Self-Monitoring of Blood Glucose Levels Requires Intensive Training for Use of Meters to Obtain Reliable and Clinically Relevant Measurements

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Abstract

Background:

Anecdotal reports from pediatric sites have indicated that some blood glucose meters may display wrong and misleading numbers rather than error indications, when operated in deviation from the instructions for use (IFU), e.g., by manipulating the strip during the count-down phase.

Methods:

This study was performed with 60 patients with diabetes [32 female, 28 male, 21 type 1, 39 type 2, age (mean ± SD): 56 ± 11 years] who measured their blood glucose levels twice with five different blood glucose meters [Precision® Xceed™ (Abbott Medisense), Freestyle Mini™ (Abbott Medisense), Accu-Chek® Comfort (Roche Diagnostics), Accu-Chek® Aviva (Roche Diagnostics), and Ascensia Contour® (Bayer Vital)]. The first measurement was performed in accordance with the IFU, and the second by manipulating the test strip using a standardized inflexion/release procedure during the count-down phase. A standard glucose oxidase method (SuperGL) served as laboratory reference.

Results:

All meters worked in full compliance with current accuracy standards when operated according to the IFU. When manipulating the test strip, the results varied considerably: While changes in reliability were acceptable for two devices (Precision® Xceed®, Freestyle Mini™), the other devices produced an unacceptable number of errors and a series of entirely wrong values without error indication.

Conclusions:

The use of all devices is recommended when used according to the IFU. The use under the artificially induced impaired testing conditions is a major concern. This study underlines the importance of appropriate patient training regarding adherence to the IFU of glucose meters.

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Introduction

Daily self-monitoring of blood glucose (SMBG) is a common practice for patients with type 1 or type 2 diabetes. In particular, patients who require insulin are highly dependent on reliable glucose monitoring. It is well known that frequent glucose control is proportional to improvement of glycemic control as assessed by reduction of HbA1c value.[1,2,3,4] Recently, the importance of glucose self-monitoring was impressively shown in type 1 diabetes mellitus patients by Nathan et al.[5] In that study, one patient group received intensive diabetes care, consisting of treatment with insulin based on at least four glucose self-monitoring measurement throughout a day. This intensive therapy was followed by reduced risks of cardiovascular disease by 42%, and by 57% for heart attacks, stroke, or cardiovascular disease-related death after 17 years in comparison to the control group receiving conventional diabetes care. Additionally, a study by Martin et al.[6] revealed a decreased diabetes-related and a reduced all cause-related death rate for a group of patients with type 2 performing SMBG in comparison to a non-SMBG control group.[6]

Therefore, it is mandatory that glucose meters that are used by the patients are reliable with easy to follow instructions for use. Anectodal reports from clinical sites have indicated that some blood glucose meters (BGMs) may displace wrong or misleading values. This has prompted us to investigate the robustness of BGMs with regard to handling errors during the investigation. This study was designed as a comparator study where BGMs are used in accordance with or including deviations from the respective instructions for use.

Subjects and Methods

Patients

This study was performed in accordance with the Guidelines for Good Clinical Practice and after approval by the responsible ethics review board. Prior to study participation, patients gave written informed consent for the blood draws and subsequent measures. The trial was designed as a one day, open label, single center study. A total of 60 patients with type 1 and type 2 diabetes mellitus were enrolled into the study.

Measurements

The study was conducted with the five self blood glucose monitoring devices (Precision® Xceed™ [Abbott Medisense], Freestyle Mini™ [Abbott Medisense], Accu-Chek® Comfort [Roche Diagnostics], Accu-Chek® Aviva [Roche Diagnostics], and Ascensia Contour® [Bayer Vital]), when used by the patients in accordance to or with a standardized deviation from the instructions for use. The introduced deviation was a mechanical strip stress (vertical elongation of the test strip, sudden release and swinging) during the measurement procedure.

After testing with an established laboratory reference blood glucose test method (Super GL Glucose-/Lactate-analyzer; glucose oxidase method), the patients were asked to perform a series of measurements with all five devices with and without a mechanical stressor. Thereafter, the standard reference method was applied again to allow for consideration of blood glucose changes in the analysis. The mechical stress was introduced by flexing and subsequent immediate release of the test strip during the countdown period of the measurement procedure. All measures were performed in the presence of experienced healthcare professionals (investigator or study nurse). Thereafter, the patients ingested a carbohydrate-containing drink (300 ml regular coca-cola or apple juice, approximately 2BE) to increase blood glucose levels and the procedure was repeated after approximately one hour. The second measurement series was performed identically to the first measurement series.

Laboratory Reference

Reference glucose values were measured with the CE-certified Super GL-Glucose/Lactate-analyzer (Dr. Müller Gerätebau GmbH, Freital, Germany). Closeable sample cups were filled with capillary blood drawn from the fingertip before and after the measurements performed with the handheld devices for determination of blood glucose levels with the Super GL-Glucose/Lactate-analyzer. Conventional end-to-end capillaries were employed. All laboratory glucose reference determinations were made at the central laboratory of the ikfe GmbH.

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Statistics

All analyses were performed in an exploratory sense with appropriate standard descriptive methods and error-grid analyses according to Clarke et al.[7] Deviation of measures from each laboratory standard value were classified into five zones A, B, C, D and E as described in detail earlier.[7, 8] Zones A and B are considered to comprise the clinically acceptable values, whereas the zones C, D and E represent the clinically unacceptable values, which would lead to incorrect treatment decisions.

If the two standard laboratory reference values were within a 5% range, indicating stable glucose control, the mean values of the two standard laboratory tests were used as the comparator value for each data set for the error-grid analysis or the calculation of the mean absolute percent deviation. If the difference was larger, a device specific comparator value was calculated based on the assumptions of a linear change of glucose concentrations in the observation period and an equal time requirement for each testing procedure. Prior to the analysis, the BGM values were corrected with a factor of 1.1 to take into account that the blood glucose-self measurement devices calculate the numeric values for venous blood in contrast to the laboratory reference method, which reports the numeric value for the capillary blood.

The determination of the accuracy was performed by evaluating the mean absolute percent deviations (MAPD) and the number of *correctly* performed readings, as indicated by a numerical value without error signal or any other indication of disturbed measurement procedure.

Statistical significance was tested using two-sided Student's *t* test. P-values of p<0.05 were considered statistically significant. All calculations were made with the SPSS statistical package (version 12.0, SPSS Inc., Chicago).

Results

Sixty patients with diabetes were enrolled. The cohort consisted of 21 patients with type 1 diabetes (35%) and 39 patients with type 2 diabetes (65%). Patient ages were a mean of 55.9 ± 11.4 years old, and a range 41 - 75 years. Overall, 116 data sets with complete numeric values including device error indications could be included into the analysis (96.7% of the theoretical maximal number) per blood glucose measuring device and test condition. Reasons for exclusions were implausible differences between the laboratory values at baseline and endpoints that would represent blood glucose changes > 5mg/dl*min (1 case) or withdrawal of the patients from the trial after the first measurement series (3 cases) due to high baseline glucose values.

Data were available from 1076 measurements in the regular procedure and measurements with the mechanical strip stress test. In the former group, numeric values could be obtained from 578 (53.7%) measures. In mean, 98.5% clinically acceptable numeric values were derived in this group, compared to the reference values. In the measurements with the deviations from IFU, 498 (46.3%) numeric values could be obtained. Overall, 82.2% clinically reliable numeric values, compared to the reference values were derived in this group.

Overall, 82 error messages occurred during the study. The test performance according to the IFU lead to 2 error messages (error). Applying mechanical stress to the test strip lead to 80 error messages (58 low, 22 error). During the study, the non-numeric value *high* did not occur for any of the tested devices.

The results of the error grid analysis for each test device and condition are given in **Figure 1**. **Table 1** provides the distribution (in percent) the paired values into the classical error grid zones. The Error-Grid analysis revealed comparable results for both normal and impaired testing conditions for the trial devices Precision® Xceed™ (A+B: 99.1/ 99.1 [normal/impaired]), Freestyle Mini™ (A+B: 98.3/ 97.4 [normal/impaired]). For the devices Accu-Chek® Comfort (A+B: 98.3/ 87.1 [normal/impaired]) and Accu-Chek® Aviva (A+B: 97.4/ 90.5 [normal/impaired]) the analysis revealed slightly differing values from the normal and impaired testing conditions. The blood glucose meter Ascensia Contour® (A+B: 99.1/37.1 [normal/impaired]) showed greatly alternating results in the analysis.
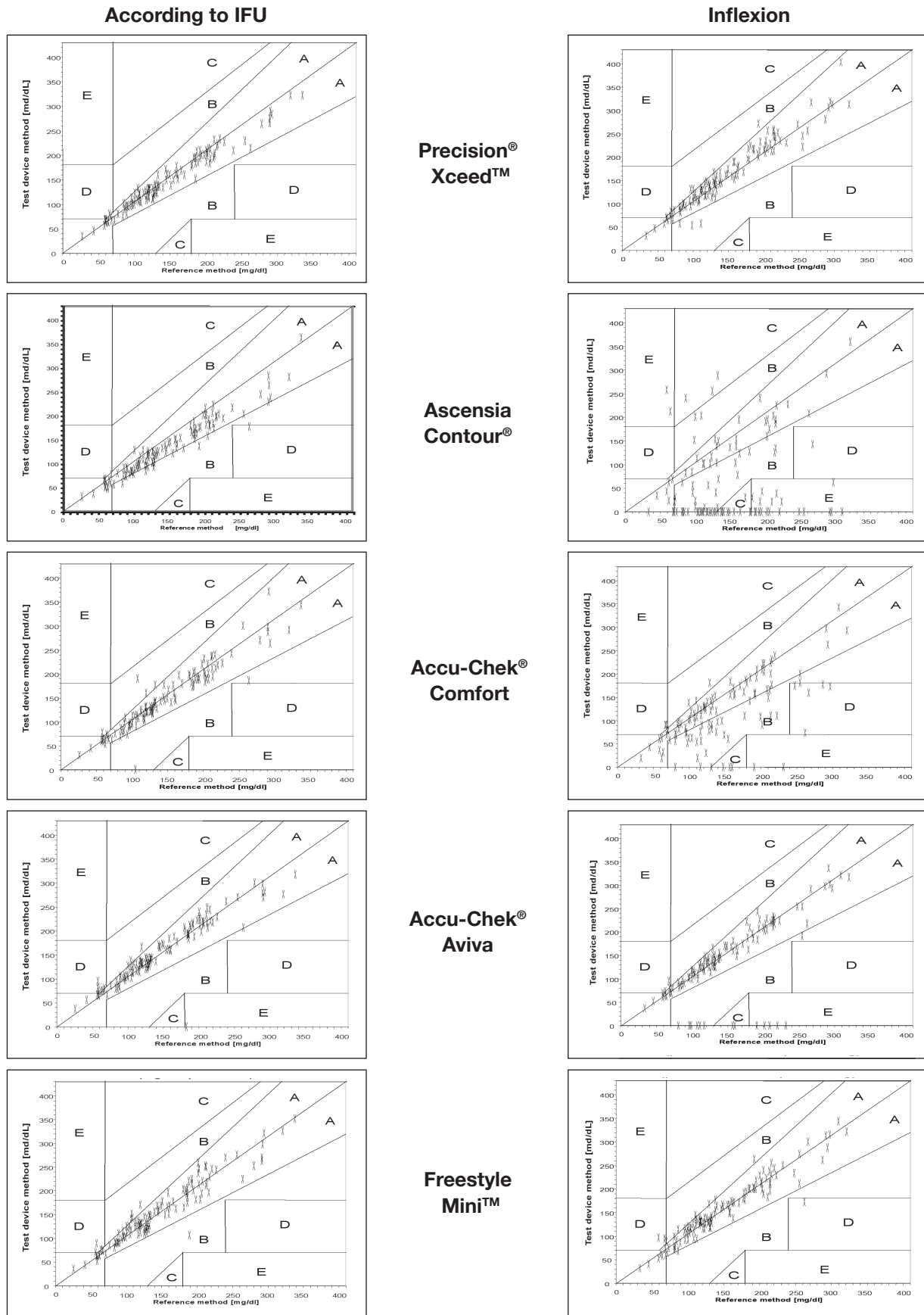
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According to IFU　　　　　　　　　　　　　　**Inflexion**

Figure 1: Error-Grid Analysis for the five test devices (Precision® Xceed™, Freestyle Mini™, Accu-Chek® Comfort, Accu-Chek® Aviva, and Ascensia Contour®) devices under normal conditions in accordance with the instructions for use (left column) and under disturbed testing conditions performed by strip inflexion and release during test period (right column).

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Normal					
Zone	**Precision® Xceed™**	**Accu-Chek® Comfort**	**Ascensia Contour®**	**Accu-Chek® Aviva**	**Free-style Mini™**
A	98.3%	94.8%	92.2%	95.7%	94%
B	0.9%	3.4%	6.9%	1.7%	4.3%
C	0%	0%	0%	0%	0%
D	0.9%	0.9%	0.9%	1.7%	1.7%
E	0%	0%	0%	0%	0%
Error	0%	0.9%	0%	0.9%	0%
Inflexion					
Zone	**Precision® Xceed™**	**Accu-Chek® Comfort**	**Ascensia Contour®**	**Accu-Chek® Aviva**	**Free-style Mini™**
A	94%	59.5%	19%	88.8%	92.2%
B	5.2%	27.6%	18.1%	1.7%	5.2%
C	0%	0%	3.4%	0%	0%
D	0.9%	6%	0.9%	2.6%	2.6%
E	0%	0%	7.8%	0%	0%
Error	0%	6.9%	50.9%	6.9%	0%

Table 1: Distribution (in percent) of the paired values into the classical error-grid zones (according to Clarke *et al.*)[7]

No statistical significance ($p > 0.05$) could be observed when comparing the mean absolute percent deviation (MAPD) values of the normal vs. the impaired testing conditions for the trial devices Precision® Xceed™ (normal/impaired MAPD: 7.0/8.9), Freestyle Mini™ (normal/impaired MAPD: 10.7/10.8) and Accu-Chek® Aviva (normal/impaired MAPD: 10.0/9.0). For the meters Accu-Chek® Comfort (normal/impaired MAPD: 8.2/21.5) and Ascensia Contour® (normal/impaired MAPD: 11.6/49.1) the difference in MAPD was statistically significant ($p < 0.001$).

Discussion

In the present study, five commercially available self blood glucose monitoring meters (Precision® Xceed™, Freestyle Mini™, Accu-Chek® Comfort, Accu-Chek® Aviva and Ascensia Contour®) were compared regarding their accuracy and reliability when used by sixty patients with type 1 or type 2 diabetes mellitus. The test was performed with comprehensive range of regular and disturbed measurement conditions. In general, all devices revealed excellent and reliable results in accordance to the current technology standards when used according to the instructions for use. Furthermore, the obtained results demonstrate the improvement in blood glucose testing technologies when compared to earlier studies performed with the same clinical and laboratory infrastructure.[9]

The mechanical manipulation procedure which resembles the use of SMBG´s by untrained patients (e.g. children or the elderly) show comparable and stable performance for the devices Precision® Xceed™ and Freestyle Mini™. A slightly impaired outcome is observed for the blood glucose meters Accu-Chek® Aviva and Accu-Chek® Comfort and a significant deterioration is seen with the Ascensia Contour®. The latter device produced large magnitude errornous results under these conditions that could mislead the patient by indicating wrong numbers without indicating the impaired measurement conditions in about a third of the measurements. Additionally, the device showed a high number of *low* messages, although the blood glucose level was in the regular range, which could also lead to clinically significant erroneous intervention by the patient.

The reason for the differences between the devices may be found in the different design specifications of the test strips. The Ascensia Contour strip uses capillary adhesion of the blood sample into the strip without further measure to keep the blood in place during the measurement procedure. Rapid strip movement can lead to removal of the blood from the sensor. In the best case, an error alarm could be produced, but wrong values displayed on the screen are also likely.

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While this does not play a major role when patients are using the devices in accordance to the instruction manuals, it may pose a growing concern for unreliable patients, like children, who might not adhere to the given instructions. This becomes even more relevant due to the emerging incidences of diabetes in children and adolescents.[10,11] Thus, the reliability of SMBG is of utmost importance for patients with diabetes. It enables the patient to make important treatment decisions. Additionally, reliable SMBG results might protect the patients from comorbidities.[6]

In conclusion, close adherence to the instruction for use is a stringent requirement for patients using blood glucose self-measuring devices. Additionally careful selection of the meters is especially recommended in pediatric patient populations.

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