Research Article

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The comparison of two glucose measurement systems: POCT devices versus central laboratory

İki glukoz ölçüm yönteminin kıyaslanması: Hasta başı cihazları ve merkezi laboratuvar cihazları ile ölçüm

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Abstract

Background: Glucose meters are used for two purposes: point-of-care testing and the self-monitoring of glucose, both of which are very important in the management of diabetes, hypoglycemia, or hyperglycemia and in therapeutic decisions.
Objective: The aim of this study was to determine the test reliability of glucose meters and to compare their results with those of the clinical laboratory method.
Material and methods: Evaluation was made of five different types of glucose meters which are generally used for hospitalized patients. Capillary and venous specimens were obtained concurrently from each patient. The former were analyzed in the glucose meters, and the latter in the laboratory analyzer.
Results: Of 1837 glucose meters read-outs, 1748 capillary and venous comparisons were evaluated. The majority of the glucose meter measurements were within acceptable limits. The error percentage distribution of glucose meters indicated that the accuracy of glucose meters is higher in the prediabetic/diabetic measurement range than at normo-/hypoglycemic levels.
Conclusion: In general, the glucose meters and laboratory method were observed to be compatible. However, health care professionals and self-monitoring diabetic patients should be aware of the evaluation of glucose meter results, and should cross-check, as frequently as possible, with laboratory values.

Keywords: Glucose levels; Glucose meters; Point-of-care testing; Reliability.

Özet

Giriş: Glukometreler; diabet, hipoglisemi ve hiperglisemi takibinde ve terapötik karar oluşturmada büyük önem arz eden kan glukoz seviyesinin takibi amacıyla hasta başı testi olarak ve kendi kendine kan glukoz düzeyi takibinde kullanılırlar.
Amaç: Bu çalışmanın amacı, glukometrelerin test güvenilirliğini belirlemek ve sonuçlarını klinik laboratuar yöntemiyle karşılaştırmaktır.
Materyal ve metod: Hastanemizde yatan hastaların glukoz takibi için rutin olarak kullanılan beş farklı glukometre değerlendirildi. Her bir hastadan aynı anda kapiller ve venöz örnekler alındı. Kapiller örnekler glukometrelerde, venöz örnekler ise laboratuvar analizöründe analiz edildi.
Sonuçlar: 1837 glukoz ölçüm cihazının okunması sonucu, 1748 kapiller ve venöz örneklerin karşılaştırma sonuçları değerlendirildi. Glukometre ölçümlerinin çoğu kabul edilebilir sınırlardaydı. Glukometrelerin hata yüzdesi dağılımı, glukometrelerin doğruluğunun prediabetik/diyabetik ölçüm aralığında normo-/hipoglisemik seviyelere göre daha yüksek olduğunu gösterdi.

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Tartışma: Genel olarak, glukometreler ve laboratuvar metodu uyum içindeydi. Ancak, sağlık uzmanlarının ve glukometre ile glukoz seviyesi takibi yapan diyabetik hastaların glukometre sonuçlarının değerlendirilmesi hususunun farkında olmaları ve glukometre ölçüm sonuçlarının olabildiğince sık aralıklarla laboratuvar değerleriyle çapraz kontrollerinin yapılması gerekmektedir.

Anahtar Kelimeler: Glukoz seviyeleri; Glukometreler; Hasta başı test; Güvenilirlik.

Introduction

In order to sustain the normoglycemic state of patients and achieve adequate metabolic control and treatment, it is essential to obtain immediate blood glucose measurements with monitoring devices as point-of care testing (POCT) or self-monitoring as needed. These measurements enable health care professionals and diabetic patients to effectively control blood glucose levels [1–6]. Diabetic patients, especially those requiring multiple insulin injections daily, are strongly recommended to measure blood glucose at least three times a day, as this has been shown to be essential to prevent diabetic complications in several studies [1, 7]. Moreover, all patients with abnormal glucose test results are advised to measure their blood glucose levels even if they are non-insulin dependent [1, 2, 8–10].

Analytical performances of GMSs are open to dispute. Therefore, international standards define requirements associated with the permissible analytical error of GMSs [11–13] in order to provide definitive quality criteria of glucose measurements. Tighter criteria have been suggested by the American Diabetes Association (ADA) [14, 15], and less stringent ones by others [2, 7, 8]. The fact that there has been no agreement as yet on objective criteria means a lack of consensus in respect of the quality goals for these devices.

In POCT glucose meters, glucose measurement methods involve an enzymatic reaction. After adding the sample, the reaction occurs, and the final response is measured using photometric (colorimetric) or amperometric (electrochemical) methods. For this purpose, two different enzymes are commonly used: Glucose oxidase (GO, 1.1.3.4) and glucose-1-dehydrogenase (GDH, 1.1.1.47) [16, 17]. In photometric systems, using reflectance spectrophotometry, water and glucose of the sample are taken and the blood cells are consequently excluded, resulting in a homogenous spread of the sample on the layer where the reaction occurs. The capillary fill system is used by the electrochemical strips [18, 19].

The quality control (QC) materials for glucose meters, provided by manufacturers, are not real QC materials and do not mimic fresh human blood. They are only used to observe whether the measurement is within the acceptable range, which is too wide to use as a guide for interpretation of the results obtained. In some types of glucose meter, the acceptable range is determined by control strips, and they only control the device performance not the test strips themselves. Therefore, a standard laboratory method is required for the quality control of glucose meters.

Since the improvement in the accuracy problem of the GMSs and production of reliable results are very important, the present study aimed to evaluate the performance of glucose meters used in different clinics and units of the hospital by correlating the glucose results of glucose meters and those of the laboratory analyzer. Therefore, the performances of each device were monitored on a monthly basis and the data were evaluated.

Materials and methods

This study was conducted in Clinical Biochemistry Laboratory of Ataturk University Research Hospital by using the blood samples taken from hospitalized patients. The study was a method comparison study. The glucose meters included in the study used glucose oxidase (GO, 1.1.3.4) for enzymatic reaction, and electrochemical strips for amperometric determination. The devices used whole blood (ranging from 5 to 20 μL). The linearity ranged from 0 to 600 mg/dL. The imprecision of each device was first determined as within-day intra-assay coefficient of variation (CV%) in order to include GMS into the study and the routine usage. Before the specimen was taken from the patients, each patient was informed about the sampling. Then, a skin puncture was made and five determinations were executed regardless of the fasting state of the patient, which took no more than 2 min. A CV% less than 5.0 was accepted for inclusion of the device in the study and for routine usage appropriateness, according to the literature [7] and the general acceptance rules of our laboratory. The reference glucose (GLU) measurements were made using a clinical chemistry analyzer (Beckman Coulter AU 5811, Mishima, Japan) with the enzymatic UV test (Beckman Coulter Glucose kit, hexokinase method, OSR6121). For the laboratory analyzer, monthly imprecision and daily

internal QC studies were executed, and the results were recorded.

Five different types of GMSs (GMS-A, -B, -C, -D, and -E) with different commercial trademarks which were being used as POCT devices in the hospital underwent quality assessment with the laboratory method. All samplings were performed in clinics by professional medical staff. During the 36-month period, 1,837 determinations were made using 86 GMSs; with a total measurement of 96 for GMS-A, 448 for GMS-B, 243 for GMS-C, 385 for GMS-D and 576 for GMS-E respectively. At the beginning of each month, capillary and the venous samples were obtained concurrently. The two samples of each patient were immediately analyzed in the GMS and laboratory analyzer. If the error was ≤±20%, which is the minimal accuracy criteria requirement of ISO 15197:2003 [7], the GMS was accepted for further patient testing. If the error was >20%, the result of the GMS was rejected and the comparison study of this device was repeated with a new sampling. For the second setting, if the error was again >20%, the GMS was rejected and excluded from the study. If, in repetition, the error was ≤±20%, the GMS was accepted for further patient testing and included in the study.

The analytical process was repeated for each device on a monthly basis for a period of approximately 36 months. During this period, some devices were rejected due to error, and new ones were included in the study. The capillary sample was analyzed in the glucose meter immediately after sampling. The venous blood sample in a serum separation tube with gel (Becton Dickinson, Tamse, Switzerland) was transferred to the laboratory with a pneumatic system, and after preanalytical processes, the serum was analyzed within 30 min in the clinical chemistry analyzer.

The error % of the glucose meter was calculated from the difference between the results of the glucose meter and that of the standard laboratory method using the simultaneously-obtained capillary and venous blood from the same patient. After a little modification, the following formula, as previously described by Solnica et al. [20] was used for the error calculation.

$$\text{Error } (\%) = 100 \times [(\text{GLU})_{\text{cap}} - (\text{GLU})_{\text{ven}}] / (\text{GLU})_{\text{ven}}$$

$(\text{GLU})_{\text{cap}}$: capillary glucose concentration measured by glucose meter; $(\text{GLU})_{\text{ven}}$: venous glucose concentration measured by laboratory method.

An error of 20% was taken as the cut-off value. A GMS measurement of ≤±20% was considered to be an analytical goal or an accepted result as suggested by error grid analysis [8]. A GMS measurement >±20% was considered to be an error or a rejected result [7, 8].

Ethical statement

Blood samples collections were performed according to the local ethical and legal requirements.

Statistical analysis

Statistical analysis was made using the SPSS 20.0 program (SPSS, Chicago, IL, USA) and Med-Calc Statistical Software (version 12, MedCalc Software, Mariakerke, Belgium). Gaussian analysis of all measurements was first performed to assess conformity to normal distribution of the data. The Kolmogorov-Smirnov test was used to verify the normality of the parameters. On the basis of this statistical evaluation, Pearson correlation was used for GMS-C, and the Spearman correlation test for GMS-A, -B, -D, and -E. The results of the two analyzers, GMS and laboratory analyzer, were compared using Passing-Bablok and Bland-Altman plots for association and differences, and the difference plots were obtained. A value of $p < 0.05$ was considered statistically significant.

Results

The mean ± SD values of within- and between-day imprecisions and CV (%) values of the laboratory analyzer were calculated as follows: Intra-assay CV: 1.60% and 1.61% for target values of 100 ± 1.66 mg/dL and 228 ± 3.69 mg/dL, respectively. Inter-assay CV: 1.29% and 1.06% for target values of 98.9 ± 1.28 mg/dL and 232 ± 2.46 mg/dL, respectively. Repetitions were performed for 20 times for both within-day and between-day imprecisions. Within-day imprecisions of all GMSs was calculated on 86 GMS by repeating the same measurement five times on each device and CV% was determined as 3.33.

A within-day coefficient of variation (CV) <5% was accepted as an acceptable performance of GMSs [10]. The performance of the laboratory analyzer was recorded periodically as part of the internal quality control procedure using control materials (Beckman Coulter control serum 1, ODC0003 and control serum 2, ODC0004).

Table 1 shows the comparison characteristics of GMSs. The number of total comparisons and the number of positive (≤+20%) and negative (≤–20%) errors of GMSs, calculated from the difference between the result of the glucose meter and that of the standard laboratory method in the respective samples, are shown in Table 1. The number of positive errors (1130; 64.6%) was higher

Table 1: The comparison characteristics and error analysis of GMSs.

	The number	%
Characteristics		
The number of GMS measurements	1837/1837	100
The number of GMSs passed at the first attempt (error <±20%)	1365/1837	74.3
The number of GMS sent for second measurement (error >±20%)	472/1837	25.6
The number of GMSs passed at the second attempt (error <±20%)	383/1837	20.8
The number of GMSs failed at the second repetition or excluded	89/1837	4.8
The number of GMS – laboratory method comparisons	1748/1837	95.1
Error analysis		
The number of total comparisons	1748	(100%)
The total number of positive (≤+20%) errors	1130	(64.6%)
The total number of negative (≤–20%) errors	618	(35.4%)
The mean and SD of positive errors	(9.3)	±5.8
The mean and SD of negative errors	(–7.1)	±3.9

than that of negative errors (618; 35.4%) The mean of positive errors was calculated as 9.3 ± 5.8, and that of negative errors as –7.1 ± 3.9, indicating a higher positive error rate of the devices. The statistical evaluation of error % of individual devices and of all GMSs (taking absolute values of negative errors) was as follows: 8.43 ± 5.25 for GMS-A, 8.46 ± 5.49 for GMS-B, 6.60 ± 5.59 for GMS-C, 8.83 ± 5.76 for GMS-D, 8.96 ± 5.53 for GMS-E and 8.44 ± 5.61 for all GMSs.

The means of errors of all GMS are close to each other, with that of GMS-C being the lowest. The GLU concentrations measured by GMSs ranged from 45 to 606 mg/dL,and those by laboratory method from 50 to 619 mg/dL.It was first examined whether all the measurements were Gaussian and whether the data were normally distributed. Descriptive statistics were applied to the GMSs. GMS-C showed no normal distribution. Therefore, in order to obtain the correlation coefficients of the comparisons, Pearson correlation analysis was applied for GMS-C, and Spearman correlation for the remainder. Correlation analyses were made between total GMSs and the laboratory method, and between individual devices (A – E) and the laboratory method (Table 2). GLU of 100 mg/dL was taken as the cut-off value, and the results of the GLU measurements were divided into two groups: those >100 mg/dL and those ≤100 mg/dL. The correlations at the concentrations <100 mg/dL (GLU) and at those >100 mg/dL (GLU) were determined for all

Table 2: Statistical analysis of GMS-laboratory method comparisons.

Correlation	r	p-Value	n
All GMSs – laboratory comparison	0.955	0.01	1748
All GMSs – laboratory comparison [(GLU) ≤ 100 mg/dL]	0.545	0.01	543
All GMSs – laboratory comparison [(GLU) > 100 mg/dL]	0.958	0.01	1205
GMS-A – laboratory comparison	0.965	0.01	96
GMS-A – laboratory comparison [(GLU) ≤ 100 mg/dL]	0.704	0.01	25
GMS-A – laboratory comparison [(GLU) > 100 mg/dL]	0.962	0.01	71
GMS-B – laboratory comparison	0.966	0.01	448
GMS-B – laboratory comparison [(GLU) ≤ 100 mg/dL]	0.518	0.01	116
GMS-B – laboratory comparison [(GLU) > 100 mg/dL]	0.967	0.01	332
GMS-C – laboratory comparison	0.984	0.01	243
GMS-C – laboratory comparison [(GLU) ≤ 100 mg/dL]	0.651	0.01	93
GMS-C – laboratory comparison [(GLU) > 100 mg/dL]	0.980	0.01	150
GMS-D – laboratory comparison	0.938	0.01	385
GMS-D – laboratory comparison [(GLU) ≤ 100 mg/dL]	0.652	0.01	175
GMS-D – laboratory comparison [(GLU) > 100 mg/dL]	0.958	0.01	210
GMS-E – laboratory comparison	0.952	0.01	576
GMS-E – laboratory comparison [(GLU) ≤ 100 mg/dL]	0.442	0.01	175
GMS-E – laboratory comparison [(GLU) > 100 mg/dL]	0.954	0.01	401

and for each individual GMS type. Significant correlations were found for all GMS – laboratory comparison [for all GLU, for GLU ≤100, and GLU >100; r = 0.955, 0.545, 0.958, respectively], for GMS-A – laboratory comparison (0.965, 0.704, 0.962), for GMS-B – laboratory comparison (0.966, 0.518, 0.967), for GMS-C – laboratory comparison (0.984, 0.651, 0.980), for GMS-D – laboratory comparison (0.938, 0652, 0.958), and for GMS-E – laboratory comparison (0.952, 0.442, 0.954). Very strong correlations were seen for all GLU measurements and for those >100 mg/dL, and weak correlation coefficients were found for GLU values ≤100 mg/dL. The number of comparisons at glucose concentrations >100 mg/dL was higher than that of comparison at the concentrations ≤100 mg/dL (1205 vs. 543). A similar tendency was present in individual GMSs.

The results of the Passing-Bablok regression analysis are shown in Table 3. All GMS results were compared with those of the laboratory method on the basis of the slope and intercept of the Passing-Bablok regression lines. The Bland-Altman plots of the all GMSs are presented in Figure 1.

As seen in Figure 1, except for GLU levels < 100 mg/dL very close equivalent slopes were observed applying Passing-Bablok regression fits, and most of the comparisons, except for GLU levels <100 mg/dL, yielded slopes of around 1.000 and near-zero intercepts. In order to show the compatibility between the two series of GLU measurements, Bland-Altman plots were obtained as seen in Figure 1.

Considering the current draft revision of ISO 15197 (13), the error percentage distribution of GMSs is shown in Table 4 on the basis of the data of the comparative method. The accuracy of GMSs within all limits stated in Table 4 was higher in prediabetic and diabetic measurement range [(GLU) >100 mg/dL] than in normo- and hypoglycemic levels [(GLU) ≤100 mg/dL]. The percentages of accepted results were 74% (within <±15%), 59% (within <±10%), and 30% (within <±5%) in the former and 68% (within <±15%), 40% (within <±10%), and 17% (within <±5%) in the latter.

Discussion

The assessment of analytical accuracy of any laboratory instrument, as in the case of quality control routinely carried out in the laboratory, is not possible for glucose meters. In this study, the comparison of the GMS result with that of the laboratory reference method was considered to be a means of quality assessment for these devices, and the simultaneously obtained capillary and venous sample of the same patient was taken as "the same control material" to manage the performance of hospital GMSs.

A within-day coefficient of variation (CV) <5% was accepted in this study as acceptable performance of GMSs, since a CV <5% for glycemic control other than hypoglycemia may be acceptable as suggested by Skeie et al. [21]. However, Boyd and Bruns [22] recommended strict imprecision rules for GMSs as a CV of 2% for proper insulin dosage.

The permissible error must be defined for the comparison of GMS and the laboratory method. What degree of analytical error is permissible for GMS remains a subject of debate. The fact that no objective criteria have been agreed means a lack of consensus with respect to the quality goals for these devices. For example, depending on the level of blood glucose to be measured, ≥95% of the measurements should be ranged within ±15 mg/dL in glucose concentrations <75 mg/dL or maximally within ±20% range in glucose concentrations ≥75 mg/dL for measurement accuracy as stated by ISO 15197-2003 (E). For minimal accuracy of GMSs, another criterion states that ≥95% of GMS measurements must fall within ±15 mg/dL in glucose concentrations <100 mg/dL and within ±15% in glucose concentrations ≥100 mg/dL as stated by ISO 15197-2013 (E) [13]. Another study [2] considered biological variation criteria and suggested a total error (including both bias and imprecision) of ≤6.9%. The National Committee of Clinical Laboratory Standards (NCCLS) (currently Clinical and Laboratory Standards Institute) and ISO recommendations allow error of up to ±20% [7]. In the current study, ±20% was accepted as the cut-off value regardless of the glucose concentration measured. It should be noted that in previous studies, when glucose meter results are compared to the laboratory results, the differences are expressed as mg/dL for GLU values <70 or 100 mg/dL, while differences are expressed as percentages for GLU values >70 or 100 mg/dL. In the present study, all differences were expressed as percentages for all glucose levels, since, especially in hypoglycemic levels, a difference of ±15 mg/dL GLU may be approximately the same as ±20%.

The performance gap between GMSs and the laboratory reference method has been the object of intense focus [23]. Undoubtedly, GMS performances have increasingly improved [22]. Unfortunately, a recent report evaluating the accuracy criteria of GSM stated an inaccuracy of >40% [24]. As can be seen in Table 2, the data of the current study show that 75% of the GMS measurements met the defined acceptance criteria, as 1365 accepted

Table 3: The results of the Passing-Bablok regression analysis.

GLU	All levels	≤100 mg/dL	>100 mg/dL
GMS-A (y), venous (x)			
Regression equation	y = 6.000 (0.403 to 12.225) + 1.000 (0.951–1.042)x	y = 10.231 (–14.800 to 25.764) + 0.912 (0.7059–1.228)x	y = 18.000 (9.000–24.672) + 0.934 (0.881–1.000)x
Cusum test for linearity	p > 0.10	p > 0.10	p > 0.10
GMS-B (y), venous (x)			
Regression equation	y = 3.299 (–0.538 to 6.040) + 1.014 (0.991–1.046)x	y = 30.020 (14.642–2.230) + 0.680 (0.538–0.857)x	y = 11.557 (8.000–15.352) + 0.971 (0.941–1.000)x
Cusum test for linearity	p > 0.05	p < 0.01	p > 0.10
GMS-C (y), venous (x)			
Regression equation	y = 0.000 (0.000–3.49) + 1.0000 (0.973–1.000)x	y = 11.750 (0.000–30.486) + 0.875 (0.675–1.000)x	y = 6.080 (0.000–13.217) + 0.960 (0.913–1.000)x
Cusum test for linearity	p < 0.01	p > 0.05	p < 0.01
GMS-D (y), venous (x)			
Regression equation	y = – 2.186 (–6.587 to 2.117) + 1.069 (1.034–1.108)x	y = 29.718 (16.400–40.656) + 0.687 (0.562–0.828)x	y = 3.733 (–2.480 to 8.000) + 1.033 (1.000–1.080)x
Cusum test for linearity	p < 0.05	p < 0.05	p < 0.01
GMS-E (y), venous (x)			
Regression equation	y = – 0.593 (–3.805 to 2.752) + 1.046 (1.018–1.074)x	y = 14.666 (0.000 to 27.076) + 0.833 (0.692–1.000)x	y = 7.762 (4.770–12.920) + 0.994 (0.960–1.020)x
Cusum test for linearity	p > 0.05	p < 0.05	p > 0.05
All GMSs (y), venous (x)			
Regression equation	y = 1.394 (–0.370 to 3.150) + 1.026 (1.009–1.041)x	y = 21.461 (14.692 to 27.800) + 0.769 (0.700–0.846)x	y = 10.661 (7.862–13.500) + 0.967 (0.950–0.987)x
Cusum test for linearity	p < 0.01	p < 0.01	p < 0.01

Regression equations are presented as y = a (95% CI) + b (95% CI)x. 95% CI – confidence intervals of 95%. a – regression line intercept. b – regression line slope. $p < 0.05$ was considered statistically significant.

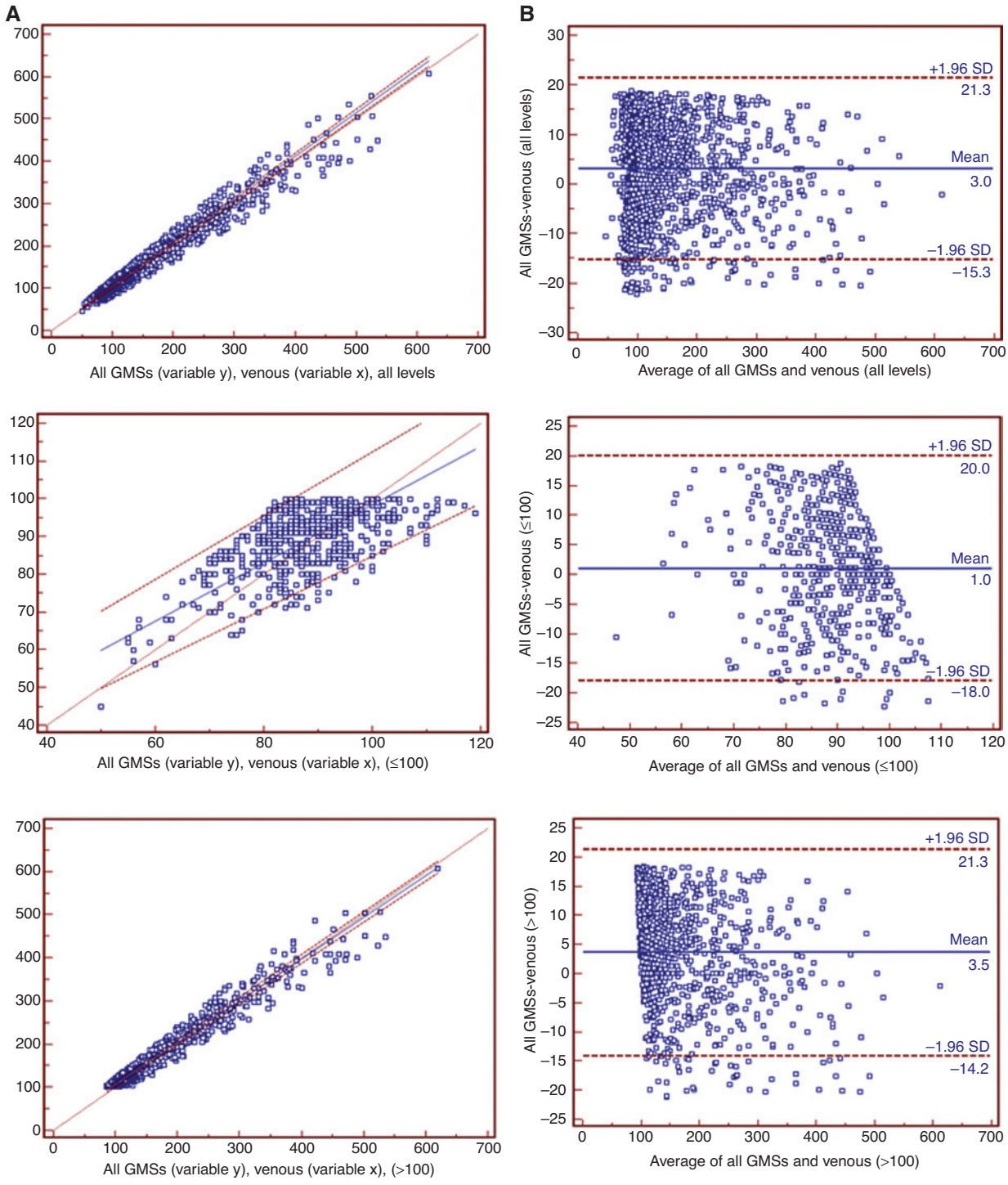

Figure 1: Passing-Bablok regression graphs (A) and Bland-Altman plots (B).
(A): Passing-Bablok regression fits for comparisons of all GSMs and venous determinations for [GLU] of all levels, ≤100, and >100. Solid line – regression line. Dashed lines – 95% CI for the regression line. Dotted line – identity line (X = Y). 95% CI – 95% confidence interval.
(B): Bland-Altman plot shows the compatibility of the GLU results obtained with all GSMs and laboratory method. Solid line (mean) – mean difference. Dashed lines (SD) – standard deviation.

results (74.3%) and 472 rejected results (25.6%). After repetition of the rejected measurements, these figures became 1748 accepted results (95%) and 89 rejected ones (5%), meaning that this external quality assessment prevented 472 inaccurate read-outs within a 3-year period in the hospital.

Table 4: Error percentage distribution of GMSs (according to the draft revision of ISO 15197).

	Within <±5%	Within <±10%	Within <±15%	Within <±20%	Exceeds ±20%
GLU ≤100 mg/dL					
X/Y	101/583	234/583	401/583	583/583	36/619
%	17	40	68	100	6
GLU >100 mg/dL					
X/Y	355/1165	697/1165	864/1165	1165/1165	62/1227
%	30	59	74	100	5

X: the number of samples within the specified difference from the comparative method; Y: the number of total measurements.

Capillary, arterial, and venous blood samples of the same patient may show significant differences in terms of glucose concentrations [16, 17]. Consequently, it is inevitable that the glucose values measured with glucose meters may give false results compared to the venous or arterial samples used in the laboratory reference method [25]. GMSs use whole blood (capillary blood) specimens for glucose testing. It has been reported that the usage of capillary blood in these devices results in measurements of glucose levels at ratios 10–15% lower than in plasma [26]. Although the majority of these devices have been calibrated to give plasma glucose results, some devices can measure exact plasma levels of glucose, since they use strips capable of filtering the plasma from the applied whole blood, reading-out the plasma glucose concentration. The concurrently-drawn plasma and serum glucose concentrations of the same patient, on the other hand, has been considered the same [27]. However, capillary blood glucose levels may be higher than those of venous blood samples in a non-fasting state [28, 29].

Some GMSs measure the glucose in lysed blood. Therefore, a discrepancy between GMS and the laboratory method is attributed to the difference in whole blood and plasma. These types of GMSs, which are whole blood analyzers and use lysed blood, apply a correction factor in order to report exact plasma glucose concentrations [17]. However, the majority of GMSs determine the glucose concentration in unlysed whole blood, with glucose levels being equivalent to those in plasma [17, 30]. In the present study, all the GMSs included were of the plasma-filtering type, meaning that sample type did not contribute to the total GMS error.

To date, several studies have been conducted on the performances of GMSs, and different aspects of the topic have been evaluated [2, 31, 32]. Several factors affect the hospital GMS results. These factors include hematocrit value, drug interactions, sampling region, contamination, device-related factors (storage conditions of test strips, enzyme used in the system, environmental conditions), and user-based errors [33–35]. The Diabetes Educator Guide to Blood Glucose Meter Selection and Monitoring for Accuracy and Safety 2017 by the American Association of Diabetes Educators (AADE) [36] and the Blood Glucose Monitoring Test Systems for Prescription 2016 by the US Food and Drug Administration [37] provided a long list of the source of errors or failures of GMSs, which are associated with the operator, reagents (strip), instrument, environment, and sample.

The majority of the errors may be related to the operator, including incorrect specimen collection, insufficient or incorrect application of blood to the strip, inappropriate sampling site, application of the specimen to the strip more than once, incorrect insertion of the strip into the meter, inaccurate timing, poor meter maintenance or cleaning, and poor storage of consumables of the device. The operator errors have been reported in one study as 12% [38]. Similarly, Schmid et al. [39] listed such operator errors as the application of an insufficient volume of blood, milking the finger to acquire sufficient blood, using outdated test strips, using alternative sites, using a malfunctioning meter, and using a dirty meter. However, the GMS usage errors can largely be avoided by training the users/operators properly. On the basis of the current study data about this type of error, it can be concluded that the high numbers of rejected GMS read-outs were improved at the second series of measurements and that the inaccurate read-outs may have been caused by the users. Of 472 rejected read-outs, 383 passed after the second measurement, suggesting user error at the first attempt and improvements in procedure at the second attempt.

The statistical evaluation of the results has shown that GLU results comparable with the laboratory method were observed for the majority of the glucose meters used in the hospital and that the performance of these devices is better in prediabetic (from 100 to 125 mg/dL) and in hyperglycemic (>126 mg/dL) GLU levels as stated by previous studies [40] but not in normo- and hypoglycemic (<100 mg/dL) GLU levels. A good correlation or concordance for the measurement at GLU concentrations >100 mg/dL is supported (Figure 1) when Passing-Bablok regression was

applied. Most of the comparisons yielded slopes of around 1.000 and near-zero intercept (Table 3). All the regressions associated with GLU concentrations >100 mg/dL showed good concordance between GMSs and the laboratory method. Conversely, lower correlation or poor concordance for the measurement of GLU concentrations <100 mg/dL was observed (Figure 1) by Passing-Bablok regression fits and by the lower correlation coefficients.

Bland-Altman plots showing the compatibility between GMSs and laboratory measurements are presented in Figure 1. A good concordance of both GLU measurements in GLU concentrations >100 mg/dL can easily be seen when one considers the results of the Bland-Altman difference plots and the biases. However, an acceptable, or moderate, performance of both GLU measurements in GLU concentrations <100 mg/dL can easily be predicted by the results of the Bland-Altman difference plots and the biases. The findings of this study also show that there is a tendency for a read-out with positive error (≤+20%) in GMSs. Both the number of positive read-outs and the mean of positive read-outs were found to be higher than those of negative errors (≤−20%). Our study has such limitations as: glucose concentrations may be different in capillary and venous blood samples especially in critically ill patients. Catecholamine administration to critically ill patients may also influence POCT glucose levels. Although the glucose oxidase method is specific for blood glucose concentration, it should be considered that blood oxygen concentrations may influence POCT devices based on glucose oxidase technique. The skin puncture method for POCT glucose meter analysis is performed by different medical professionals in different clinics and this may cause little variations.

It was concluded that a compatibility of the results of glucose meters to those of the laboratory could be obtained provided that the error sources were minimized. However, healthcare professionals and diabetic patients who are self-monitoring, should be aware of the evaluation of the glucose meter results, and they should check their devices, as frequently as possible, with laboratory determinations as a part of external quality assessment. Otherwise, unacceptable systematic and/or randomized errors are inevitable. Checking the glucose meter results at regular intervals as recommended by almost all diabetic societies should be mandatory. In order to achieve the analytical quality of GMSs, it is critical to educate the device users and to assure a defined analytic quality as a part of management of glycemia. The error percentage distribution of the GMSs indicated that the accuracy of GMSs is higher in the prediabetic/diabetic measurement range than at normo-/hypoglycemic levels.

Conflict of interest statement: The authors declare that there is no conflict of interest.

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