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Testing quality of a self-monitoring blood glucose sensor with an auto-coding mechanism when used by patients versus technicians

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ABSTRACT

Background: In response to the problem of erroneous readings due to miscoding when performing self-monitoring blood glucose (SMBG), this study introduces a user-friendly SMBG biosensor with an innovative auto-coding module on the meter and strip. Actual users characterized the performance of the SMBG systems.
Methods: A total of 105 patients were incorporated in the study and Clarke error grid analysis (EGA) was administered to evaluate the clinical accuracy of the results obtained by the patients versus the technicians. All patients used the questionnaires to comment on the use of the auto-coding sensor.
Results: In the imprecision test, the total CV of the 5 BG levels was 2.1%. In the EGA plot, the results of the auto-coding sensor were 96.2%, both lots A and B, in zone A for the patients and 99.0% and 97.1% for the technician. The paired *t*-test demonstrated no statistically significant difference between the patient and technician measurements. Regression analysis also demonstrated that the measurements taken by the patients agreed with those obtained using the laboratory method.
Conclusions: The patients achieved satisfactory performance using the auto-coding SMBG sensor and derived similar results with both laboratory reference and operation by a technician.

1. Introduction

Self-monitoring of blood glucose (SMBG) is essential for diabetes patients to monitor their glycemia and accordingly moderate their behaviors such as diet and exercise, and is also essential for individuals using insulin or oral agents [1–3]. Regular management of blood glucose (BG) concentration helps patients with type I or type II diabetes by mitigating the onset or progression of diabetic associated complications [4]. The American Diabetes Association (ADA) recommends that individuals with diabetes should routinely monitor their BG level, at least four times daily for those with type I diabetes and once daily for those with type II diabetes [3]. Nevertheless, the monitoring frequency of BG level using SMBG biosensor remains well below the level suggested by ADA. Possible reasons for this situation include pain resulting from skin puncture, difficulty in inserting test strips, trouble applying sufficient blood volume, and questions regarding test accuracy, all of which create enormous demand for more user-friendly BG sensors [5].

Skeie et al. assessed the quality of five different SMBG systems and observed significant differences between the BG values performed by patients and technicians [6]. Compared to the values obtained using the laboratory method, the analytical results obtained by the technicians were more accurate than those obtained by the patients. Another investigation by Kristensen et al. showed that the measurements taken by the patients deviated more from the limits required by the ISO standard than did those taken by the technicians [7]. SMBG manufacturers have examined the discrepancies between the results obtained by patients and technicians when operating SMBG systems. These discrepancies are primarily attributable to the special usage techniques associated with the SMBG system, the background knowledge of users, and the robustness of SMBG systems. The quality of SMBG systems is limited by current technology, which requires strict operating techniques for SMBG systems to ensure accurate outcomes. Techniques applied to SMBG systems include, but are not limited to, cleaning the fingertips before puncturing the skin, using the systems under appropriate ambient conditions, using the test strips with the corresponding calibration codes, and applying sufficient blood to the test strips. Earlier investigations found that 16% of 183 patients [7] and 16% of 201 patients [8] used incorrect codes for SMBG operation during a single clinic visit. This incidence of miscoding has placed a strong focus on caregivers. Baum et al. designed an experiment to compare the analytical results obtained from incorrectly and correctly coded SMBG systems [9]. They concluded that the analytical errors associated with incorrectly coded

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systems exceeded ±30%. A simulation of insulin dosage based on miscoded SMBG systems further demonstrated the importance of coding systems for patients undergoing insulin administration [10,11].

Most of the commercially available amperometric type SMBG biosensors are calibrated using code chip/code key or manual coding. In the case of manual-coding biosensors operated via a single button, users must press and hold that button to go over all the codes until the correct one shows up. On the appearance of the correct code, the button must be immediately released to avoid missing the correct code. Otherwise, the user must repeat the whole process. These processes are intended to protect patients against misleading BG information; however, such complex and time consuming processes may discourage them from performing SMBG.

2. Materials and methods

2.1. SMBG instrument with auto-coding mechanism

This study applied an SMBG biosensor, Bionime Rightest GM550 (Bionime Corp) that incorporated an innovative auto-coding module on the meter and strip. The coding module on the meter is assembled with code pin, rubber, grounding material, ball, and spring, all assembled in series. Each code pin engages with the specific flat or concave hole on the strip and can then define to binary coding information, 1 or 0, which the black pins embedded into concave holes on the strip represent binary coding 1, while the white pins embedded into flat holes on the strip represent binary coding 0. The combination of all the binary coding information can obtain a predefined parameter from the meter. The strip contains 12 code pins and can thus provide up to 2^{12} combinations of coding patterns. Each test strip in the same lot has the same code pattern and each lot is assigned a specific parameter. By precisely detecting the combinative coding pattern, the auto-coding sensor can automatically perform calibration using a single defined parameter. This function markedly reduces errors in usage technique that result from miscoding.

2.2. Subjects

A total of 105 diabetes and non-diabetes participants (44 males and 61 females from 24 to 87 years old) were enrolled in this clinical study at Min-Sheng General Hospital, Taoyuan City, Taiwan. The study participants were not necessarily users of the auto-coding BG monitors. The protocol was approved by the Institutional Review Boards for studies involving human subjects (MSEIRB Authority No. 0980110) with the informed consent of all participants. All participants were asked to provide information on their age, gender, type of diabetes, duration of personal diabetic history and time using BG sensors. At the end of the test, participants also completed a questionnaire on their experience of using the auto-coding BG sensor during the clinical study.

2.3. Test procedure

The imprecision test of the auto-coding sensor was assessed by a technician using two strip lots, A and B. Venous blood samples were collected via venipuncture and spiked at five glucose concentration levels. A hundred measurements were taken from 10 meters with 10 replicates at each glucose level, and 1000 measurements were obtained by the completion of testing.

The general procedures used to evaluate clinical accuracy are as follows: (1) a patient received basic instructions regarding SMBG before the tests; (2) after reading these instructions, a 200-μl of capillary blood was collected from the fingertip of the patient by a technician and centrifuged. The BG value of the plasma was measured using the hexokinase method (Olympus AU640 Clinical Analyzer, laboratory reference method); (3) on completion of the blood collection, the patient performed SMBG themselves and obtained two measurements, strip lots A and B, respectively; (4) two further measurements with strip lots A and B were obtained by the technician immediately after the patient finished SMBG; (5) immediately after the technician obtained the two measurements, an additional 200-μl of capillary blood was collected from their fingertip. The capillary blood was centrifuged and the BG value of plasma was measured using the laboratory reference method. Steps (1) to (5) were repeated for all 105 patients. Imprecision test and clinical accuracy evaluation were performed according to ISO 15197:2003 [12].

2.4. Statistical analysis

The imprecision was expressed in terms of the coefficient of variation (CV). The pooled imprecision at each glucose concentration level was determined by including measurements from strip lots A and B in the calculation, and the total imprecision expressed in terms of the overall testing range was calculated using all the measured test values. The Clarke error grid analysis (EGA) was conducted to evaluate the clinical accuracy of the auto-coding sensor compared to the reference method [13,14]. The Clarke EGA requires over 95% of the BG measurements to fall within zone A and 100% to fall within zone A+B. EGA contains 5 zones (A, B, C, D, and E). Zone A represents bias within 20% of reference values or the hypoglycemic region. Zone B denotes bias outside of 20% of the reference values but no/benign treating effect. Values in zones C, D, and E may cause unnecessary corrective treatments, failure to administer treatment, and incorrect treatment, respectively. Notably, results within zones A or B are clinically acceptable, whereas those within zones C, D, or E are completely intolerable. In this investigation, the agreement between whole blood glucose values obtained from meters and plasma BG values obtained from the laboratory reference method was further assessed via regression analysis.

3. Results

3.1. Imprecision test

Table 1 lists the results of the imprecision test with strip lots A and B. The pooled CVs of the auto-coding BG sensor were 2.0% and 1.9% at the lowest and highest BG levels, respectively. At levels II, III and IV, the pooled CVs of the auto-coding BG sensor were 1.3%, 1.2%, and 1.8%, respectively.

3.2. Clinical accuracy evaluation

The clinical accuracy assessment of the Bionime Rightest GM550 biosensor with two strip lots (lot A and B) was conducted by the patients and the technician, and the results were determined based on the Clarke EGA. Table 2 lists the percentages of measurements that fall within zones A and A+B in the EGA plot. The results of the auto-coding BG sensor were 96.2%, both lots A and B, in zone A when operated by the patients, and 99.0% and 97.1% when operated by the technician. No results fell in zones C, D, or E. Furthermore, the paired *t*-test for comparing the results obtained by the patients and the technician (i.e. *p*-value) obtained results of 0.84 and 0.49 for lots A and B, respectively. Fig. 1(A) presents regression analysis comparing the results obtained from the patients and the technician with those obtained using the reference method in the EGA plot, where the slope and intercept were 0.94 and −1.26 by patients, and 0.95 and −3.88 by the technician. Fig. 1(B) illustrates the correlation between the results obtained by the patients and the technician. The slope and intercept was 0.99 and 0.16.

3.3. Questionnaire responses

Table 3 shows the statistics obtained from the questionnaire in relation to patient SMBG characteristics and patterns. Some 53.6% of diabetes patients claimed experience of using SMBG sensor. Moreover, up to 93.3% of participants were satisfied with the auto-coding function of the