MD CONFERENCE EXPRESS

Laboratory Medicine and Diabetes Care

Clinicians use glucose and hemoglobin A1c (HbA1c) levels to determine whether or not their patients are in control of their diabetes. Just how precise are these values and the established guidelines? That was the question this informative discussion tried to answer.

Mitchell Scott, PhD Washington University, gave an overview of the measures of laboratory test precision and the types of error that contribute to the inaccuracy of results. The coefficient of variation (CV) is a measure of between run precision. It is calculated by dividing the mean by the standard deviation and is the most useful value for clinicians to consider. At his lab (Barnes Jewish Hospital), a glucose value of 88mg/dl has a 1.4% CV and a confidence interval (CI) of 85-91. A glucose of 283 mg/dl has a 1.1% CV and a CI of 276-290. In his experience, the glucose meters used in the hospital are less accurate than the main lab, with an 8.4% CV, a range 153-210, and CI of 139-195.

There are several types of errors that contribute to the overall error of the result. Biological variability includes within patient and between patient variability. The biological variability alone of fasting plasma glucose is quite high (6.9% CV), which means that a glucose value of 126 mg/dl has a CI of 103-149 (Sacks et al, *Clinical Chemistry* 2002; 48:436). Additional routine sources of error include sample misidentification, inappropriate sample storage, drawing at the incorrect time, phlebotomy technique, drawing in incorrect tubes, and IV contamination. Processing and storage delays can cause major problems: if samples are not centrifuged promptly, glucose in the sample decreases 7% per hour at room temperature. Dr. Mitchell strongly suggests that clinicians centrifuge their samples promptly, repeat any borderline glucose values, and call the lab if lab results do not correlate with their clinical observations.

David B. Sacks, MB, ChB, FRCPath of Harvard Medical School presented changes to the HbA1c test and the global implications for clinical practice. The concentration of glycated hemoglobin (GHb) represents integrated glucose in blood over a 6-8 week period. It is therefore a very useful criterion for glucose control and in most major clinical trials it is used as a predictor of the risk of complications. The ADA recommends regular monitoring of GHb, but there are 30 different tests available world-wide.

The objective of the National Glycohemoglobin Standardization Project (NGSP) is to standardize the HbA1c result (a measure of GHb) so clinicians can easily compare results and accurately assess risk. The NGSP works with manufacturers to calibrate instruments, certify methods, and certify individual labs via proficiency testing. This effort has led to improved reproducibility and consistency: in 1993, 50% of labs were reporting HbA1c as a measure of GHb; in 2006, 99% are reporting HbA1c. NGSP methods are used in the European Union, India, China, Australia, Latin America, North America, South Africa, and Russia.

Yet there is a potential source of confusion for clinicians. The IFCC (International Federation

of Clinical Chemistry) has also set out to develop an HbA1c reference method and primary reference materials. As it turns out, the IFCC values are lower than NGSP values. For example, a 7.0 NGSP = 5.3 IFCC. There is a formula that can be used to convert between the two, but this makes it more difficult to accurately determine a patient's glycemic control. Although the guidelines may be changing in the future, a consensus has not been reached at this time. It is therefore important that clinicians continue to follow their current guidelines for HbA1c when monitoring their patients.

Screening in Pediatric Diabetes

Pediatric diabetes patients should be screened for celiac disease, thyroid disease, dyslipidemia and microalbuminuria when certain indications are present. These diseases are all serious and can effect the treatment of diabetes. Diabetes may also mask their presence and complicate their effects.

Celiac diseases

In type 1 diabetics (T1D), celiac disease (CD) causes unexplained hypoglycemia. Up to 16% of T1D patients develop autoantibodies to tissue transglutinase (TG IgA), a marker of CD. 70-90% of T1D patients have a positive intestinal biopsy for CD (Rewers et al. 2004).

Marian Rewers, MD, University of Colorado Medical Center, Denver, CO, recommends that T1D patients be screened for TG IgA at onset of diabetes and at least bi-annually until age 10, or if symptomatic. In symptomatic cases, a biopsy should be recommended. All patients whose CD biopsy was positive should be put on a gluten-free diet, regardless of symptoms. A patient's insulin dose usually needs to be increased when he/she is on a gluten-free diet.

Thyroid disease

15-30% of patients with type 1 diabetes have hypothyroidism. The coexistence of T1DM and autoimmune thyroid disease (AITD) is considered autoimmune polyglandular syndrome (APS Type III), explained Linda DiMeglio, MD, MPh, Riley Hospital for Children, Indianapolis, IN. Autoimmune thyroiditis is associated with human leukocyte antigen [HLA] genotype as well, which may be synergistic with HLA type for development of both T1DM and TAI.

"It is important to know the thyroid status of patients with T1DM because untreated hypothyroidism results in reduced insulin degradation and could cause hypoglycemia," said Dr. DiMeglio.

Hyperthyroidism affects only one percent of those with T1D, with Graves' disease being the most common cause of hyperthyroidism in young children and adults. Hyperthyroidism can be associated with worsening glycemic control and thyrotoxicosis may reveal latent diabetes mellitus.

Serum thyroid stimulation hormone (TSH) is the most reliable and sensitive screening test for thyroid dysfunction.

Lipid Profiles

Dyslipidemia in childhood is a risk factor for development of atherosclerosis and increased cardiovascular (CV) risk. The goals of identifying and treating dyslipidemia are to prevent or delay atherosclerosis and to diminish CV risk associated with diabetes and dyslipidemia (*NEJM* 1998).