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GLUCOSE METER - A BOON TO THE 21st CENTURY

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ABSTRACT

Glucose meters are widely used today both in the inpatient and outpatient settings, and by the patient himself at home to monitor therapy. The glucose meters use whole blood. For good performance both technical accuracy and clinical accuracy is very important. Technical accuracy tells us about the closeness of agreement between a measured value and true value of a parameter whereas clinical accuracy compares the agreement between the test result and the medical decisions which is based on the tet result. Many factors can affect glucose meter results, including environmental exposure, operator technique, and patient factors. This article reviews the history, technical accuracy, clinical accuracy, meter performance, interferences involved in glucose meter reading.

KEY WORDS: Glucose meter, accuracy, interference,

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INTRODUCTION

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The insulin was discovered in 1920s, since then the development of self-monitoring of blood glucose (SMBG) is probably another important development in the control of diabetes mellitus (DM). Today glucose meters are used in emergency rooms, hospitals, ambulatory medical care, outpatient clinics, and at home for self-monitoring. Glucose meter enables rapid analysis of blood glucose and helps in management of hypoglycemic and hyperglycemic disorders.

HISTORY OF GLUCOSE METER

Ernie Adams in 1963 invented a paper strip that develops a blue color whose intensity was proportional to glucose concentration and could be read by visually comparing the strip color to a color-concentration chart. In 1970, Anton H. Clemens developed the first blood glucose meter and glucose self-monitoring system, the Ames Reflectance Meter (ARM) to detect reflected light from the paper strip, for physician use. [1] Richard K. Bernstein developed a meter based on ARM that could be used by patients. Glucose meters have wide range of applications in medicine both for diagnostic purposes and for management. Hyperglycemia needs early and rapid diagnosis and management, as prolonged hyperglycemia can lead to dehydration, metabolic disturbances, and long-term cardiovascular and renal complications. American Diabetes Association (ADA) recommends SMBG for DM as a key component of their disease management program. [2] Tight glycemic control is needed in the management diabetes. The ADA recommends target range of 110–140 mg/dl (6.11–10.0 mmol/liter) for critically ill patients and the American Association of Clinical Endocrinologists recommendation of 110 mg/dl (6.11 mmol/liter) as the upper cutoff concentration for glucose in critically ill patients. [2, 3] Glucose meters are used by a diverse patients and diverse acute medical conditions. Like other medical device, glucose meters do have limitations. There are many preanalytic variables which should be considered when interpreting blood glucose results. [4, 5] Reliability and quality of results can be affected by environmental effects, by the operators themselves, patient condition, medication, and other metabolic factors.

PRINCIPLE OF GLUCOSE DETECTION

Glucose meters have two parts: an enzymatic portion and the detector. The enzyme portion of the glucose meter is in the form of a disposable strip or reaction cuvette usually in dehydrated state. The patient's blood sample rehydrates and glucose reacts with the enzymes to produce a product that is detected by detector. Some meters generate hydrogen peroxide or an intermediary that can react with a dye, resulting in a color change proportional to the concentration of glucose in solution. Some meters incorporate the enzymes into a biosensor. There are three principle enzymatic reactions currently utilized by glucose meters: glucose oxidase, glucose dehydrogenase, and hexokinase. The enzymes are proteins which denature and inactivated at extreme temperature. Exposure of anhydrous enzymes to humidity can prematurely rehydrate the proteins and limit their reactivity. The detector portion of the meter is composed of electronics, so it must also be protected from extremes of temperature, humidity, moisture. Today most meters have internal temperature checks that allow them to operate within acceptable tolerance range and display error code if it is outside the manufacture range. For good performance both technical accuracy and clinical accuracy is very important. Technical accuracy is the measurement of closeness of agreement between a measured quantity value and a true quantity of glucose. Clinical accuracy compares the medical decisions based on the test results.

TECHNICAL ACCURACY

The National Institute of Standards and Technology's frozen serum standards (glucose concentration determined by isotope dilution mass spectrometry) are available which can be used to determine method accuracy for laboratory instruments analyzing serum specimen. Routinely, glucose meters accuracy is assessed by comparing it with a method used in the clinical laboratory, this establishes meter comparative accuracy but not reference accuracy to a recognized standard. Glucose meters analyze whole blood. The use of whole blood samples for accuracy comparison requires consideration of the effect of glycolysis which decrease glucose concentration in a sample at the rate of 5–7% per hour as long as the serum/plasma remains in contact with the red blood cells. [6,7] Separation of serum/plasma from cells generally within 30 min is recommended for whole blood analysis on glucose meter for establishing meter accuracy. Glucose meters differ in their method of analysis. Some meters take a fixed volume of patient whole blood, lyse the cells, and analyze the amount of glucose in that volume of lysate. Widely meters utilize a series of absorbent pads to separate the cellular portion of a sample from the serum/plasma portion. This allows only serum/plasma to react with the enzymatic reagents. To harmonize glucose results, it is widely recommended to report results from glucose meters such that the value closely matches that of a laboratory method. [8] Capillary, arterial, and venous specimens may be analyzed by a glucose meter, depending on the clinical situation especially in hospitalized inpatients. Alternate collection sites like forearm, leg and abdomen are being tried and are popular due to decreased pain compared to the fingertip. In the fasting state, arterial glucose levels are about 5 mg/dl (0.27 mmol/liter) higher than capillary and 10 mg/dl (0.55 mmol/liter) greater than venous concentrations. [9] The difference can be increased by pH differences between arterial and venous blood samples, decreased perfusion and oxygenation. During fasting, capillary glucose is slightly (2–5 mg/dl) higher than venous glucose. In the postprandial state, capillary blood may be 20–25% or greater than venous levels. [10] Poor perfusion, as in shock can lead to capillary and venous difference in glucose. Hematocrit among hospitalized may vary from the normal, but the manufacturers of glucose meter assume and use normal hematocrit for meter calibration and correction functions. This can be a source of bias when using glucose meters in these patients.

CLINICAL ACCURACY

Clinical accuracy compares the medical decisions based on the test results. Despite apparent analytical difference in results, same or different clinical decisions may be made depending on whether the result is utilized for screening, diagnosis or management in people care. Clarke and associates developed an error grid analysis method to evaluate the clinical significance of the glucose meter result against a comparative method. [11] There are five accuracy zones in the Clarke error grid. Zone A or B - there is mild discrepancy between the glucose meter result and the comparative method, would lead to no change in clinical decision. Zone C, D, or E – there is larger differences between the glucose meter and laboratory comparative method, with potential failure to detect hypoglycemia or hyperglycemia. Clarke error grid was modified by Parkes et al to avoid discontinuities between risk zones where small changes in blood glucose levels can result in dramatic changes in risk. [12]. Today a major tool for evaluating glucose meter accuracy error grid analysis. Variability or precision of the glucose meter may give rise to difference in glucose meters analytical and clinical agreement. [13-15] The Monte Carlo simulation model study evaluated the clinical significance of glucose meter precision and concluded that total precision of <1–2% was required for the glucose meter to ensure similar insulin dosage compared to the laboratory methods more than 95% of the time. [16]

CRITERIA FOR GLUCOSE METER PERFORMANCE

Different accuracy acceptability criteria have been set by different standards organizations and professional societies. The ADA has recommended that glucose meters agree to within ±15% of the laboratory method at all concentrations, and future performance goal of ±5% agreement at all glucose concentration. [17,18] As per the International Organization for Standardization and U.S. Food and Drug Administration the accuracy criteria is ±20 mg/dl (1.11 mmol/liter) for levels <100 mg/dl (5.6 mmol/liter) or ±20% for glucose levels >100mg/dl (5.6 mmol/liter) for at least 95% of results. [19, 20] The determination of accuracy of glucose meter may vary by country and recommendation utilized for the judgment. [21-24]

POSSIBLE INTERFERENCES

Many factors can affect glucose meter results (Table 1). Operator dependent inaccuracy is the most significant source of blood glucose errors, especially in outpatient setting. [5,25] The most common outlined reasons for the discrepancy in result obtained by a patient against a medical laboratory technician are dirty meters, site of testing not cleaned properly, inappropriate samling, presence of blood clots or bubbles in the sample, while handling if mechanical pressure is applied on the strips Modern meters do not need time reactions, do not need pretest strip wipe, need less sample blood, can store patient results, be connected to a computer and display result graph.

Table 1
Glucose meter potential interferences

Environmental	• Exposure Of Strips To Air • Humidity • Altitude • Temperature
Operational	• Generic Test Strips • Reuse Of Strips • Arterial And Catheter • Anticoagulants • Hemolysis • Volume Of Sample
Physiologic	• Hematocrit • Ph • Oxygenation • Hyperlipidemia • Prandial State
Drugs	• Acetaminophen and Ascorbic acid consume peroxide, which results in lower blood glucoses. • Mannitol interferes with some glucose-oxidase-based meters. • Icodextrin, commonly used as an osmotic agent for peritoneal dialysis, can be metabolized to maltose that cross-reacts as glucose, falsely increasing results on some glucose dehydrogenase based meters. • Dopamine can affect glucose results on glucose-dehydrogenase-based meters.
Medical problems	• Hypotension • Anemia • Polycythemia • Academia • Oxygen therapy depress results in glucoseoxidse based meters • Hypoxia causes falsely elevate glucose results in glucoseoxidse based meters • Infants in neonatal intensive care unit (due to polycythemia) • Anemia secondary to any medical or surgical causes like cancer, chemotherapy, blood loss and in postsurgical recovery period, glucose levels can be overestimated. • Specimens should never be collected by finger stick below a catheter, especially in patients with poor perfusion or edema. • Low pH (<6.95) falsely depresses glucose readings, while high pH increases readings for meters utilizing glucose oxidase.

Calibration is an important aspect of any laboratory instrument. Some meters require the operator to insert a calibration code based on the lot of test strip utilized for analysis. Proper meter coding is very important on the meter results and clinical decisions. [26] Some SMBG devices have an automatic calibration or coding feature does not face these problems. Thus calibration can be another source of glucose meter error Patient compliance remains another major problem, especially in certain groups such as adolescence. Patient education is very important to accurate glucose results. Meter accuracy can be improved by periodic inquiry regarding storage of strips, observation of patient testing technique, teaching the need of proper calibration, and periodic testing of control solutions (provided with the glucose meter) to verify technique and reactivity of meter and test strip reagents. The glucose meter can also be checked against a meter of known accuracy or by comparing a specimen against a laboratory method.

CONCLUSION

Glucose meters accept only whole blood, but the present day standards are serum based. As technical accuracy defines meter performance and clinical accuracy establishes how treatment decisions agree between meter results and laboratory glucose results glucose meters should be evaluated before use. The meter selection should be based on technical and clinical performance in the patient population for whom it is intended to be used. Several factors affect the accuracy of glucose meter results, like environmental exposure, patient physiologic and medication effects, and operator technique. Hence clinicians should consider the many factors that can affect meter accuracy and glucose meter results must be interpreted with respect to its potential interference and questioning glucose meter results whenever the results do not match the clinical scenario.

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