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ORIGINAL ARTICLE

Dynamic Electrochemistry: A Step in the Right Direction

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Abstract

Variation in hematocrit is a serious but underappreciated interference to accurate point-of-care glucose measurement. Using a meter employing new technology of dynamic electrochemistry, Musholt and colleagues present *in vitro* data in this issue of *Journal of Diabetes Science and Technology* demonstrating improved glucose accuracy over a wide range of hematocrits. Although this may have some importance for patients testing in the home environment, the essential application of this new technology will be in the critical care and perioperative environment, where wide swings in hematocrit are common. Because these meters are in use with great frequency in the hospital where accurate glucose measurement is vital, mitigating this interference is a welcome addition to our diagnostic armamentarium.

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Introduction

The ability of patients with diabetes to measure their own blood glucose has arguably been the most significant advancement in diabetes care since the 1980s. Although the ease of use, cost, and accuracy of these devices have improved considerably, the perfect point-of-care (POC) meter has yet to be realized. In addition to continuing accuracy concerns raised by diabetes experts and government regulators, a number of significant interferences to accurate measurement remain. The majority of these obstacles are, however, not significant issues in the self-testing "home" environment. Where POC glucose measurement device accuracy becomes a significant concern is with migration of these meters into the hospital environment of the critically ill and perioperative patient. In this setting, some of these interferences are potentially fatal.

In this issue of *Journal of Diabetes Science and Technology*, Musholt and colleagues[1] report on the accuracy of a glucose meter that uses a relatively new technology that successfully mitigates one of the most severe measurement interferences—variation in hematocrit. This technology, dynamic electrochemistry, differs somewhat from the methodology of the Nova Biomedical StatStrip®, which directly measures hematocrit and compensates with a correction factor. The technology reported herein by Musholt and colleagues[1] makes repeated measurements of the blood sample, using differing frequency and voltage conditions, and then applies a mathematical algorithm to account for a number of interferences, including hematocrit. Readers with further interest in this technology should see the thorough discussion by Rao and associates.[2] Accuracy of the tested meter, the BGStar,

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Abbreviations: (POC) point of care

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was excellent at the low glucose range of 79–84 mg/dl, with a deviation of 6.1% between highest and lowest hematocrit tested. Accuracy was not nearly as good (14.5%) at midrange glucose concentrations (150–161 mg/dl) and excellent again (3.9%) at high glucose values (301–314 mg/dl). However, even with the higher reported deviation in the midrange, accuracy is still within the 20% zone A error (leading to correct clinical action) on a Clarke grid.[3] Because our major concern in critically ill patients is accuracy at low glucose values,[4] these results seem more than acceptable.

As the authors remind us, there are a number of common outpatient conditions that lead to swings in hematocrit, including altitude changes (~10%),[5] exercise (~1–2%),[6] hemodialysis (~5%),[7] and even seasonal variations (~3–7%).[8] With a nonhematocrit compensated POC glucose device, patients with diabetes may experience inaccurate measurements under these conditions. The authors are to be commended for not only testing various meters for the hematocrit effect, but, as importantly, (re)alerting practitioners to this problem. Tight glucose control is not easy to accomplish. It is even more difficult when one has to account for interferences that cause glucose measurement inaccuracies.

Glucose Measurement in the Critically Ill

These relatively small outpatient hematocrit changes may affect glucose meter accuracy, but there are multiple examples in the hospital environment of hematocrit shifts that are markedly more severe. With the migration of these POC glucose meters into critical care environments, encouraged by hospital administrators because of rapid results and primarily reduction in costs, accurate glucose measurement with rapidly changing hematocrit is very relevant. For example, in trauma patients who sustain significant hemorrhage or those who sustain life threatening gastrointestinal bleeding, it is not uncommon for hematocrit to change from normal levels in the 40s down to the low teens with initial crystalloid resuscitation and then return to near normal levels with subsequent red blood cell transfusion. In addition, during complex surgical cases, blood loss can easily exceed a patient's blood volume, and very large changes in hematocrit are common. Likewise, operations involving cardiopulmonary bypass and hemodilution easily result in 50% fluctuations in hematocrit.

These large, rapid changes in hematocrit can lead to critical errors in glucose measurement, resulting in potentially catastrophic consequences. Musholt and colleagues[1] report glucose deviations of approximately 25–40% with large hematocrit variations when using traditional meters. Because such hematocrit shifts commonly occur in the sickest patients, it is easy to envision how morbidity and even mortality may result. Furthermore, this error is the result of just one interference (hematocrit). It is even more concerning when consideration is made for other possible simultaneous interferences commonly noted in this population such as PaO_2 changes, pH variation, and hypoperfusion effects.[9] Moreover, stacking these interferences in the same direction can result in disaster.

Why is there such concern for glucose control in the critically ill and perioperative patient? Although the exact target for glucose values in the intensive care unit and perioperative patient is far from settled, clear evidence exists that glucose control is important for infection control,[10] reduction of brain injury in neurosurgery patients,[11] and even survival in trauma patients.[12] Accurate measurement is an obvious requirement to achieve required glucose control.

Further Challenges

Is dynamic electrochemistry the ultimate correction needed for POC glucose meters? Although this is an interesting first report, it does not explore hematocrits less than 25, a common clinical scenario. In addition, an *in vivo* trial, preferably using a critically ill and perioperative cohort, would go a long way toward establishing a final answer. Because this measurement is done with electrochemistry, other interferents are certainly possible. *In vitro* work done in our laboratory[13] showed substantial interference from clinical doses of saline, commonly used for initial resuscitation of trauma patients, on electrical conductivity, which is directly translated into errors in conductivity-based hematocrit measurement in devices such as the iStat®. Does dynamic electrochemistry correctly overcome this potential fluid-induced error in hematocrit measurement, or does it fall into the same trap as the iStat technology? We do not yet know. Does heparin mixed with the blood sample affect the accuracy with dynamic electrochemistry? Musholt and colleagues'[1] protocol called for glucose testing of heparinized samples. Heparin is a highly charged molecule, and results from our laboratory[13] showed an increase in whole blood conductivity at heparin concentrations used in blood collection and testing. This also calls for further analysis.

The exciting technology reported in this issue of *Journal of Diabetes Science and Technology* by Musholt and colleagues[1] is an initial step in providing evidence that dynamic electrochemistry may be a key to compensating for dangerous interferences in glucose measurement. Although Musholt and colleagues[1] point out common outpatient reasons for hematocrit variation, the increasing use of POC glucose meters with intensive care and perioperative patients demands accurate correction, so that appropriate glucose management is enabled.

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