POCT17

Use of Glucose Meters for Critically Ill Patients

This white paper includes an overview of glucose meter limitations with practical advice for use of glucose meters in critically ill patients.

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NOTE 1: The findings, recommendations, and conclusions in this white paper are those of the authors, and have not been reviewed through the CLSI consensus process. They do not necessarily reflect the views of the organizations the authors represent. CLSI does not, in any way, endorse the off-label use of waived glucose meters.

NOTE 2: Mandates are generally reserved for CLSI standards, but are occasionally allowed in CLSI white papers. In CLSI white papers, use of the term "must" is either 1) based on a requirement or 2) indicative of a necessary step to ensure patient safety or proper fulfillment of a procedure. The authors evaluated use of the term "must" and deemed it appropriate.

Abstract

Glucose meters, used for self-monitoring and in a myriad of healthcare settings, provide for frequent and rapid measurement of glucose levels using a capillary fingerstick blood sample. However, due to their limitations, self-monitoring glucose meters based on strip technology were never intended for use in acute care settings. Hematocrit, oxygen therapy, drugs, and metabolites can falsely increase or decrease glucose test results in hospitalized patients. Problems observed during the use of glucose meters in critically ill patients has raised awareness of their safety for professional use in hospitalized patients. Hospital laboratories should note the limitations of their glucose meter methodology and recognize conditions for intended and off-label use of the test system. Originally, all glucose meters were cleared as over-the-counter (OTC) products. By definition, the OTC labeling made these devices waived for use in hospitals based on the Clinical Laboratory Improvement Amendments of 1988 (CLIA). In the United States, off-label use of glucose meters changes the meter classification from CLIA-waived to CLIA high complexity. This shift to high complexity classification may limit the staff who can perform testing and necessitates additional resources to meet CLIA compliance. These consequences must be considered for glucose meter testing in the critically ill and for other patient conditions for which the manufacturer may not have thoroughly evaluated the analytical performance of a meter in all patient care settings.

This white paper explores the limitations of strip-based glucose meters, distinguishes between intended and off-label use, and identifies the consequences of using a glucose meter outside of the manufacturer package insert recommendations, including the actions required to meet CLIA high complexity requirements. This white paper does not define "critically ill," but provides readers with the factors to consider in developing their own definition of "critically ill." The contents of this white paper represent the opinions of CLSI volunteers, and each organization using blood glucose meters should determine whether it is practicing off-label use and collaborate with its internal quality and regulatory departments to develop an appropriate plan to manage this off-label use. Alternatively, organizations should be advised to review their management plan with the Centers for Medicare & Medicaid Services and US Food and Drug Administration (FDA) representatives, if necessary.

Introduction

Glucose meters are the standard of practice for point-of-care monitoring of blood glucose concentration and treatment management in diabetic patients. Using a single drop of blood, glucose meters provide rapid test results for immediate medical decisions and prompt initiation of therapy or help guide long-term treatment decisions. They are widely available for patient self-monitoring, physician office practices, use by long-term nursing home facilities, and the care of hospitalized patients, not all of whom are diagnosed with diabetes. Many glucose meters were first introduced to the market for patient self-testing, and later the same methodology was used in meters intended for professional use in a hospital setting. The analytical performance in home settings for patient self-testing may not meet the same needs for hospitalized patients,

given the physiological differences between these patient populations (eg, hematocrit ranges, oxygenation, perfusion, drugs, and metabolites). Glucose meters have been promoted for management of inpatient glycemic control in the ICU and non-ICU hospitalized settings in consensus statements from the American Association of Clinical Endocrinologists and the American Diabetes Association.[1]

Although fast and convenient, glucose meters have limitations. Glucose meters, like all other analytical test devices, are known to have a number of interferences, ranging from operator technique to physiological factors.[2] Extremes of hematocrit can variably affect meters, increasing results in some meters while decreasing results in other meters, depending on the methodology and initial concentration of glucose in the sample.[3] Oxygen therapy can affect meters with glucose oxidase reagents.[4] Drugs can interfere; eg, high doses of ascorbic acid when used for ICU burn patients.[2] Maltose found in some intravenous solutions and medications can be recognized as glucose by a few glucose dehydrogenase methods, falsely increasing glucose results.[5,6] Other sugars, like galactose, can also be sensed as glucose by some meter reagent enzymes, falsely elevating test results. Exposure of test strips to heat, cold, light, humidity, altitude, and other environmental factors can variably affect meter results.[7-9] These interferences represent only a partial list of the many factors that could affect the quality of glucose meter results. Given the rapid development of new therapies and medications on the market, not all possible interferences have been thoroughly evaluated or are even known by meter manufacturers.

Because most glucose meters have not been evaluated by the manufacturer in patients receiving intensive medical intervention and therapy, the US Food and Drug Administration (FDA) requires a limitation qualification to be added to manufacturer package insert sheets regarding the use of strip-based glucose meters in critically ill patients. This limitation states that a specific glucose meter has not been evaluated in critically ill patients. Critically ill patients present with extremes of disease and physiology that challenge the analytical performance of most strip-based technologies.

The critically ill limitation in the package insert warns the health care professional that the manufacturer has not designed the meter or evaluated the performance of the meter for use in critically ill patients. Additionally, it indicates the FDA has not reviewed manufacturer claims for use in critically ill patients. This limitation should raise awareness of the potential for glucose meter interference by factors found in critically ill patients. To date, only one strip manufacturer has performed studies in patients with clinical conditions and medications that could affect the accuracy of its glucose meter in order to receive FDA clearance for use in critically ill patients. This meter's manufacturer received clearance for analysis of venous and arterial whole blood specimens for all hospitalized patients. Currently, no strip manufacturer has provided studies for FDA clearance to support the use of its meter on capillary whole blood specimens collected from critically ill patients.

This white paper specifically discusses glucose meter use in hospitalized patients for which its use may not be in accordance with the manufacturer's instructions. For the purpose of this white paper, the term glucose meter does not apply to a meter system using cartridges, cassettes, and cuvettes, only those using reagent strips. Although specific reference is made to FDA and Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations, the concepts discussed apply worldwide. Because of the possible risk to patients whenever implementing off-label use, caution and documentation by health care professionals are required when any deviation from the manufacturer's recommendations occurs.

Discussion

Intended Use vs Off-Label Use

The intended use is defined as the use for which a product, process, or service is intended according to the specifications, instructions, and information provided by the manufacturer.[10] The intended use of an *in vitro* diagnostic device is determined by the manufacturer during the device development stage. Typically, the intended use of an *in vitro* diagnostic device identifies the disease or condition the device will diagnose,

Related CLSI Reference Materials*

EP05 **Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline. 3rd ed., 2014.** This document provides guidance for evaluating the precision performance of quantitative measurement procedures. It is intended for manufacturers of quantitative measurement procedures and for laboratories that develop or modify such procedures.

EP06 **Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. 1st ed., 2003.** This document provides guidance for characterizing the linearity of a method during a method evaluation; for checking linearity as part of routine quality assurance; and for determining and stating a manufacturer's claim for linear range.

EP07 **Interference Testing in Clinical Chemistry. 2nd ed., 2005.** This document provides background information, guidance, and experimental procedures for investigating, identifying, and characterizing the effects of interfering substances on clinical chemistry test results.

EP09 **Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 3rd ed., 2013.** This document addresses the design of measurement procedure comparison experiments using patient samples and subsequent data analysis techniques used to determine the bias between two *in vitro* diagnostic measurement procedures.

EP15 **User Verification of Precision and Estimation of Bias. 3rd ed., 2014.** This document describes the estimation of imprecision and of bias for clinical laboratory quantitative measurement procedures using a protocol that can be completed within as few as five days.

EP17 **Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures. 2nd ed., 2012.** This document provides guidance for evaluation and documentation of the detection capability of clinical laboratory measurement procedures (ie, limits of blank, detection, and quantitation), for verification of manufacturers' detection capability claims, and for the proper use and interpretation of different detection capability estimates.

EP28 **Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory. 3rd ed., 2010.** This document contains guidelines for determining reference values and reference intervals for quantitative clinical laboratory tests.

* CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

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