A Rosetta Stone for Insulin Treatment: Self-Monitoring of Blood Glucose

In the daily management of type 1 diabetes, self-monitoring of blood glucose (SMBG) is the recommended glycemic monitor, or “Rosetta stone”, that enables improved glycemic control (1). By measuring real-time glucose, informed patients can modify their diabetes management acutely or prospectively to sustain glucose in a narrow range near normal. A recent study from the Veterans Administration demonstrated improved glycemic control with lowered hemoglobin A1c in patients with insulin-treated type 2 diabetes who performed SMBG (2). A wide range of insulins is now available with various durations of action that can help to improve glycemic control. The greatest therapeutic advances entail the use of recombinant DNA-engineered insulin analogs. Novel insulins such as lyspro-insulin [lysine(B28), proline(B29)] have a very rapid onset of action (15–30 min), peak effect (1–2 h), and limited overall duration of action (3–4 h), whereas glargine (\(^{\text{a}}\text{Gly}-30\text{a-L-Arg}-30\text{b-L-Arg-human}\)) has no peak and a duration of action of 24 h or longer.

Maintaining blood glucose at or very near the normal range decreases the frequency of new-onset microvascular complications and delays the progression of established microvascular complications in both type 1 and type 2 diabetes (3–5). In non-insulin-treated patients, before 2002 there were few data to suggest that SMBG improved clinical outcome (6). However a recent study from France found that SMBG lowered hemoglobin A1c in monitored, non-insulin-treated type 2 diabetes (7), as did a study from Germany (8).

Accurate and precise blood glucose measurements are no doubt helpful and important to achieve optimal diabetic care (9). However, unless patients alter their care (e.g., acute adjustments in diet, exercise, or insulin dosing) in response to the real-time blood glucose or in anticipation of changes in blood glucose, even the most accurate and precise glucose measurement will not improve glycemic control. Simply put, knowledge of blood glucose, without patient action based on these data, will be ineffective in lowering the hemoglobin A1c concentration. The development of patient-care algorithms to normalize blood glucose is the responsibility of the physician and healthcare team providing care to the patient with diabetes (10). The responsibility of the laboratorian and the diagnostics industry is to ensure that blood glucose monitors provide accurate and precise measurements. One of the greatest fears of insulin-treated individuals is the development of hypoglycemia. This emphasizes the need for optimal low-end analytical performance. Severe untreated hypoglycemia can be deadly (11).

In this issue of Clinical Chemistry, Kristensen et al. (12) provide a proposed procedure for “cost-reasonable” strip and meter evaluation (~$20 000/evaluation). Kristensen et al. remind us that patients do not perform SMBG as precisely as medical laboratory technologists. This is not a novel revelation (13); nonetheless, the documentation of this fact is worthwhile. The authors identify several factors that contribute to lower glucose precision in patients performing SMBG compared with medical laboratory technologists, including (a) higher rates of inadequate sample volume applied to the detection strip (i.e., difficulties with the physical delivery of blood to the strip), (b) failure of patients to further recognize inadequate sample delivery; and (c) meter coding errors by patients. It is refreshing to know that patient education does improve precision. Concerning factors outside the control of the patient, for one of the two analyzers evaluated, one of three lots of strips displayed reduced analytical performance.

What can be done to further improve the analytical and daily performance of SMBG? The answers can be divided into technical improvements in the SMBG systems and improved patient education. The first recommendation taken from this Technical Brief (12) is that all strips and meters should have mechanisms to detect inadequate sample delivery. Regarding one of the two meters evaluated, the data indicated that almost one in four samples had an inadequate volume. To use a strip/meter system that does not detect adequate sample volume risks recurrent “short-sampling”. Furthermore, inadequate sample delivery does not guarantee a negative bias to the result (see the filled circles in Fig. 1 of Kristensen et al. (12)]. Overestimation of blood glucose could lead to hypoglycemia from overtreatment, whereas underestimation of blood glucose could lead to hyperglycemia from undertreatment. Certainly other technologic improvements can be made in strip/monitor systems, such as a patient-lockout capacity if controls are not run and/or are out of range; alarms for short-sampling; simplification of sample loading; talking devices that advise the patient of errors; electronic controls that are run daily and provision of liquid controls that can be run weekly or more often; easier availability of data downloads to personal computers or the web for interface with the healthcare team; internal algorithms that could track current and past blood glucose readings, time of day, food intake, previous insulin doses, and exercise to provide recommended insulin adjustments; interfaces between the glucose meter and continuous subcutaneous insulin infusion pumps that regulate the rate and pattern of insulin infusion (i.e., an artificial pancreas); alarms that notify the patient that it is time to check blood glucose; and user-friendly keypads and displays designed for individuals with a limited education.

Improving the analytical performance of the meter balances cost vs accuracy and precision. Better measuring devices and strips will likely be more expensive. However, if up to 25% of certain SMBG blood glucose results are “wasted” because of inadequate sample delivery or other technical failures, is it any bargain not to use the best systems available? Manufacturers caution that if
precision and accuracy targets are tightened, the cost of strip/device systems will likely increase. If the cost increases significantly and interferes with the availability of testing, has the medical community advanced the care of people with diabetes? This debate must continue among patients, clinicians, laboratorians, medical-care payers, and strip/device manufacturers until they reach a consensus as to what more should be achieved analytically at an affordable price. Certainly there should be no shortage of investment capital available for product development in the diagnostics industry, seeing that the worldwide market for SMBG approaches US $3 billion annually (14).

Patient education concerning the proper use of strips and devices should be an obligate part of routine patient care similar to recommendations for periodic measurement of hemoglobin \(A_1C\), blood pressure, and microalbumin excretion. Indeed, the American Diabetes Association (ADA) clinical practice guidelines state that “it is important for healthcare providers to evaluate each patient’s monitoring technique, both initially and at regular intervals thereafter” (9). Furthermore, the ADA states that “Use of calibration and control solutions on a regular basis by patients helps ensure accuracy of results”. However, this author is skeptical about the number of patients who run controls and the frequency with which healthcare teams evaluate the accuracy of self-monitoring devices (15).

Some have suggested a paradigm shift that avoids the requirement for blood samples for glucose monitoring. Unfortunately, use of sweat, tears, or saliva as surrogates for the measurement of blood glucose is fraught with problems (16–18). Recall that the results of testing of the first nonblood body fluid routinely tested for glucose (urine) also correlated poorly with blood glucose. Transcutaneous glucose measurements in the form of the GlucoWatch (Cygnus) have, at best, fair precision and accuracy and are applicable only for problem solving and are not suitable for routine blood glucose assessment (19). The Continuous Glucose Monitoring System (CGMS; Minimed) measures subcutaneous glucose as a surrogate for blood glucose (20). Like the GlucoWatch, the predominant use of the CGMS should be problem solving, which greatly limits its widespread applicability. Body fluids that demand thorough scientific and clinical examination are vitreous and anterior chamber fluid, which could be evaluated by spectroscopic analysis (21–23).

In summary, improvements in the analytical performance of point-of-care testing strips and monitors are desirable. Preanalytical factors do influence the quality of the SMBG data, as illustrated by the report of Kristensen et al. (12). These authors also propose a mechanism to assess meter performance that includes their use by real patients. The diabetes healthcare team, through patient education with a clear focus on the preanalytical performance of SMBG, can dramatically improve the precision of SMBG. At the present time, the only suitable body fluid that can be used routinely to measure blood glucose is blood. Because the body carefully guards against blood loss, skin punch is the only practical method available for obtaining blood. Certainly the scientific community must seek out patients’ opinions about the required levels of performance of meters that would meet patient needs (24, 25). An interesting report published in 2001 addressed patients’ perceptions concerning analytical meter performance and adjusting care based on SMBG results (26). Just as important as accurate and precise blood glucose data is the need for patients to modify their care on the basis of their blood glucose result. On a hopeful note, despite the limitations of current self-monitoring systems (e.g., both preanalytical and user-related problems and glucose measurement problems), patients can often achieve usable glucose data (27) and improve their glycemic control. The Food and Drug Administration (28) and ADA (29) provide helpful web sites for patients concerning SMBG.

References

William E. Winter
University of Florida
Department of Pathology, Immunology and Laboratory Medicine
Box 100275
Gainesville, FL 32610-0275
Fax 352-846-2149
E-mail winter@pathology.ufl.edu

DOI: 10.1373/clinchem.2004.033167