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Fig. 1. Difference between Glucometer Dex or GlucoMen Glyco results (first measurement) and reference method results (mean of two measurements) plotted against the reference method results.

(A), patients (n = 93 and 90 for Glucometer Dex and GlucoMen Glyco respectively); (B), MLT (n = 95 and 92 for Glucometer Dex and GlucoMen Glyco, respectively).
Measurements with strips filled incompletely with blood are indicated with closed symbols. Open symbols indicate measurements with different lots of test strips. Lines represent limits suggested from American Diabetes Association (inner lines) (9) and in ISO/FDIS 15197 (outer lines) (5).
measurements with strips not completely filled with blood. The MLT also observed whether the instrument was coded correctly. Finally, the patients completed two questionnaires, one about the user manual and one about the user-friendliness of the device. The study protocol was approved by the Norwegian Regional Committee for Medical Research Ethics.

The comparison method for the Glucometer Dex was a glucose dehydrogenase method using hemolyzed blood with reagents from Bayer (GlucoMen Glyco, II; prod. no. B01-597-01). Both methods were 1650 with reagents from Bayer (Glucose Hexokinase method that measures glucose in plasma on an Advia 1650). The comparison method for GlucoMen Glyco was a glucose dehydrogenase method using hemolyzed blood on a Cobas Faran centrifugal analyzer (Roche Diagnostics). The comparison method for GlucoMen Glyco was a method that measures glucose in plasma on an Advia 1650 with reagents from Bayer (Glucose Hexokinase Method II; prod. no. B01-597-01). Both methods were verified by SRM 965 from the NIST and by control solutions verified by the isotope dilution–gas chromatography/mass spectrometry reference method.

Imprecision (SD and CV) was calculated by use of paired measurements, based on the formula:

$$SD = \sqrt{\frac{\sum d^2}{2n}}$$

where $d$ is the difference between measurements, and $n$ is the number of duplicate samples. The criterion promoted by Burnett (6) was used for detection of outliers. According to ISO/FDIS 15197 (5) and the NCCLS (7), the number of measurements deviating more than ±20% (results ≥4.2 mmol/L and >0.83 mmol/L (results <4.2 mmol/L) should be <5%. None of the meters met these requirements when used by patients, but the GlucoMen Glyco met the requirements when used by the MLT (Fig. 1 and Table 1). However, several other, usually stricter quality specifications have been suggested (8–11), e.g., the American Diabetes Association suggests a total error of ±10% (9).

As can be seen in Table 1, the measurements performed by the patients had significantly poorer precision than measurements performed by the MLT ($p <0.05$). On the basis of patient-derived quality specifications and simulation studies, it has been suggested that imprecision should be <5% (9, 10). In a study where the analytical quality of five SMBG systems was investigated, the CV varied from 5% to 11% when patients used the instruments compared with 2.3–5.9% when a MLT used them (12), which is in line with our results.

One important issue of incorporating a user test in the evaluation of SMBG devices is to discover user errors that will not be detected by the MLT. This was found for the GlucoMen Glyco, but not for the Glucometer Dex. For the GlucoMen Glyco, 6% of the measurements performed by the patients were done with too little blood, whereas the MLT had no such measurements. In addition, 16% of the patients had not coded the instrument correctly (Fig. 1 and Table 1). If measurements related to these errors were excluded from the calculations, the analytical quality of the meter would also be acceptable in the hands of the patients. Regarding the Glucometer Dex, there was a problem with the strip that led to poor uptake of blood. As many as 24% of the measurements performed by the patients with the Glucometer Dex at the consultation were done with too little blood. The MLT, as well as the patients who received training, had significantly fewer incompletely filled strips at the consultation than the group of untrained patients (15%, 18%, and 31%, respectively; Fig. 1 and Table 1). This problem thus would have

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### Table 1. Analytical quality.

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Examined by</th>
<th>n</th>
<th>Deviation &gt; ISO standard, %</th>
<th>n</th>
<th>Mean, mmol/L</th>
<th>Results excluded, n</th>
<th>CV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucometer Dex</td>
<td>MLT</td>
<td>95</td>
<td>11.6 (5.9–19.8)</td>
<td>187</td>
<td>10.5</td>
<td>2</td>
<td>5.6 (5.2–6.1)</td>
</tr>
<tr>
<td></td>
<td>Patients at consultation</td>
<td>93</td>
<td>24.7 (16.3–34.8)</td>
<td>92</td>
<td>10.3</td>
<td>4</td>
<td>9.8 (8.8–11)</td>
</tr>
<tr>
<td></td>
<td>Patients at home</td>
<td>396</td>
<td>9.0</td>
<td>9</td>
<td>8.6 (8.1–9.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GlucoMen Glyco</td>
<td>MLT</td>
<td>92</td>
<td>1.1 (0.1–6.1)</td>
<td>191</td>
<td>9.0</td>
<td>0</td>
<td>4.3 (4.0–4.7)</td>
</tr>
<tr>
<td></td>
<td>Patients at consultation</td>
<td>90</td>
<td>6.7 (2.4–14.0)</td>
<td>94</td>
<td>9.2</td>
<td>2</td>
<td>6.8 (6.1–7.8)</td>
</tr>
<tr>
<td></td>
<td>Patients at home</td>
<td>411</td>
<td>8.5</td>
<td>5</td>
<td>6.4 (6.1–6.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Excluding results related to incorrect coding and incompletely filled strips

Excluding results from incompletely filled strips

- a Percentage of measurements (first of duplicate) that deviate from the reference method (mean of duplicate) by more than the difference allowed by the ISO standard (5). When calculating the accuracy only measurements from the MLT’s instrument for which all three lots were included are presented.
- b Calculated from duplicate measurements from patients or from the MLT. When calculating the imprecision for instruments used by the MLT, measurements for both meters were included.
- c Mean (95% confidence interval).
- d Results were excluded based on the criterion promoted by Burnett (16).
- e 95% confidence interval in parentheses.
been detected by the MLT, but was more obvious when the patients used this meter.

To evaluate the lot-to-lot variation, we included only the measurements performed by the MLT. For the Glucometer Dex, the analytical quality of one lot was significantly poorer than the quality of the two others, even when we excluded the results for incompletely filled strips. For the GlucoMen Glyco there was no difference in analytical quality among the three lots, but all had a negative bias compared with the reference method, as shown in Supplement 2 in the online Data Supplement. Lot-to-lot variation may be a considerable problem with SMBG devices and could be a major factor in loss of analytical quality (12). From 2004 onward, the quality of all lots on the Norwegian market will be examined.

Educational efforts might influence the performance of SMBG (13–15). For the Glucometer Dex, the precision obtained both at the consultation and at home was better for the patient group trained on meter use by the MLT compared with the group that received only written instructions [CV, 12% and 28% for the trained patients and the untrained patients, respectively, at the consultation (P < 0.05) vs 5.6% for the trained patients and 8.8% for the untrained patients at home (P < 0.05)]. For the GlucoMen Glyco, the precision obtained at home was better for the trained group than for the nontrained group (CV, 5.2% vs 7.6%; P < 0.05). However, 12 patients in the nontrained group compared with 2 patients in the trained group had coded the GlucoMen Glyco incorrectly.

User errors that were assessed in the evaluations were highlighted in the questionnaires (Supplements 3 and 4 in the online Data Supplement). Regarding the Glucometer Dex, ~25% of the patients commented on the problem of poor uptake of blood. In the case of the GlucoMen Glyco, 13% answered that it was difficult to apply blood to the test strip, and 17% found it difficult to code the instrument. Manufacturing of SMBG instruments according to patients’ wishes may lead to improvements in acceptability, compliance, and glucose control (16).

Each evaluation lasted ~5 months. One month was used to prepare the work, 2.5 months were needed to complete the practical work, and 1 month was needed for result evaluation. The costs were estimated to be approximately NOK 150 000 (US $20 000) for each evaluation.

It is essential that important shortcomings of SMBG devices are disclosed before the instruments are made commercially available. A procedure for evaluating new instruments and strips should therefore be standardized, including both a user part and a part that deals with analytical quality in the hands of experienced technologists. The evaluation should not be too costly to perform. We believe that our procedure fulfills these demands, and the Norwegian Health Authorities have decided that all SMBG instruments marketed in Norway should be examined by a procedure similar to the one described in this study. In addition, all lots of strips on the market will be tested in a special survey because they cannot be included in the procedure for practical reasons.

The Glucometer Dex and GlucoMen Glyco instruments and strips used and tested by the MLT and the patients in the study were kindly supplied by Bayer Diagnostics (Tarrytown, NY) and Menarini (Firenzi, Italy), respectively. The National Office for Social Insurance in Norway provided financial support for the study. The study is part of the Global Campaign of Diabetes Mellitus launched by the IFCC.

References


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Elimination of the Cardiac Natriuretic Peptides B-Type Natriuretic Peptide (BNP) and N-Terminal proBNP by Hemodialysis, Hans Günter Wahl,1* Stephanie Graf,2 Harald Renz,1 and Winfried Fassbinder2 (1 Klinikum der Philipps-Universität Marburg, Department of Clinical Chemistry and Molecular Diagnostics, 35033 Marburg, Germany; 2 Klinikum Fulda, Department of Internal Medicine III, Fulda, Germany; * author for correspondence: fax 49-6421-2865594, e-mail hg.wahl@med.uni-marburg.de)

The measurement of natriuretic peptides for the diagnosis of heart failure has been a major breakthrough in cardi-