Performance Analysis of a Real-time Glucose Monitor

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Introduction

The fear of hypoglycemia often dictates the way nurses and physicians manage blood glucose (BG) levels—such as frequently as every 5 minutes (Figure 1). The device has been tested both in vitro and in vivo for linearity, bias, and precision in response to glucose [10]. This small-scale study was devised to evaluate the VIA’s performance in terms of accuracy compared to the HemoCue B-Glucose Analyzer (HC; HemoCue AB, Angelholm, Sweden). BG was measured simultaneously using the VIA and HC every 10 minutes over an 8.5 hour period in 14 separate experiments. These paired measurements were analyzed using the techniques of linear regression and difference against mean.

Data Collection

who, subjects

- Twelve adults (5 type 1 diabetic patients and 7 non-diabetics volunteers) participated in the study.
- Participants ranged in age from 27 to 51 (mean age was 37).
- Body mass index averaged 23 ± 3 kg/m².
- One diabetic patient was studied on three separate occasions for a total of 14 experiments.

what, experimental protocol

- Each experiment lasted 8.5 hours.
- Each participant ate two identical meals of fixed caloric content and exercised on a stationary bicycle for 30 minutes.
- Each diabetic patient was placed on continuous intravenous regular insulin infusions and dosed using a standardized algorithm with a constant basal rate (0.5U/hr) and boluses given with each meal [5,6,7,8,12].
- BG levels were measured every 5 min using the VIA.
- Venous blood samples (from the same line) were also collected every 10 min (every other VIA measurement) for glucose reference measurements and for determination of plasma insulin.
- In addition, capillary blood was sampled hourly by fingerstick and assayed for glucose concentration using the Accu-Chek Instant glucometer (Roche Diagnostics, Basel, Switzerland).
- Each experiment yielded between 48 and 52 paired data points (where the blood glucose was measured simultaneously by the VIA and the HC).

and where…

- The Artificial Pancreas Center at Jefferson Medical College, Thomas Jefferson University in Philadelphia.

Data Analysis

BG values were divided into separate groups to study the effect of BG level when comparing the two devices. The three groups were defined by the ranges: hypoglycemia (L) <80 mg/dl, near-normal glycemia (N) 80 to 180mg/dl, and hyperglycemia (H) >180 mg/dl. Linear regression analysis yielded the correlation coefficient and linear regression equation using the paired measurements over the entire range of BG values. The chosen parameters of the linear regression equation minimized the squared error between the estimated and actual BG values. Normal quantile plots for each group were generated to determine normalcy of the residuals. Comparison of the data also included the method of Bland and Altman [1]. The relationship between the difference (VIA – HC) and the mean ([VIA + HC]/2) was used. Agreement between the VIA and HC measurements were assessed in each range to determine if the BG level affects the performance of the device. Statistical analysis was performed using SPSS for Windows (SPSS Inc., Chicago, IL) and Matlab (The Mathworks, Inc., Natick, MA).

Results

Linear regression analysis yielded a regression line equation, \( VIA = 0.82 \times HC + 29 \). Agreement between the VIA and HC measurements were assessed in each range to determine if the BG level affects the performance of the device. Statistical analysis was performed using SPSS for Windows (SPSS Inc., Chicago, IL) and Matlab (The Mathworks, Inc., Natick, MA).

Discussion

Linear regression analysis illustrated a well-defined difference in performance between the two devices. Although the paired measurements are well correlated, there will be significant differences in their performance at certain BG levels. Most critical is the discrepancies observed in the hypoglycemic range. It is important to determine the onset of hypoglycemia and initiate the proper treatment to avoid complications. A direct comparison of the two devices was made using the techniques described by Bland and Altman [1]. The plot of the difference against the mean illustrates a trend in the data where the bias between the two devices is more pronounced as the BG increases. In the L and N ranges, the VIA measurements are consistently higher than the HC.

<table>
<thead>
<tr>
<th>Glucose range</th>
<th>VIA Mean Bias (mg/dl)</th>
<th>HC Mean Bias (mg/dl)</th>
<th>N (paired samples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L (&lt;80 mg/dl)</td>
<td>12.0</td>
<td>9.6</td>
<td>5</td>
</tr>
<tr>
<td>N (80 to 180 mg/dl)</td>
<td>0.9</td>
<td>-8.8</td>
<td>160</td>
</tr>
<tr>
<td>H (&gt;180 mg/dl)</td>
<td>17.9</td>
<td>-7.8</td>
<td>1</td>
</tr>
</tbody>
</table>

The frequent one-point recalibration of the VIA is dependent on the concentration of glucose in the flush solution used to clean the sensor after each measurement. Errors in the preparation of the flush solution could result in an improper calibration of the device, leading to the BG level dependent discrepancies observed in the hypoglycemic range. Torjman et al. [17] and Dahlberg and Whitelaw [2] both concluded that the HC produces BG measurements below reference values in the hypoglycemic range. But, these claims are contradicted in other studies [14,18,20].