

Research Paper

medical science

Current concepts in blood glucose monitoring

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ABSTRACT	Blood glucose monitoring has evolved over the last century. The concept of adequate glycemic control and minimum

Blood glucose monitoring has evolved over the last century. The concept of adequate glycemic control and minimum glycemic variability requires an ideal, accurate and reliable glucose monitoring system. The search for an ideal blood glucose monitoring system still continues. This review explains the various blood glucose monitoring systems with

special focus on the monitoring systems like self-monitored blood glucose (SMBG) and continuous glucose monitoring system (CGMS). It also focuses on the newer concepts of blood glucose monitoring and their incorporation in routine clinical management of diabetes mellitus.

KEYWORDS : glucose monitoring.

INTRODUCTION

The effect of adequate glycemic control on the progression of micro-vascular and macro-vascular complications have been well described by the Diabetes Control and Complications Trial (DCCT)[1] and the United Kingdom Prospective Diabetes Study (UKPDS)[2] trials. The concept of adequate glycemic control and minimum glycemic variability requires an ideal, accurate and reliable glucose monitoring system. This quest to achieve an adequate glycemic control has led to the development of science of blood glucose monitoring systems.

HISTORY AND EVOLUTION OF BLOOD GLUCOSE MONITORING SYSTEMS

Blood glucose monitoring has evolved from obscure methods like urine tasting to colorimetric blood glucose strips. Then came the era of the glucose sensors and manually calibrated glucometers. Presently, we are in the modern era with auto-calibrated accurate glucometers with biosensors for SMBG. Estimation of glycated hemoglobin (HBA1c) remains the gold standard of glucose monitoring as an end point for drug intervention trials. It is postulated that glycemic variability and glycemic excursions are the basis for early development of complications through the development of oxidative stress and free radical injury.[3] To achieve minimum glycemic variability the technique of CGMS was developed making the dream of artificial pancreas a much possible reality.

Hemoglobin A1c (HBA1c)

In 1968, Rahbar first showed that hemoglobin A1 represented a glycated form of hemoglobin which was increased in diabetes.[4] HBA1c measures a physiologic process of non-enzymatic glycation, which is a surrogate for glycation of other proteins in the body and a precursor of diabetes complications. Therefore, the HBA1c represents a measurable indirect estimate of complications of diabetes.[5] It gives an average estimate of plasma glucose over the preceding three months (equal to the lifespan of red blood cells). However, 50% contribution is of the last one month.

Monnier *et al.*, have described an important concept of relative contributions of the fasting and the post-prandial blood glucose levels to the HBA1c.[6] For HBA1c less than 8.4% is the post-prandial glucose values, which are more contributory and as the HBA1c increases, the relative contribution of fasting plasma glucose values increases.

The Diabetes Control and Complications Trial (DCCT)[1] and UK Prospective Diabetes Study (UKPDS),[2] both long-term studies had HBA1c as the primary index of glycemic control. Since then, utility of HBA1c has been well validated as an end point in therapeutic diabetes trials.

Recommendations for HBA1c ADA 2013[7]

- Perform at least twice yearly in patients meeting treatment goals and have stable glycemic control
- Perform quarterly in patients whose therapy has changed or who are not meeting glycemic goals.

USE OF OTHER BIOMARKERS FOR GLUCOSE MONITORING Fructosamine assays 1,5 Anhydroglucitol assay (1,5-AG) Self- monitored blood glucose (SMBG)

Self-monitored blood glucose is the easiest and the most widely used method of short-term glucose monitoring throughout the world. Fingerstick glucose testing using a glucometer is the prototype of SMBG. These points of care devices have revolutionized the concept of home-based glucose monitoring.

Types of glucometers

Glucometers can be broadly classified into two types depending on the enzymes used: Glucose oxidase and glucose dehydrogenase (GDH) with various cofactors like (FAD/NAD/Pyrroloquinoline). Each of these types has their own advantages and disadvantages.

Frequency and pattern of SMBG

A European expert recommendation for SMBG in type-2 diabetes patients issued in 2011 recommended two patterns of SMBG depending on the therapy and the basal control of the patient.[8]

Less intensive pattern

It involves paired meal testing (pre- and post-prandial) once in a day to identify the dynamics of glycemia in response to a meal. The duration of testing is one paired meal testing per month, 1 week/month, 3-7 days/week, continuous paired testing depending on individual case. It is to be used in patients on medical nutrition therapy or a single oral hypoglycemic agent (OHA).[8]

Intensive pattern

Intensive testing involves seven tests per day over a minimum of 3 days up to 7 days. It focuses on the dynamics of glucose levels per day and tries to identify the variability of glucose levels. The duration of testing is a minimum of 3 days/week to 1 week/month, with continuous SMBG.[8] It is mainly used in those with poor metabolic control and those on multi-dose insulin injections or multiple OHA with basal insulin.[8]

RECOMMENDATIONS

ADA 2013

Patients on multiple-dose insulin or insulin pump therapy should do SMBG especially prior to critical tasks like driving and exercise as well as post-meals and suspected hypoglycemia.

In non-insulin treated type-2 diabetes patients also SMBG is useful but is not clearly defined by ADA 2013.

Limitations of SMBG

Calibration and accuracy of glucometers is a very important limitation of SMBG and has to be standardized as described earlier. SMBG cannot predict the future trends of blood glucose and its efficacy is dependent on adherence and compliance. Repeated lancet injuries are a major cause of poor compliance and non-adherence. Concerns of contamination and possible spread of blood borne pathogens like hepatitis are also being studied.[9] Center for disease control (CDC) has also issued timely statements recognizing the importance of universal precautions in SMBG, especially the assisted blood glucose monitoring.[10]

Continuous glucose monitoring systems (CGMS)

Through the understanding of the limitations of SMBG and the concept of glycemic variability emerged the technology of continuous glucose monitoring systems. The first CGMS device was approved by FDA in June 1999 and manufactured by Medtronic Minimed.[11]

Technology

The principle of CGMS is based on the continuous measurement of interstitial glucose levels. Hence it has the ability to provide information about the direction, magnitude, duration, frequency of fluctuations in blood glucose levels. It is an effective tool to measure the glycemic variability and glycemic excursions. There are two main types of CGMS devices: Retrospective also called as 'Professional CGMS' and 'Real time or Personal CGMS'. The Retrospective CGMS gives a retrospective data of 3-5 days depending on the duration of use. It records readings every 5 minutes giving about 288 readings every day. The recorded data is downloaded in the physician's office and hence this type of CGMS does not give us real-time values and cannot be linked with an insulin pump. On the contrary, Real time CGMS gives continuous real time results and has built-in alarm system which provides warnings in rapid fluctuations of blood glucose. The monitor shows trends and predicts future glucose readings. The real time readings help in immediate feed-back and appropriate therapeutic action and can be linked to an insulin pump.

Every CGMS device has a sensor which measures interstitial fluid glucose levels and is inserted using an inserter. The real-time CGMS has a monitor which displays the glucose readings and predicts future trends. In case of retrospective CGMS other components include a docking site which helps download the data from the sensor.

Currently approved CGM devices utilize glucose oxidase based electrochemical subcutaneous sensors. Electric current generated by the sensor as the glucose is oxidized is transmitted to the receiver or monitor.[12]

RECOMMENDATIONS ADA 2013

Continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens can be a useful tool to lower a1c in selected adults (<25 years) with type 1 diabetes. (Level A Evidence).

Glucose monitoring in gestational diabetes mellitus

Controversies exist about the intensity of glucose monitoring in gestational diabetes as well as about the monitoring systems to be used. [13] SMBG through many studied has shown benefit but uncertainty exists about the optimal frequency and timing of self-monitoring. [14] The utility of HBA1c is presently limited to periconceptual period. [15] In some studies, however, weekly HBA1c has shown to be beneficial. Through few studies, CGMs has shown to be beneficial in insulin-treated gestational diabetes, especially for those whose blood sugars are difficult to control or may have nocturnal hypoglycemia, but still this technology needs additional evaluation with larger randomized controlled trials.[14]

Future of glucose monitoring

Non-invasive glucose monitoring forms the future of glucose monitoring systems. Raman spectroscopy, optical coherence tomography, photo-acoustic spectroscopy and fluorescence show the greatest promise in achieving the goal of an ideal glucose sensor.[16] However, at present none of these devices meet the criteria for the ideal sensor and an ideal/accurate biosensor of a closed-loop system remains elusive.

Concept of artificial pancreas: Closing the loop?

CGMS connected to continuous insulin infusion systems in a closed loop forms the basic structure of an artificial pancreas.[17] Thus CGMS forms the key link towards realization of the unrealistic dream of artificial pancreas.

CONCLUSIONS

To summarise, the options of glucose monitoring are varied and each option has its own merits and flaws. We have to bear in mind that at the end of the day the goal of adequate glycemic control has to be achieved in every diabetic patient with minimum hypoglycemia and with utilization of available resources of monitoring.



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