Sibioc Symposium - The latest advances in diabetes clinical and laboratory research

DIABETES: TIME FOR A RETHINK ? (PLEASE CHECK SESSION WITH ORGANISERS

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The global epidemic of diabetes shows no signs of remitting. Both Type 1 diabetes and type 2 diabetes have substantial heterogeneity. Type 1 diabetes is considered a disease of childhood-onset, yet it usually presents in adulthood, often initially without requiring insulin therapy. The immunogenetic phenotype of adult-onset type 1 diabetes is similar to children diagnosed after the age of 13 years but different from those diagnosed under age 7 years. Their progression to insulin dependence is less rapid and often the disease is less severe. Recognising adult-onset type 1 diabetes in distinction from type 2 diabetes can be difficult. Yet it is important, given the poor management of these cases, their relative hyperglycaemia as well as hypoglycaemia and both retinopathy and macrovascular disease. Recent guidelines have suggested approaches to both the classification and management of adult-onset type 1 diabetes in order to limit those risks. Heterogeneity also exists within Type 2 diabetes and has highlighted the role of diet and the range of available drugs, specifically drugs that target cardio-renal disease. Recognising that heterogeneity in diabetes at all ages through precision medicine will be key to improving management of the disease in the future.

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ROLE OF GLYCATED ALBUMIN FOR DIAGNOSIS AND MANAGEMENT OF DIABETES MELLITUS

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There is growing interest and use of alternative markers of hyperglycemia such as glycated albumin or fructosamine in diabetes care. Alternative markers could be complementary to HbA1c and/or potentially used in settings were HbA1c is unavailable or problematic (e.g., hemoglobinopathies, anemia, altered red cell turnover). Statements from diabetes and laboratory organizations have suggested that glycated albumin may be useful, but its diagnostic performance and long-term prognostic value are unclear.

We have conducted a series of diagnostic and epidemiologic studies to understand the clinical value of glycated albumin in diabetes care. We have found that, in persons with diabetes, glycated albumin is highly correlated with HbA1c and fasting glucose and is associated with prevalent retinopathy, incident kidney disease, incident cardiovascular disease, and mortality. In adults with diabetes, associations of glycated albumin with clinical outcomes similar in magnitude to those for HbA1c. We also performed diagnostic studies to characterize the performance of glycated albumin for screening and diagnosis of diabetes and prediabetes. In a general population of US adults, glycated albumin was highly specific to identify people with diabetes, however, it lacked sensitivity as compared to other glycemic biomarkers to screen for prediabetes. Glycated albumin did not perform well as a screening biomarker in children or for hyperglycemia in pregnancy. We also demonstrated that glycated albumin is strongly affected by excess adiposity and its performance appears altered in persons with obesity.

Ultimately, our body of research shows that glycated albumin is a highly specific biomarker of hyperglycemia and may be useful for monitoring glycemic control in persons with diabetes when HbA1c testing is problematic or not available. Glycated albumin is not sufficiently sensitive to be used as a general screening test.

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DIABETIC KIDNEY DISEASE: NEW CLINICAL AND THERAPEUTIC ISSUES

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Recent epidemiological studies have disclosed the clinical and anatomical heterogeneity of diabetic kidney disease (DKD). In fact, two new phenotypes have emerged in addition to the classical albuminuric phenotype. Nonalbuminuric renal impairment is characterized by reduced estimated glomerular filtration rate (eGFR) associated with normoalbuminuria and has become at least as frequent as the albuminuric phenotype among diabetic individuals with reduced eGFR, especially those with type 2 diabetes (T2D), possibly due to the increasing occurrence of remission/regression of albuminuria. Progressive renal decline is characterized by eGFR loss that progresses unidirectionally to end-stage kidney disease (ESKD) at a variable rate independently of albuminuria. These new phenotypes indicate that DKD progression toward ESKD may occur through two distinct pathways, albuminuric and nonalbuminuric, heralded by a progressive increase of albuminuria or by a decline of renal function irrespective of albuminuria, respectively. Moreover, increasing evidence indicates that, in addition to the typical microvascular lesions with predominant glomerular injury (glomerular basement membrane thickening, mesangial expansion, and glomerulosclerosis), atypical (macro)vascular and/or tubulo-interstitial lesions with no or minimal glomerular involvement may be observed in diabetic individuals, especially those with T2D. The atypical histological features seem to be more frequent in patients presenting with the nonalbuminuric phenotype, whereas the typical glomerular lesions appear to prevail among those with the albuminuric phenotype, though the paucity of biopsy data does not allow demonstrating clear clinico-anatomical relationships. During the last decade, new anti-hyperglycemic drugs with the lowest safety threshold within the reduced eGFR range have become available for treatment of patients with T2D and DKD. Cardiovascular and renal outcome trials have shown that glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter 2 (SGLT2) inhibitors provide cardiovascular and renal protection beyond their glucose-lowering effect, with SGLT2 inhibitors reducing eGFR decline and albuminuria, whereas GLP-1 receptor agonists being effective only on macroalbuminuria.