Identifying Sources of Error in Self-Monitoring of Blood Glucose

Lois Jovanovic-Peterson, MD
Charles M. Peterson, MD
Jacqueline D. Dudley, RN
Charles Kilo, MD
Barbara Ellis, RN

The use of glucose oxidase reagent strips by patients with diabetes has become increasingly prevalent over the last decade (1,2). A number of patient management systems rely on these technologies as a monitoring system to avoid hyper- and hypoglycemia (3) and to normalize daily blood glucose levels (4).

Most studies of glucose oxidase reagent strips have found them to be precise and accurate, but few of these studies have been performed in the "real world" of patient use (5). Several concerns have been raised about the accuracy and precision of patient-determined glucose values. Recently, a request for a less user-dependent system was made by health-care professionals at a consensus conference on the self-monitoring of blood glucose (SMBG) (6).

This study was designed to *1*) evaluate the precision and accuracy of patient-determined blood glucose measurements and *2*) quantitate the contribution of blood removal and timing to the errors encountered in patient use of these systems by using a second-generation technology.

MATERIALS AND METHODS

Subjects in this study were diagnosed with diabetes mellitus and trained in the technique of SMBG with the use of glucose oxidase reagent strips. Systems previously used by the subjects included all of those tested, except the One Touch System (Lifescan, Mountain View, CA) and one other system not included in the study. No more than 5 patients had previously used any one particular system used in this study. The age range of the subjects was 20–71 yr with a mean age of 47.7 yr at the Sansum Medical Research Foundation (SMRF) and 52.2 yr at the Kilo Diabetes and Vascular Research Foundation (KRF). The SMRF had 22 subjects (16 women, 6 men), 19 of whom were treated with insulin and 3 of whom were treated with oral agents. The KRF had 23 subjects (11 women, 12 men), 17 of whom were treated with insulin and 6 of whom were treated with oral agents.

Ten milliliters of venous blood was drawn into a heparinized tube from each subject. The subject was then instructed on the use of the five test-method systems used in the study (Chemstrip bG, Boehringer Mannheim, Indianapolis, IN; Glucometer II, Ames, Miles, Elkart, IN; Accu-Chek II, Boehinger Mannheim; Tracer, Boehinger Mannheim; and One Touch) according to the manufacturer's instructions. Chemstrip bG was selected as a representative of a visually read system, and the Glucometer II, Accu-Chek II, and Tracer were selected as examples of standard first-generation meter-read technologies that rely on patient placement of blood, removal of blood, and timing. The One Touch System was chosen as a second-generation system because it is less dependent on patient performance of the above tasks in that it is activated with the placement of blood on the reagent strip, and neither timing nor removal of blood by the patient is required.

Subjects first received instruction on one system then performed three practice tests with the appropriate glucose control solution. Each subject used a pipette to transfer his/her own heparinized venous blood to the test strip and obtained duplicate blood glucose determinations. At the same time, on the same sample of heparinized venous blood, a glucose determination was performed on the glucose analyzer (model 23A, YSI, Yellow Springs, OH) (YSI). The YSI uses the glucose oxidase method. After completion of testing with the first system, the process of instruction, practice, and blood testing was repeated with the other systems. Testing was completed on all methods within 2 h. With the exception of the visual method, which was always read first to minimize bias, the order of presentation was controlled by a computer-generated randomization schedule to ensure that balance in presentation order was achieved. Teaching was performed in groups of three to four subjects. A sufficient number of prechecked accurate meters were available, whereby every subject was provided with his/her own system. Participants used watches with second hands to time the Chemstrip bG reaction.

The data were analyzed with several statistical methods. The accuracy of the five SMBG methods was assessed by comparing the absolute percent deviation of each of the duplicate determinations from the YSI reference standard. The percent deviations were then analyzed parametrically by analysis of variance and nonparametrically by Freidman's rank test (7,8). Absolute percent deviations were also grouped by blood glucose level, although the bias at different blood glucose levels was not examined.

Accuracy of the five methods was assessed by the same statistical methods applied to the logarithm of the difference between the duplicate blood glucose determinations. With two observations, these variates were constant multiples of the sample variance, and the distribution was improved by logarithmic transformation.

The precision and accuracy of the devices compared to the YSI standard were assessed with a weighted least-squares regression procedure (9). Additionally, the root mean square percent (MS%) error, an overall measure of both precision and accuracy was used. This statistic

TABLE 1
Regression statistics for individual test results by system

System	*n*	Slope	Intercept	C.V. (%)	Root percent error	R^2
Combined						
Chemstrip bG	90	0.987	−4.47	14.63	15.31	.9775
Glucometer II	90	1.038	3.25	17.02	18.12	.9756
Accu-Chek II	90	1.089	−10.70	9.61	12.12	.9911
Tracer	90	1.016	−4.27	13.42	14.00	.9820
One Touch	90	0.995	3.60	5.86	6.49	.9968
SMRF						
Chemstrip bG	44	1.022	−5.01	13.22	13.38	.9830
Glucometer II	44	1.077	1.48	16.24	18.31	.9793
Accu-Chek II	44	1.129	−11.51	11.06	15.45	.9890
Tracer	44	1.056	−5.01	16.80	17.61	.9741
One Touch	44	0.995	3.63	5.88	6.80	.9969
KRF						
Chemstrip bG	46	0.992	−9.64	15.53	16.95	.9739
Glucometer II	46	0.969	10.00	17.69	17.95	.9731
Accu-Chek II	46	1.073	−12.88	6.79	7.66	.9955
Tracer	46	0.977	−3.16	8.33	9.32	.9928
One Touch	46	0.996	3.21	5.96	6.19	.9967

SMRF, Sansum Medical Research Foundation; KRF, Kilo Diabetes and Vascular Research Foundation.

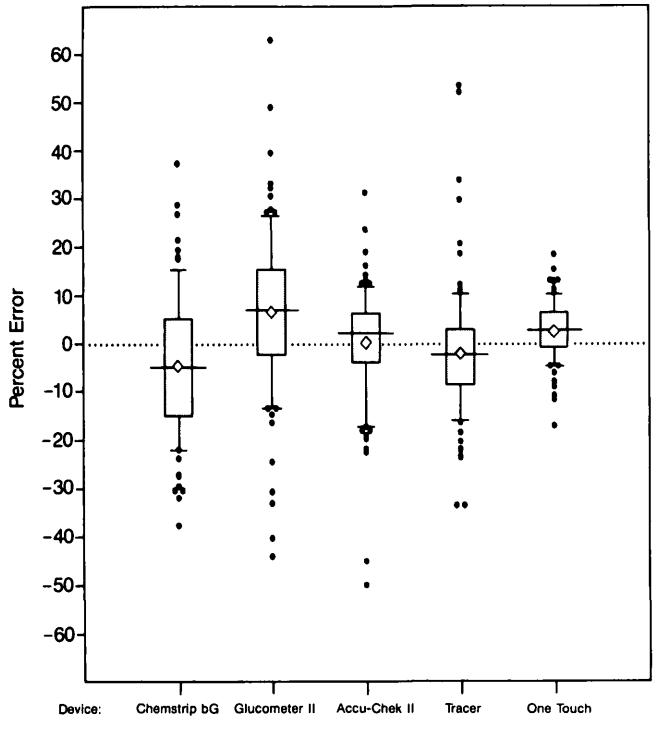

FIG. 1. Box plots of percent error by device pooled from 2 centers. Each box plot gives data on 90 samples. ◇, Mean; *horizontal line*, median. *Box* covers 25th to 75th percentiles of all individual data points; *vertical lines* extend to 10th and 90th percentiles of all individual data points. Remaining data are plotted as individual points.

is composed of the sum of precision (C.V.) and accuracy as measured by the deviation of regression from the ideal (bias squared).

RESULTS

Table 1 summarizes the regression statistics from the two research centers. These statistics indicate the linearity of all five systems. Overall, no bias was shown with any system. As shown in Table 1, the C.V. and MS% error encountered with the One Touch System are less than those encountered with the other systems. Pairwise ANOVA tests between the One Touch System and the other four devices yielded *P* values for the absolute percent error data of ≤.003.

Figures 1 and 2 show the box plots of the MS% error by device and the percent C.V. by device of the pooled data from the two centers. Both figures document the decrement in error and variation achieved with the One Touch System. No patient had results from all five methods that were all >10% from the YSI.

Table 2 summarizes the absolute MS% error versus the YSI within three different glucose ranges (0–100, 101–200, and 201–300 mg/dl) for each of the five systems. Chemstrip bG, Glucometer II, Accu-Chek II, and Tracer systems had at least 21% of the results in the 0- to 100-mg/dl glucose range that were >20% from the YSI. The One Touch System had no results >20% from the YSI.

DISCUSSION

It is difficult, at best, to devise real-world tests to duplicate how precisely and accurately patients would perform SMBG on a daily basis. Therefore, this study, conducted under the best of conditions, attempted to eliminate user errors such as sample size, sample hemolysis, lack of appropriate user training, expired reagent strips, poor meter maintenance, and system malfunction.

The results of this study give credence to the hypothesis that the lack of precision and accuracy in results of patient-performed blood glucose measurements can partly be improved by a system that minimizes the potential for user error. Use of a system that eliminated the need for blood removal and timing resulted in a decrease in the variability of results. Consistent results from both research centers lends strength to this observation. This study did not attempt to determine whether lack of precision or accuracy was due to timing or inadequate blood removal technique. It was found that the accuracy and precision error associated with testing on a first-generation system was significantly reduced by a system that eliminated the need for the patient to start the test, time the test, and remove blood.

It is unlikely that other factors could have contributed to the results mentioned. The research centers involved in the trial did not have patients in the study who had used the One Touch System previously. Although differences in optics or strip technologies probably contributed to the results seen in this study, minimizing

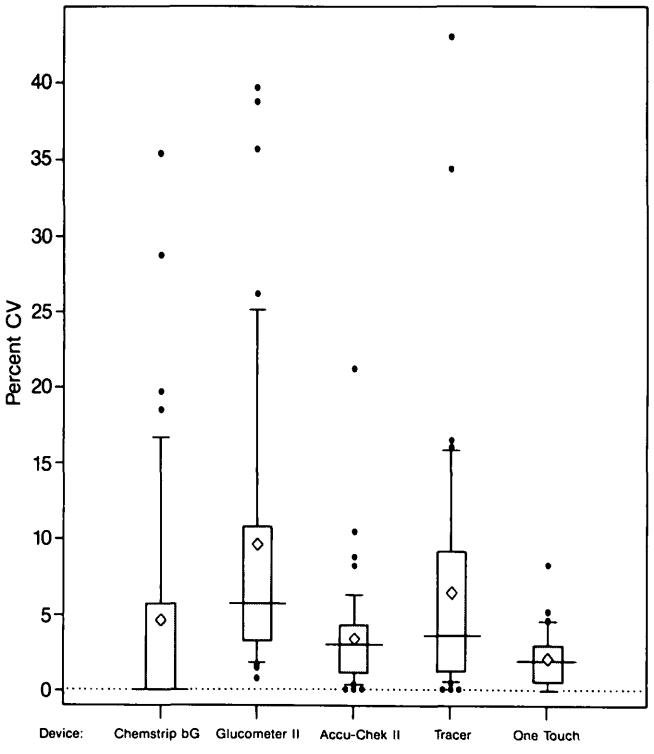

FIG. 2. Box plots of percent coefficient of variation by device pooled from research centers. Each box plot gives data on 45 samples and 90 test results. ◇, Mean; *horizontal line*, median. *Box* covers 25th to 75th percentiles of all individual data points; *vertical lines* extend to 10th and 90th percentiles of all individual data points. Remaining data are plotted as individual points.

TABLE 2
Absolute percent error vs. YSI within different glucose ranges by system

System	Glucose range (mg/dl)	Percent of system results within the given range of YSI			
		0–10%	10–15% (0–15%)	15–20% (0–20%)	>20%
Chemstrip bG	0–100	31	38 (69)	6 (75)	25 (100)
	101–200	54	11 (65)	22 (87)	13 (100)
	201–300	43	21 (64)	7 (71)	29 (100)
Glucometer II	0–100	42	17 (58)	17 (75)	25 (100)
	101–200	53	10 (63)	8 (70)	30 (100)
	201–300	73	15 (88)	4 (92)	8 (100)
Accu-Chek II	0–100	46	13 (58)	21 (79)	21 (100)
	101–200	83	10 (93)	5 (98)	2 (100)
	201–300	77	19 (96)	4 (100)	0 (100)
Tracer	0–100	40	20 (60)	5 (65)	35 (100)
	101–200	82	7 (89)	4 (93)	7 (100)
	201–300	77	11 (88)	8 (96)	4 (100)
One Touch	0–100	70	20 (90)	10 (100)	0 (100)
	101–200	93	7 (100)	0 (100)	0 (100)
	201–300	85	12 (96)	4 (100)	0 (100)

YSI, Yellow Springs Instrument.

patient performance variables probably played the major role.

Therefore, we conclude that a system such as the One Touch, which eliminates the need for the operator to start and time the test and remove blood, results in an improvement in precision and accuracy, relative to the YSI, of blood glucose monitoring by patients.

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From the Kilo Diabetes and Vascular Research Foundation, St. Louis, Missouri.

Address correspondence and reprint requests to Charles Kilo, MD, Kilo Diabetes and Vascular Research Foundation, 1227 Fernridge Parkway, Suite 100, St. Louis, MO 63141.

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Recommendation for Strict Control of Plasma Triglyceride in Diabetic Subjects

Gen Yoshino, MD
Tsutomu Kazumi, MD
Masahide Iwai, MD
Kohji Matsuba, MD
Ippei Iwatani, MD
Masayuki Matsushita, MD
Toshio Kasama, MD
Shigeaki Baba, MD

Atherosclerosis is the most common complication of diabetes. Hyperlipidemia or dyslipoproteinemia may account for the increased risk of atherosclerosis in diabetic patients (1). However, diabetic patients are still at a higher risk of developing atherosclerosis, even if they are normolipidemic (2,3). There is increasing agreement about the atherogenicity of intermediate-density lipoprotein (IDL) (4). Our previous work demonstrated an increased cholesterol concentration level in the Sf20–60 (IDL_1) fraction of normolipidemic, non-insulin-dependent diabetic patients (3). This study looked for clinical parameters that correlate with IDL_1 cholesterol concentration. Correlation analyses were performed between the cholesterol in IDL_1 and plasma lipids. Identification of a close relationship between IDL_1 cholesterol and plasma triglyceride enabled us to propose new guidelines for management of mild hypertriglyceridemia in diabetic subjects.

SUBJECTS AND METHODS

We examined 106 diabetic patients (63 men, 43 women) whose mean ± SD ages were 55 ± 12 yr and 41 healthy volunteers. None of the subjects received drugs that would affect lipid metabolism or had a significant impairment in renal, hepatic, or thyroid function assessed by monitoring serum enzymes. Patients with familial hypercholesterolemia were excluded. The subjects were divided into three groups according to treatment: insulin injection (group I, $n = 31$), sulfonylurea (group S, $n = 32$), or diet alone (group D, $n = 43$). All patients were brought into this study after stabilizing their blood glucose control levels and limiting their plasma cholesterol and triglyceride levels <250 mg/dl. The patients from group S were treated with glyburide, except for 7 treated with gliclazide. Nonobese age-matched healthy and normolipidemic (plasma cholesterol and triglyceride <250 and <150 mg/dl, respectively) subjects served as controls (group C, $n = 41$).

The procedures of blood sampling, lipoprotein separation, cholesterol and triglyceride assay, and statistical analysis were the same as described previously (3).

RESULTS AND DISCUSSION

Because the data on 82 of 106 patients were presented previously, the patient characteristics from this study were