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ORIGINAL ARTICLE

Within-Individual Hematocrit Variations and Self-Monitoring of Blood Glucose

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Abstract

Many self-monitoring of blood glucose (SMBG) systems have generated artefactually increased glucose results in low-hematocrit patients (e.g., intensive care unit and renal failure patients); conversely, these devices could produce artefactually decreased glucose results in high-hematocrit patients (e.g., neonates). The introduction of hematocrit-independent SMBG systems permits more accurate testing in anemic or polycythemic individuals. In this issue of *Journal of Diabetes Science and Technology*, Ramljak and coauthors have created glucose bias graphs for 19 common SMBG devices and declared certain systems to be optimally accurate because of insensitivity to hematocrit variation over a broad hematocrit range. Luckily, the average within-individual variation of hematocrit is low (between 2.9 and 3.3%). As such, a larger spectrum of SMBG devices can be regarded as optimally hematocrit independent.

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Introduction

In their systematic investigation of compromised self-monitoring of blood glucose (SMBG) testing due to hematocrit variation, Ramljak and coauthors[1] constructed unique glucose bias graphs for 19 common SMBG devices. Their work demonstrated striking patterns in meter inaccuracy due to hematocrit variation. With little effort, the reader can readily distinguish those meters that were overly biased at multiple hematocrit levels from meters that exhibited negligible bias over the entire hematocrit range. A handful of meters demonstrated biased glucose results only in the high hematocrit zone (>60%); we will advance the thesis that this last group of instruments offered analytically and clinically acceptable performance for virtually all patients, perhaps excluding neonates.

Ramljak and coauthors[1] primary supporting paper[2] cites the occurrence of enormously broad hematocrit ranges in typical patient populations. For a sample of 15,000 outpatients, they described low and high hematocrits of 20% and 60%; the limits were even broader for a sample of 45,000 inpatients: 10% to 70%. The authors did not mention that the 10% and 20% hematocrits were obtained primarily from critically ill adult patients and that the 60% and 70% hematocrits were derived primarily from neonatal patients. Barring violent injury, hematocrits do not naturally change from 70% to 10%; nor do they change from 60% to 20%. Neonates do not become adults overnight, and the transformation

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Abbreviations: (CVw) within-subject coefficient of variation, (HIF) hematocrit interference factor, (SMBG) self-monitoring of blood glucose

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of the adult to youth is still legend. The authors referenced Thirup[3], citing that hematocrit measurements can change by 15%. In Thirup's compilation of 10 studies of hematocrit variation, the within-subject coefficient of variation (CV_w) ranged from 2.9–3.3%. Larger controlled hematocrit excursions did occur with transfusion and adjustment of erythropoietin dosing.[4] The average change in hemoglobin (highly correlated to hematocrit) following transfusion in chronic renal failure patients was 0.34 ± 0.07 g/dl (around 3%). In the presence of infection or inflammation, transfusions were associated with higher variation, 0.75 ± 0.41 g/dl (around 7%).

With reference to outpatients, Ricos and coauthors[5] have published a summary of within-individual variation of hemoglobin in patients with disease. The average CV_w for these patients was between 2% and 4%, which was not that different from normal subject variation. Specifically, they found that patients with chronic renal failure had a lower CV_w than the median for healthy adults (2.3% vs 2.8%). This is especially relevant in SMBG testing because chronic renal failure is a common comorbidity and/or complication of diabetes mellitus. Van Wyck and coauthors[6] examined 30 renal dialysis patients and found the within-subject variability of both hemoglobin and hematocrit to be 4.0%. With reference to other causes of acute changes in hematocrit, the authors cited exercise. The ultramarathon is possibly the most hematocrit-destabilizing exercise. Two articles cited either no change in hematocrit[7] or a 10% decrease immediately postrun, followed by recovery 5 days postrun.[8] While significant, this latter excursion did not approach the extent implied by the authors.

There are little published data on within-subject variability of hematocrit in the neonatal population. Jopling and coauthors[9] found that neonates born at less than 29 weeks of gestational age, on average, had a 6.0% fall in hematocrit in the first 4 h of life. The changes in those born closer to term or at term were less pronounced. In calculating reference intervals, they found that in preterm infants born at 29–34 weeks of gestational age, mean hematocrit fell about 20% (absolute) over the first 28 days of life. Of note, neonates requiring transfusion were excluded from this study.

Perhaps only in the neonate is the within-individual variation close to what the authors inferred. Given this, perhaps the criteria that they have arbitrarily chosen are not optimal. If the goal in selecting an SMBG was one size fits all, such as a government-run program, such stringent criteria may have been prudent. However, given that no single individual will span the entire range of possible hematocrit values, the authors' "hematocrit interference factor" (HIF) may have been a too-strict criterion. Closer study of the individual glucose bias figures becomes more relevant. The authors have accomplished very useful work in identifying several SMBGs in which the performance was clinically (and analytically) unacceptable. The six systems that "passed" were clearly reliable over any range of hematocrit. What about the systems that did not fit into either of those groups? Are they safe to use?

One approach could be to determine three HIFs: one for low-hematocrit patients (e.g., 20%), one for normal-hematocrit patients (35%), and another for high-hematocrit patients (50%). A meter that has low HIF for all three regions would be deemed an acceptable meter. Another approach would be to look at the slope of the curves rather than absolute maximums/minimums. For example, consider the Contour Meter® (Bayer HealthCare, LLC, Tarrytown, NY). The curve is relatively flat at low and normal hematocrits, with increasing bias at high hematocrits, as demonstrated by a steeper slope. This could be an indication that the Contour is an acceptable SMBG for adults (inpatients and outpatients) but should be used with caution in neonates. Both of these approaches could be better elucidated with data points at more hematocrit levels to better characterize the glucose bias.

The work of Ramljak and coauthors[1] is highly encouraging in that a good number of hematocrit-independent SMBG devices are now available. The patient with diabetic nephropathy, the woman with newly discovered gestational diabetes, and even the highly conditioned athlete with diabetes will experience fewer occasions when their serial SMBG values demonstrate a hematocrit-dependent bias. We caution health systems that are acquiring newer generations of SMBG devices: sometimes the manufacturer may not have total control of the process that maintains hematocrit insensitivity. In some meter evaluations, we have discovered hematocrit sensitivity in specific meters, contrary to what was documented in the scientific literature. The divergence between our findings and published reports might be based on variation in different lots of manufactured strips. Until hematocrit insensitivity becomes an essential and intrinsic property of SMBG devices, we recommend that the acquiring health system test the new generation of SMBG devices for hematocrit sensitivity (and employ multiple-strip lots).

Disclosures:

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