Whole-Blood Glucose Testing at Alternate Sites

Glucose values and hematocrit of capillary blood drawn from fingertip and forearm

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OBJECTIVE — To measure hematocrit (Hct) and glucose concentration in capillary blood drawn from the fingertip and forearm of a group of 50 nonfasting subjects with diabetes.

RESEARCH DESIGN AND METHODS — Hct was determined indirectly by measuring Hb with the HemoCue B-Hemoglobin Photometer. Glucose was assayed with the HemoCue B-Glucose Analyzer, chosen as the independent control assay, and the Sof-Tact Blood Glucose System. Testing session with each subject lasted ~30 min and consisted of a sequence of tests with each device (SofTact, HemoCue Glucose, and HemoCue Hemoglobin), performed on the arm and then on the fingertip. This sequence was performed three times, so all tests were done in triplicate. Additional fingersticks were performed on each subject at the start and end of the session to measure net change of glucose status during the experiment with a YSI Glucose Analyzer. The mean of the triplicate assays was used to calculate each subject’s percent of glucose difference between arm and finger [(arm glucose – finger glucose)/finger glucose]. Because of the order in which replicates were performed, time-dependent changes in the glucose status of subjects had little effect on the mean values. Thus, the percent of glucose difference calculated herein reflects the intrinsic difference between forearm and fingertip.

RESULTS — Hb concentration and Hct were found to be significantly higher in the arm than in the finger. When intraperson differences were calculated, the difference for Hb and Hct was found to be 1.8 ± 1.1 g/dl (mean ± SD) and 5.3 ± 3.0%, respectively. In contrast to Hb, the percent of glucose difference between arm and finger was statistically insignificant. When measured with HemoCue, the percent of glucose difference was ~0.1 ± 8% for all 50 subjects, −1 ± 6% for 20 subjects, for whom blood glucose varied <9 mg/dl during the experiment, and 2 ± 10% for 15 subjects, for whom blood glucose varied >18 mg/dl. Thus, irrespective of how much blood glucose changed among the subjects, the glucose difference between forearm and fingertip was insignificant and less than measurement errors. A major source of error in the calculated differences was variability between replicates. No correlation was observed between an individual’s Hct bias and his or her percent of glucose difference, as measured with HemoCue. The results with Sof-Tact were similar, with percent of glucose difference again being statistically insignificant. The measured difference was −4 ± 13% for all 50 subjects, −1 ± 13% for 20 subjects, for whom blood glucose varied <9 mg/dl during the experiment, and −1 ± 12% for 15 subjects, for whom blood glucose varied >18 mg/dl. There was no correlation between a subject’s Hct bias and his or her glucose difference, as measured with Sof-Tact.

CONCLUSIONS — In this cross-sectional study of 50 nonfasting subjects whose blood glucose concentration changed to various degrees during the experiment, no significant glucose difference was observed between the capillary beds of the forearm and fingertip, regardless of whether glucose was assayed with HemoCue or the Sof-Tact Blood Glucose System. On the other hand, Hb concentration and Hct were found to be significantly higher in the capillary blood of the forearm.

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During the past decade, several studies have clearly established the importance of frequent daily self-monitoring of blood glucose to control one’s glycemic condition and thereby reduce the onset of complications caused by diabetes (1,2). Pain associated with finger lancing is one of the major barriers to frequent daily testing (3). Consequently, it has been argued that skin lancing at less sensitive parts of the body would increase testing compliance. Suzuki (4) was the first to perform such alternate-site testing. In response to the need for less painful testing, several manufacturers have now released products that are specifically designed to be used at body sites other than the fingertip.

The Sof-Tact Blood Glucose System (Abbott Laboratories/MediSense Products, Bedford, MA) is one such product. It is a fully integrated system that combines the functionalities of a lancing device and a glucose meter into a single device. Its recommended use is on the forearm, upper arm, and thenar prominence of the thumb. Many studies have been performed with it using standard lancets, and its less painful performance has been documented (5–7).

Although testing at alternate body sites has many advantages (e.g., less pain, sparing of fingertips), its full acceptance ultimately depends on how accurately glucose levels of alternate sites reflect one’s glycemic state. Several recent publications have addressed this issue (8–13), but questions on glucose equivalence still remain (14).

The primary objective of our study was to rigorously test ways in which glucose results could differ between the fore-
Capillary glucose and Hct of arm and finger

arm and the fingertip. First, we needed to test glucose accurately independent of the Sof-Tact System. Technology for alternate-site testing is so recent that no glucose reference assay has yet gained general acceptance for alternate-site tests, which yield a limited volume of blood. We chose the HemoCue B-Glucose Analyzer (HemoCue, Angelholm, Sweden) for our independent control assay based on its performance. Second, we tested the hematocrit (Hct) value of the capillary blood because Hct modifies, to some degree, the results of nearly all glucose assays.

RESEARCH DESIGN AND METHODS — The study population was recruited from patients visiting an urban hospital. Half of the subjects were women, 52% had type 1 diabetes, and 54.2% of the subjects with type 2 diabetes received insulin treatment. In terms of mean ± SD (range), subjects were 45.4 ± 11.3 (18–65) years of age, their duration of diagnosed diabetes was 17.9 ± 11.4 years (1–40), their BMI was 27.9 ± 5.5 kg/m² (18.3–45.6), and their HbA₁c level was 8.2 ± 1.8%. Participants were predominantly Caucasian, with 2% African and 12% Hispanic representation. Twenty-four percent of the subjects were active smokers. Diabetes complications were common: 46% of the subjects showed some signs of retinopathy, 44% showed some signs of nephropathy, 38% showed some signs of neuropathy, 20% showed some signs of cardiovascular diseases, and 40% showed some signs of hypertension.

Procedures

Experimental procedure with each subject followed the following sequence: 1) finger was lanced for initial assay with the YSI 2300 Glucose Analyzer (Yellow Springs Instruments, Yellow Springs, OH); 2) arm was lanced for consecutive assays with Sof-Tact, HemoCue for glucose, and HemoCue for Hb, with each assay requiring separate lancing; 3) fingertip was lanced once, and ~100 μl blood was collected for consecutive assays with Sof-Tact, HemoCue for glucose, and HemoCue for Hb; 4) steps two and three were repeated twice so each assay was performed in triplicate; and 5) finger was lanced for final assay with the YSI Glucose Analyzer.

Testing of individual subjects took ~30 min. All assays were performed by two trained operators so that interperson variability in the operation of the devices was minimized.

A complete data set was obtained for all triplicate glucose assays on every subject at each body site with both Sof-Tact and HemoCue. The mean of triplicates was used to calculate each subject’s percent of glucose difference between arm and finger [arm glucose − finger glucose]/finger glucose]. The data set for Hb assays was incomplete, as only duplicate measurements could be obtained from the arm for three of the subjects. We could not record either an initial or a final YSI value for two subjects, so their degree of glucose stability over the course of the experiment remained unknown. For another 13 subjects, either the initial or final YSI measurement was not performed in duplicate. These measurements were missing due to insufficient sample volumes from subjects. Analysis was performed using the entire data set, with none of the data removed.

Assays

The HemoCue B-Glucose Analyzer was chosen as the control test for glucose because of its low volume requirement (5 μl), its low imprecision (3.5–1.6% coefficient of variation [CV]) over its dynamic range of 0–400 mg/dl), and its claimed insensitivity to Hct. Another HemoCue product, the B-Hemoglobin Photometer, was used to measure Hb. It is also an optical assay that requires slightly larger sample volumes (7–10 μl) to fill its microcuvettes. This meter directly measures Hb concentration in units of g/dl, which multiplied by three gives a corresponding Hct value within 3% (15). According to the product label, imprecision for Hb assays is <1.6% CV at all concentrations. When calculated for the triplicate assays performed in this study, mean imprecision had a 6% CV.

The Sof-Tact meter was used per manufacturer’s instructions, using port 1 for testing the forearm and port 2 for the fingertip. A standard lancing device (MidiSense auto-Lancet; manufactured by Palco Labs, Santa Cruz, CA) was used for all fingersticks and for lancing the arm. For HemoCue assays, a partial vacuum was used to collect the required sample volume from the arm. A partial vacuum was applied to the lanced site for ~15 s; conditions were equivalent to that used by Sof-Tact for alternate-site testing.

Control experiments

Because sample collection differed between armsticks and fingersticks, several control experiments were performed to determine the contribution of various physical factors (evaporation and deoxygenation) that could alter results during vacuum collection. The effect of vacuum on Hb and glucose concentrations was tested with isolated blood drops. A 5-μl drop of either venous or capillary blood was deposited on a surface, an 8 psi partial vacuum was applied for up to 30 s with the upturned syringe system, and then the drop was transferred to microcuvette for HemoCue assay. The vacuum had no detectable effect on Hb concentration; the initial concentration was 14.5 ± 0.3 g/dl and was found to be 14.5 ± 0.2 g/dl after vacuum (n = 10). Similar results were obtained for glucose in a separate experiment: 199.9 ± 6.3 mg/dl with and 196.7 ± 3.8 mg/dl without vacuum (n = 10). Thus, vacuum application did not have any significant effect on the concentration of either Hb or glucose in our blood samples.

Control experiments were also performed to test identical performance of the two Sof-Tact ports. In one test, we compared results when both ports were tested per normal operation with the same aqueous glucose solution. A syringe pump was used to slowly deliver solution to strips in port 1. Glucose difference between the ports was found to be 5.4 ± 5% (mean ± SD, n = 100). In another test, we compared results when the assay with port 1 (which normally works under partial vacuum) was performed under the same ambient pressure as port 2, with samples of aqueous glucose solution applied to test strips. The difference between ports was ~0.1 ± 0.01%. Results of these control experiments indicate that vacuum had no significant effect on Sof-Tact results and that its two ports produced equivalent results.

RESULTS

Site-to-site differences in Hb

Hb concentration was found to vary significantly between the capillary beds of the forearm and fingertip. For all 50 subjects, Hb concentration in the arm was 15.7 ± 1.8 g/dl, ~1.7 g/dl higher than in
the fingertip, which was 14.0 ± 1.9 g/dl. This difference between sample means is not significant because interperson variability masks individual bias. However, the difference between the two body sites becomes significant when intraperson differences are calculated. Intraperson Hb bias was found to be 1.8 ± 1.1 g/dl, which corresponds to a mean Hct bias of 5.3%. This bias was not a sampling artifact. Approximately 90% of the subjects had a higher Hb concentration in their arm than in their fingertip. Based on the Kolmogorov-Smirnov method (16), intraperson Hb difference was significantly different from a distribution centered on zero bias (at P < 0.01). Thus, the Hb and Hct content of capillary blood can significantly differ between different sites on the skin.

**Intraperson glucose variation during testing**

As expected for any random sampling of nonfasting individuals, the rate of change in blood glucose for the duration of the experiment varied with subjects. Change was <9 mg/dl for 42% of the patients and >36 mg/dl for 8%. The impact of such variation on results is discussed below.

**Site-to-site differences in glucose**

Mean glucose value was calculated at each body site for each individual. Because of the order in which replicates were collected, the two sites were equally affected by time-dependent changes such as glucose drift, and therefore, the mean values should reflect the effects of intrinsic factors, if any, that could alter local glucose concentrations. The most direct way of presenting observed differences is to plot the glucose result of the arm against that of the finger for each subject (Fig. 1). Symbols vary in the plot depending on the extent to which a subject's glucose concentration changed during the experiment. As can be seen, all data points are closely scattered along the line of equality, indicating no significant differences between the two variables.

To determine central tendency, average deviation from line of equality was derived for the entire data set in Fig. 1. Each subject's glucose difference was calculated relative to finger, [(arm - finger)/ finger], and then the group average was taken. As indicated in Table 1, the mean glucose difference between arm and finger for all participants was −0.1%, which is statistically insignificant with measurement errors being ~8%. Mean glucose difference was also calculated for subsets of subjects, whose glucose varied <9, <18, or >18 mg/dl. For all three groups, glucose difference between sites was small and insignificant. Thus, even for subjects in whom glucose changed >18 mg/dl within half an hour, glucose differences between test sites were insignificantly small and without much clinical relevance.

Another method for deriving glucose difference between sites is to perform regression analysis on the data of Fig. 1. The degree to which the slope of a regression line deviates from unity is an indication of the nonequivalence of the two sites. Standard regression analysis has been routinely performed in similar studies (4,11), even though one of its assumptions, namely negligible error for independent variable (16), is not met for plots such as Fig. 1. Regression analysis is also an inappropriate method for determining central tendency because points at extreme ends of the data range have disproportionately

![Figure 1](image.png)

**Figure 1**—Glucose values of the capillary blood of the forearm compared with the corresponding values taken from the fingertip of the same subject, as measured with HemoCue. Each data point represents a subject \((n = 50)\). Symbol type represents subject’s glycemic stability during the experiment: (+) for a glucose change >18 mg/dl, (■) for 9–18 mg/dl, (○) for <9 mg/dl, and (●) for change unknown. Dashed lines are drawn at ±20% or ±20 mg/dl of isoline for abscissa values above or below 100 mg/dl, respectively.

**Table 1**—Percent glucose difference between forearm and finger for all subjects and for groups of subjects with various glycemic stability

<table>
<thead>
<tr>
<th></th>
<th>All subjects</th>
<th>Subjects whose glucose varied ≤18 mg/dl</th>
<th>Subjects whose glucose varied ≤9 mg/dl</th>
<th>Subjects whose glucose varied &gt;18 mg/dl</th>
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<tr>
<td>n</td>
<td>50</td>
<td>33</td>
<td>20</td>
<td>15</td>
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<td>HemoCue results</td>
<td>−0.1 ± 8%</td>
<td>−0.9 ± 6%</td>
<td>−1 ± 6%</td>
<td>2 ± 10%</td>
</tr>
<tr>
<td>Sof-Tact results</td>
<td>−4 ± 13%</td>
<td>−4 ± 13%</td>
<td>−1 ± 15%</td>
<td>−1 ± 12%</td>
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<td>Data are means ± SD</td>
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greater leverage on the regression slope. Nevertheless, if one were to apply standard regression analysis to the data of Fig. 1, regression lines with a slope of either $0.987 \pm 0.001$ for zero-intercept or $0.961 \pm 0.022$ for a self-determining intercept of $5.9 \pm 4.6$ mg/dl would be obtained. Thus, by this analysis, glucose values for the arm in our study were either $1.3 \pm 0.1$ or $3.9 \pm 2.2$% less than for the finger. Although these values are small and still without much clinical relevance, we believe, for reasons already indicated, that our method of calculation, which is based on intraperson percent of glucose difference, provides a more objective measure of site-to-site variations.

Because subjects varied somewhat in their arm-to-finger differences, we tested the possibility that individual variations were linked to the previously described Hct bias. When individual percent of glucose difference was plotted against individual Hct bias, random scatter of data points indicated that the two variables did not correlate.

**Sof-Tact performance**

Experimental results with Sof-Tact for site-to-site differences were generally similar to the ones obtained with HemoCue, with slightly greater scatter in the data. Imprecision of the triplicate Sof-Tact assays was $\sim 7\%$ for both arm and finger. This explains the higher measurement errors for this device in Table 1. On average, glucose in the arm tended to be less than in the fingertip with Sof-Tact, but the observed difference was again statistically insignificant. Overall, the results with Sof-Tact closely mirrored the HemoCue results, showing no significant glucose bias between the forearm and the fingertip. Similarity with HemoCue also extended to the lack of correlation between individual Hct bias and Sof-Tact–derived glucose differences.

**CONCLUSIONS** — The objective of this study was to measure the degree to which blood glucose and Hct varies between two distinct skin locations, namely between the dorsal surface of the forearm and the fingertip. Hct measurement was included in the study because glucose assays are generally sensitive to the presence of erythrocytes.

Our study demonstrated that Hb concentration in capillary blood can measurably vary between the fingertip and the arm. It confirmed the findings of our preliminary experiments in which we used spectrophotometry to measure Hb concentration (isobestic point analysis on diluted bloods that were collected into microcapillaries without vacuum application). From our search of the literature, reports on Hb concentration or Hct do not exist for the forearm, but measurements on the earlobe and its difference from the fingertip have been made, beginning with Chatterjee and Maaser (17). As part of its blood drive, the American Red Cross routinely pretests the Hb concentration of potential donors to exclude anemic individuals. Pretesting involves obtaining capillary blood either from the fingertip or the earlobe. Cable (18) reviewed the results of such studies, in which the same HemoCue assay was used for Hb measurements as was used by us. Cable did not report intraperson differences. He observed that for nonanemic individuals, Hb in the fingertips was $\sim 1.4$ g/dl ($15.9 \pm 2.0$ g/dl for men and $13.7 \pm 0.8$ g/dl for women), which is in close agreement with our measurement. He found a significantly greater concentration of Hb in the earlobe of the same subjects ($19.6 \pm 0.3$ g/dl for men and $17.9 \pm 0.7$ g/dl for women). The average Hb concentration that we measured in the forearm is an intermediate value between the results reported by Cable for the finger and earlobe.

To our knowledge, no explanation has yet been given for the occurrence of Hb concentration differences across the integument. Possible causes may include blood pooling and/or differential plasma skimming of arterial blood supplying the dermis. Blood pooling is less likely to be the primary factor because in a limited control experiment on posture, we found similar Hb bias in three supine subjects who were tested 30 min after assuming level position. Although the cause for Hb differences remains unresolved, all existing results on Hb measurements lead to the general conclusion that the composition of capillary blood is not always the same. Capillary bloods of the integument can differ at least in their undissolved, suspended components. Do they also differ in glucose concentration? Demonstration of this was the primary goal of our study. To be able to rigorously establish such a difference, an assay method had to be chosen that was highly accurate and well established. Unfortunately, no such laboratory reference method exists for glucose testing at alternate body sites. Reference methods currently used for fingersticks require extracted volumes $>25 \mu l$, which normally cannot be collected from the arm. In the absence of such an established reference method, we selected the HemoCue B-Glucose Analyzer as the independent control assay in our study because of its low volume requirement and low imprecision. As additional consideration, the HemoCue assay has been in use for many years, and in one study of glucose meters, it was the designated reference assay (19). Using the HemoCue data, we calculated that the mean glucose difference between forearm and fingertip was undetectable and close to zero. No strong correlation existed between mean difference and the rate at which subjects' glucose changed during the experiment. Mean glucose differences were always significantly less than measurement errors. Thus, in contrast to our previous conclusions regarding Hb differences, the HemoCue glucose results indicate no significant intraperson glucose difference between the arm and the fingertip.

Our observation on the lack of significant glucose difference across the integument is consistent with previous reports (4,8–13). Only a few of these previous studies used the same glucose meter at both testing sites to document measured differences. Based on the slope of the regression line in his plot, Suzuki (4) observed that abdominal glucose values were $\sim 4\%$ less than fingertip values. The significance of this small difference is unclear because neither intraperson differences nor measurement errors were provided. Regression analysis was apparently also the basis for Bohannon's (11) statement that forearm results were 7.9% less than those of the finger when measured with a FreeStyle monitor. Using the same device, Koschinsky et al. (13) observed no significant differences between parallel blood samples from the forearm and fingertip. Similar paired assays were performed by Fineberg et al. with Sof-Tact (7). The regression lines in their figures, which were plots of either arm or finger glucose against laboratory reference on the finger, indicate that in their study, glucose concentration of the arm was $\sim 2\%$ more than of the finger. Again, this is an insignificant difference. We have used the HemoCue glucose assay in other
studies, including oral glucose tolerance tests, and so far, we have not encountered significant glucose differences between the arm and finger. However, our studies do not rule out the possibility that significant inequalities may exist under specific circumstances. Apparently, such differences can be elicited in brittle type 1 diabetic subjects after intravenous injection of insulin (14).

In conclusion, we set out to measure the difference in capillary blood composition between the forearm and fingertip. In our study of nonfasting subjects, we observed that capillary blood of the arm has a significantly larger Hb concentration and Hct than capillary blood of the finger. However, we could not observe significant or detectable glucose differences between these sites.

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References