tight glucose control, where small variation in actual levels may have clinically meaningful results and consequences.

Adding to concerns regarding analytical rigour of portable glucose meters is a recent American Food and Drug Administration public health notification on errors in glucose meters utilising glucose dehydrogenase pyrroloquinoline quinone test strip methodology. The report advises that a number of substances may interfere with glucose measurements and lead to erroneous results. The interfering substances include some immunoglobulin preparations, abatacept, BEXXAR radioimmunotherapy agent and products containing, or metabolised into maltose, galactose or xylose (<http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/>).

These errors appear not to occur with glucose test strips using other methodologies including glucose oxidase, glucose dehydrogenase nicotinic adenine dinucleotide or glucose dehydrogenase flavin adenine dinucleotide.

Eastham and colleagues studied the prevalence of interfering substances with glucose meters in a community hospital and found that serum uric acid  $> 0.6$  mmol/l (10 mg/dl), haematocrit  $< 20\%$  or  $> 55\%$ , total bilirubin  $> 342$   $\mu$ mol/l (20 mg/dl), serum paracetamol

concentration > 53  $\mu\text{mol/l}$  (8 mg/dl) and serum triglycerides > 57 mmol/l (5000 mg/dl) interfered with glucose measured by glucose dehydrogenase pyrroloquinoline quinone methodology, in a small number of patients.<sup>11</sup>

As with all innovations, technical issues will pose challenges, but identification of problems by studies such as these will ultimately improve analytic precision and assist in attaining optimal glycaemic control for patients with diabetes mellitus.

**Fraser Pirie**  
Deputy Editor

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