Journal of Diabetes Science and Technology
Volume 4, Issue 5, September 2010
© Diabetes Technology Society

ORIGINAL ARTICLES

Analysis of the Nova Stat Strip® Glucose Meter for Real-Time Blood Glucose Determinations During Glucose Clamp Studies: "Don't Swap Horses in Midstream"

Lutz Heinemann, Ph.D.

Abstract

Proper performance of glucose clamps is critically dependent on reliable blood glucose (BG) measurements. A number of requirements have to be fulfilled by a system that aims to replace the laboratory devices that are currently in use. Many more aspects need to be taken into account besides the accuracy of BG measurement. It might very well be that the BG meter studied by Rabiee and colleagues in this issue of *Journal of Diabetes Science and Technology* fulfills most or all of such requirements; however, these aspects have to be tested more thoroughly before one switches from an established measurement method to the Nova Stat Strip® glucometer.

J Diabetes Sci Technol 2010;4(5):1202-1204

Introduction

Performance of glucose clamps requires high-precision blood glucose (BG) measurements in order to guarantee good clamp quality.[1,2] Usually, laboratory devices such as the Beckman or the YSI glucose analyzer are employed that allow accurate measurements of BG to be performed with a coefficient of variation <2%. Unfortunately, measuring blood glucose during glucose clamps is not a lucrative market. Therefore, both manufacturers of these devices have never developed systems specifically designed for this purpose, and Beckman no longer supports their system.

Rabiee and colleagues[3] studied if the Nova Stat Strip® BG meter could be used instead of these laboratory devices for glucose clamp purposes. In their summary section, they are quite confident about the measurement quality of this meter, stating, "The simplicity of Nova and its reliability, accuracy, and speed make it an acceptable replacement device for Beckman and YSI in the conduct of clamps…".[3] This is in some contrast with another sentence in the manuscript: "This result reflects an occasional tendency of the Nova glucose meter to give readings that are not sufficiently accurate for the clamp study."[3] One wonders what the definition of "occasional" is and how the user of the Nova Strip system detects that a given measurement result falls into this category.

A look at the results presented by Rabie and colleagues[3] raises some fundamental questions, such as, are the two BG profiles in Figure 1 of their article the mean curves of all 14 patients studied or that of a "typical" individual patient? The latter would be of much more interest for this evaluation. Figure 2 shows, at least in some cases,

Author Affiliation: Profil Institute for Clinical Research, San Diego, California; and Profil Institut für Stoffwechselforschung GmbH, Neuss, Germany

Abbreviation: (BG) blood glucose

Keywords: glucose clamp, glucose clamp quality, gold standard, reliability, validity

Corresponding Author: Prof. Dr. rer. nat. Lutz Heinemann, Profil Institut für Stoffwechselforschung, GmbH, Hellersbergstr. 9, D-41460 Neuss, Germany; email address *lutz.heinemann@profil-research.de*

relevant deviations between the two methods (Nova versus Beckman) [48 (4.7%) of 1004 data pairs disagreed by more than two standard deviations]. Clearly, it might very well be that these 5% of mismatched measurements are due to measurement errors caused by the "reference" methods; neither the Beckman nor the YSI glucose analyzer are "reference" methods in the full sense of the word. However, especially in such cases, one would also want to see the individual measurement results, not just the mean of the duplicate measurements. In other words, how good was the agreement between the duplicate measurements for all three measurement systems employed? All the ranges, correlation coefficients, and error grid analyses provided are of limited help when the aim of my evaluation is to see how good the agreement between glucose measurement methods is in the individual blood sample. From my perspective, the minimum requirement would be that two methods measuring the same parameter have a linear regression coefficient of near unity and a Pearson's r of 0.978 (without mention that all data pairs should be in zone A of the error grid analysis). Clearly, Bland–Altman plots are the best method, in this sense, for method comparison.

Figure 4 of Rabie and colleagues[3] shows that the differences between Beckman duplicates were considerably smaller in many samples than those between Nova duplicates. The differences with the Nova device were nearly twice as high as those of the Beckman duplicates. Assuming that, with the Nova system, there is a tendency to perform only single measurements (due to, e.g., cost considerations discussed later), it would be difficult to detect any issues with a given measurement. However, with the Beckman, triplicate or even quadruplicate measurements would be performed to clarify such a questionable measurement. Figure 4 also shows that practically all BG values were in the range of 90 to 200 mg/dl (as stated by the authors); thus it is difficult to make statements about the measurement quality at BG levels of, e.g., 50 or 500 mg/dl. The measurement quality in the low glycemic range is of particular concern with many BG meters, and therefore, additional information is needed. From my point of view, data presented by Rabie and colleagues[3] do not allow the statement to be made that the Nova device is accurate enough to serve as a replacement of the Beckman or YSI during clamp studies.

The idea of having a reliable BG measurement method that is not labor-intensive is striking, as labor costs are the major costs for performing glucose clamps. Unfortunately, the cost element was not presented in detail, although it is stated that the Nova instrument is significantly less costly to purchase and operate. An analysis of the cost per glucose measurement for each device that includes and excludes the cost of purchase would clearly be of interest.

Glucose clamps are performed for different purposes. If they are to fulfill scientific criteria *only*, then it might be acceptable to use a BG meter. However, when clinical–experimental studies are performed in the context of drug development, it is also important to keep regulatory purposes in mind. Thus, regulatory bodies such as the Food and Drug Administration not only ask for sufficient documentation on measurement methods used for studies performed during clinical drug development, but also require a validation procedure. The Nova Stat Strip Glucometer has a PC connection, but does it also support/document regular measurement of calibration/test solutions for quality control purposes? Laboratory devices do not only provide printouts, but they also request control measurements. The study by Rabiee and colleagues[3] also does not provide detailed information about factors (e.g., temperature, hematocrit, or interferences with other drugs/substances) that are known to have an impact on the accuracy of the measurement.

Their study evaluates only the accuracy of the BG meter but not the precision of the measurement. The simple reason for this is that a "sample" with a stable glycemia is usually not available. However, by means of the glucose clamp technique, it would be possible to establish certain BG levels for a given period of time and to measure glycemia repeatedly over time at each of these levels. This would allow for determining precision as well, but this approach has never been employed in the evaluation process of a BG meter thus far.

I agree with the Rabiee and colleagues that a BG meter—which allows a more rapid turnaround time, reduces the handling efforts of the blood sample, and requires less maintenance efforts—is an attractive option; however, I would suggest that additional studies be performed to investigate the aspects aforementioned in different patient groups and different laboratories before such a BG meter is used as a replacement of the laboratory systems that are in use today. The data provided thus far suggest that we should not change the horse right now: "We acknowledge that the accuracy of the Nova instrument is not as robust as the Beckman of YSI."[3]

References:

1. Heinemann L, Anderson JH Jr. Measurement of insulin absorption and insulin action. Diabetes Technol Ther. 2004;6(5):698–718.
2. Hompesch M, Rave K. An analysis of how to measure glucose during glucose clamps: are glucose meters ready for research? J Diabetes Sci Technol. 2008;2(5):896–8.
3. Rabiee A, Magruder T, Grant C, Salas-Carillo R, Gillette A, DuBois J, Shannon R, Andersen DK, Elahi D. Accuracy and reliability of the Nova Stat Strip® glucose meter for real-time blood glucose determinations during glucose clamp studies. J Diabetes Sci Technol. 2010;4(5):1195-1201.