GLUCOMETERS - NEED FOR EXTERNAL QUALITY CONTROL

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ABSTRACT

We performed a pilot accuracy study on glucometers from three sources : "Advantage" from Boehringer Mannheim (A), "Glucometer⁴" from Bayer (B) and "One Touch Basic" from Life Scan (C) and compared these results with the results on autoanalyzers -Dimension RxL (1) and Hitachi 704 (2). Each glucometer was tested with venous blood in duplicate, from three different groups of 20 patients each, at random, on three different days, in our outpatient phlebotomy section. The rest of the sample was collected into heparinized tubes & the plasma separated within 15 minutes of sample collection & analyzed on both the analyzers in duplicates. The data were analyzed for accuracy by tabulating the number and percentage of test values that vary from the analyzer (reference) method by 10% or less, by 10% to 20%, or greater than 20% and the results tabulated on the Accuracy Study Table. This being a pilot study and the numbers being small, it may be suggested from the Accuracy Study Table alone, that the results of glucose in whole blood done with glucometer (A) were comparable with that of plasma values without applying any factor; whereas the results with glucometers (B) & (C) need to be divided by 1.11 to be comparable with plasma results; statistically though, results with glucometer (C) were comparable with or without factor. Patients using glucometers need to be alerted about the variance in their glucose results when compared to laboratory results, more clearly by the respective companies in their product inserts. An external quality control material that is glucometer method specific is needed, so that the Clinical Biochemistry laboratory in any hospital setup can more effectively monitor the performance of the glucometers in the wards periodically.

KEY WORDS: Glucometers, accuracy study blood parameters, correction factor glucometers, external quality control.

INTRODUCTION

Diabetic patients, especially insulin dependent, require careful monitoring to maintain proper control of blood glucose. Glucometers have become very handy in this regard, for patients at home for self monitoring of blood glucose (SMBG) and also in hospital wards and ICUs when frequent monitoring of blood glucose is required. It is customary for the patients as well as the clinicians to cross check the glucometer results with the laboratory values periodically. When they do so, it is not uncommon for doubts arising in the minds of patients regarding the relatively high results given by the laboratory. Similarly, a clinician will be in a

fix in a situation when there is too much discrepancy in the glucometer values when compared to the laboratory results.

As we all are aware, these discrepancies are due to the difference in methodologies and type of sample adopted; glucometers requiring whole blood and laboratory auto analyzers generally requiring plasma/serum. If glucose was distributed uniformly in the water phase, then the ratio of plasma glucose to whole blood glucose would be 93/84 or 1.11. As an approximation, plasma glucose can be considered to be 10-15% higher than the corresponding whole blood glucose concentrations (1). The method to estimate glucose can have

considerable influence as the apparent difference between plasma glucose and the whole blood glucose concentration and that much of variation can be attributed to interfering substances in erythrocytes. Time of separation of plasma, type of preservative, method of precipitation of proteins and variation of hematocrit are also factors. Whether the testing is done on a glucometer or in a laboratory, Quality Control is vital.

The present study was initiated when a vast difference of about 100 mg/dl was observed between a patient's blood glucose done on a glucometer in our Casualty department and that done in our lab on Dimension RxL. An immediate revelation to us was that the commercial serum based instrument specific controls in use in our laboratory do not have any glucometer specific ranges; also the controls provided with the glucometers appeared to be only glucometer specific - some of them are too viscous to be used on the auto analyzer. The main objective of the present study was to perform an accuracy study on the glucometers of three different makes in use in our hospital as follows:

* Boehringer Mannheim - Model "ADVANTAGE" further referred to as (Glucometer - A), * Bayer - Model "GLUCOMETER4" further referred to as (Glucometer - B) and * LifeScan Johnson & Johnson - Model "ONE - TOUCH" further referred to as (Glucometer - C) and comparing these results simultaneously on the auto analyzers in our department; * Dimension RxL (Dade - Behring) - further referred to as (Analyzer - 1) and * Hitachi - 704 (Boehringer Mannheim) - further referred to as (Analyzer - 2).

MATERIALS AND METHODS

Each glucometer was tested with three different groups of 20 patients each, on three different days, in our out-patient phlebotomy section. The patients were selected at random, as they came in, consisting of 12 males and 8 females ranging from 22-78 years with (Glucometer-A); 10 males and 10 females ranging from 6 - 76 years with (Glucometer-B) and 12 males and 8 females ranging from 7 - 70 years with (Glucometer-C). The timing

of sampling was also at random consisting of 2 fasting, 10 postprandial and 8 random samples with (Glucometer-A); 6 fasting, 2 post prandial and 12 random samples with (Glucometer-B) and 4 fasting, 4 postprandial, 11 random and 1 2nd hour GTT samples with (Glucometer-C). It was not known to us whether the patients were diabetic or not. Venous samples were collected, immediately tested in duplicates on the glucometers, the rest of the samples added to heparinized tubes and sent to our laboratory. These samples were centrifuged within 15 minutes of sample collection and were analyzed on the autoanalyzers, Analyzers-1 and -2 in duplicates within one hour of sample collection. Glucose estimated on (Glucometer -A) and (Glucometer -B) was by the hexokinase method whereas with (Glucometer-C) was by the glucose oxidase - peroxidase method. A dedicated kit from Dade using hexokinase method was used on Analyzer -1 and a kit from Sigma using the glucose oxidase Trinder method was used on Analyzer-2. To prevent bias during the study, the testing was done and the results noted independently by the Consultant Biochemist and the representatives of the respective companies. Care was also taken to use the same meter and test strips from the same lot for each group of patients.

RESULTS AND DISCUSSION

The data was analyzed using the SPSS package, version 7.5. Means were calculated for each of the 20 data pairs, and four groups were formed for comparison for each glucometer as follows:

- Group - I : Comparison of means of glucose values between glucometer and Analyzer-1.
- Group - II : Comparison of means of glucose values between glucometer and Analyzer-1/1.11
- Group - III : Comparison of means of glucose values between glucometer and Analyzer-2.
- Group - IV : Comparison of means of glucose values between glucometer and Analyzer -2/1.11
- Group - V : A fifth group was made that included the means of 60 data pairs on the three days combined, comparing the values on Analyzer - 1 and Analyzer -2 due to the different methodologies used. (Table 1a & 1b).

Table 1a. Means of glucose values (mg/dl)

	Glucometer-A	S.D	Glucometer-B	S.D	Glucometer-C	S.D
Glucometer	149.7	65.5	129.3	61.1	123.8	68.8
Analyzer 1	151.6	67.1	146.4	65.7	134.5	58.8
Analyzer 1/1.11	136.5	60.3	131.7	59.3	121.0	53.0
Analyzer 2	153.0	66.6	152.5	70.0	137.4	62.2
Analyzer 2/1.11	137.7	60.0	137.5	63.6	123.7	56.0

Table 1b. Means of glucose values (mg/dl)

	Mean Glucose	Std. Deviation (n = 60)
Analyzer 1	144.2	63.3
Analyzer 2	147.6	65.6

The data was analyzed for accuracy (2) by tabulating the number and percentage of test values that vary from the reference (auto analyzer) method by 10% or less, by 10% to 20%; or greater than 20% using the formula: Reference value-Meter value/Reference value x 100 and the results tabulated on the Accuracy Study Table (Table 2)

Table 2. Accuracy study Table: Percentage Difference:Reference Method vs Test Method

Group		0 - 10%	10 - 20%	>20%
I.	A	95	5	NIL
	B	40	55	5
	C	30	60	10
II.	A	50	40	10
	B	95	5	NIL
	C	70	25	5
III.	A	100	NIL	NIL
	B	10	75	15
	C	30	45	15
IV.	A	65	30	5
	B	80	20	NIL
	C	70	25	5

Where

(Group I) = % difference : Glucometer vs Dimension RxL

(Group II) = % difference : Glucometer vs Dimension RxL/1.11

(Group - III) = % difference : Glucometer vs Hitachi 704

(Group - IV) = % difference : Glucometer vs Hitachi 704/1.11

Group - I : 95% of values fall within 10% variance, 5% of values within 10- 20% variance and none in the >20% range with (Glucometer-A); 40% of values fall within 10% variance, 55% of values within 10-20% variance and 5% in the >20% range with (Glucometer -B) and 30% of values fall within 10% variance, 60% of values within 10 - 20% variance and 10% in the >20% range with (Glucometer-C).

Group - II : 50% of values fall within 10% variance, 40% of values within 10-20% variance and 10% in the >20% range with (Glucometer-A); 95% of values fall within 10% variance, 5% of values within 10-20% variance and none in the >20% range with (Glucometer-B) and 70% of values fall within 10% variance, 25% of values within 10-20% variance and 5% in the >20% range with (Glucometer-C).

Group - III : 100% of values fall within 10% variance, none within 10-20% variance and none in the >20% range with (Glucometer-A); 10% of values fall within 10% variance, 75% of values within 10-20% variance and 15% in the >20% range with (Glucometer -B) and 30% of values fall within 10% variance, 45% of values within 10-20% variance and 15% in the >20% range with (Glucometer-C).

Group -IV : 65% of values fall within 10% variance, 30% of values within 10-20% variance and 5% in the >20% range with (Glucometer -A); 80% of values fall within 10% variance, 20% of values within 10-20% variance and none in the >20% range with (Glucometer-B) and 70% of values fall within 10% variance, 25% of values within 10-20% variance and 5% in the >20% range with (Glucometer-C).

The aim is to find out whether the difference obtained in the sample may be extrapolated to the population. Towards this end, testing the percentage difference between the different groups statistically is necessary. Hypothesis testing is a technique to determine whether it is reasonable to conclude from analysis of a sample, that the entire population possesses a certain property (3). Formally the present problem may be stated as below:

$H_0: u_1 - u_2/u_1 = 10\%$ ———> null hypothesis

Where u_1 = the mean of the reference (autoanalyzer) readings

u_2 = the mean of the glucometer readings

$H_1: u_1 - u_2/u_1 > 10\%$ ———> alternative hypothesis

What we are really interested in is not the absolute values of the means but only the percentage differences. Conceptually, what we have is not two samples, but one sample of percentage differences. If the population of percentage differences has a mean of u'_1 , we can restate our hypothesis as

$H_0: u'_1 = 10$

$H_1: u'_1 > 10$

Since the sample size is less than 30 and the population standard deviation is not known, we used the t-distribution for testing the hypothesis and since we wanted to know whether the mean percentage difference exceeds 10%, an upper tailed test is appropriate. The assumed significance level is 5% in all the cases. The critical value of t for 5% significance and 19 df is 1.729. Comparing this with the t - value calculated for each case, the hypothesis was either accepted or rejected. The results of the one sample t-test done using SPSS are tabulated below (Tables 3a,b,c).

Table 3a. Glucometer-A : Percentage Differences

	Mean	S.D	t	Hypothesis
Meter vs Analyzer-1	0.095	5.861	- 7.557	Accepted
Meter vs Analyzer-1/1.11	-9.79	6.568	-13.475	Accepted
Meter vs Analyzer-2	2.37	5.01	- 6.811	Accepted
Meter vs Analyzer-2/1.11	-8.59	5.549	-14.981	Accepted

Table 3b. Glucometer-B : Percentage Differences

	Mean	S.D	t	Hypothesis
Meter vs Analyzer-1	12.18	3.867	2.521	Rejected
Meter vs Analyzer-1/1.11	2.395	4.201	-8.096	Accepted
Meter vs Analyzer-2	15.19	4.979	4.662	Rejected
Meter vs Analyzer-2/1.11	5.775	5.732	-3.297	Accepted

Table 3c Glucometer-C : Percentage Differences

	Mean	S.D	t	Hypothesis
Meter vs Analyzer-1	10.305	9.675	0.141	Accepted
Meter vs Analyzer-1/1.11	0.26	10.793	-4.036	Accepted
Meter vs Analyzer-2	12.065	7.785	1.186	Accepted
Meter vs Analyzer-2/1.11	2.315	8.684	-3.958	Accepted

The above analysis shows the following:

1) Glucometer-A: It is seen that the percentage difference of this glucometer, when compared to both the autoanalyzers is within the generally accepted limits of 10% difference with or without correction factor and the hypothesis is accepted in all the four groups.

2) Glucometer-B : It is seen that the percentage difference of this glucometer, when compared to both the autoanalyzers is within the generally accepted limits of 10% difference only when the correction factor of 1.11 is applied; the null hypotheses are accepted i.e., the variance between the glucometer and both the autoanalyzers are within the accepted limits of 10%. When the correction factor is not applied, the values are out of range.

3) Glucometer-C : It is seen that the percentage difference of this glucometer, when compared to both the autoanalyzers is within the generally accepted limits of 10% difference with or without correction factor and the hypothesis is accepted in all the four groups. The apparent variance of these results from those obtained in the accuracy study, may be attributed to the high deviation in the percentage differences.

Group - V : With the aim to determine whether the plasma glucose values using the hexokinase method on Analyzer-1 and by the glucose oxidase method on the Analyzer-2 for the same patient sample are the same, (sample size = 60, including samples on the three days) the hypothesis testing was done using normal distribution

Ho : $u_1 = u_2$ —> null hypothesis

H1 : $u_1 \neq u_2$ —> alternative hypothesis

Where u_1 = Mean glucose values (mg/dl) on Analyzer-1

u_2 = Mean glucose values (mg/dl) on Analyzer-2

At 5% significance level, the critical value of z is 1.96. Means and Standard Deviations on Analyzer-1 were 144.18 mg/dl and 63.29 and on Analyzer-2 were 147.18 mg/dl and 65.62 respectively. $Z = 0.456$; which lies in the acceptance region (-1.96 to + 1.96). Therefore, the null hypothesis is accepted, i.e., there is no significant difference in the hexokinase and glucose oxidase methods.

CONCLUSIONS

This was designed to be a pilot study and the numbers were kept small. By looking at the Accuracy Study Table alone, it may be suggested that the results of whole blood glucose done with Glucometer-A are comparable with that of plasma values without applying any factor; whereas the results with Glucometer-B and Glucometer-C need to be divided by the factor 1.11 to be comparable with the plasma results. Statistical analysis confirms our observations in the Accuracy Study Table with reference to Glucometers-A and-B; whereas the results with Glucometer-C, being comparable with analyzer results with or without applying the correction factor, this is probably due to larger standard deviation. Regardless of the make of a glucometer, an external Quality Control material that is both glucometer and analyzer specific is needed, so that the Clinical Biochemistry laboratory can plan out a ward glucose meter program in a hospital setup that regularly checks on their

performance. It would also be very helpful to the patients who use glucometers if they are alerted about this variance in their glucose results when compared to the laboratory results in more lucid terms by the respective companies in their product inserts.

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REFERENCES

1. Teitz, N.W. 1982 Fundamentals of Clinical Chemistry, W.B. Saunders Company, Philadelphia p.242-244.
2. Life Scan Technical Bulletin, Number 204 D, August 1988. U.S.A.
3. Levin, R.I. and Rubin, D.S. Statistics for Management, 6th edn., Prentice Hall of India , New Delhi 429-432.