

ISPAD Annual Conference 2015 Highlights

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The 41st annual ISPAD meeting took place from 7 to 10 October in Brisbane, Australia as a joint meeting with the Australasian Paediatric Endocrine Group. The roving reporters present an overview of the scientific highlights of the meeting.

Can we put the brakes on diabetes

An update on SEARCH data confirmed an increase in prevalence for type 1 and type 2 diabetes (T1D and T2D). The increasing rate of obesity has made it more difficult to define diabetes types. Individuals with 'high risk' human leukocyte antigen (HLA) alleles are a decreasing proportion of new diabetes diagnosis, with lower risk alleles becoming more prominent, suggesting a change in environment rather than genetics per se.

The improvements in care achieved by national and international benchmarking, reduction in glycated hemoglobin A1c (HbA1c) with no change in severe hypoglycaemia, and a reduced prevalence of severe diabetic ketoacidosis (DKA) after introduction of the SWEDIABKIDS registry was showed. The importance of early tight control in diabetes with reduction of risk for complications, irrespective of later control was also emphasized.

Epigenetics

Developmental origins of health and diseases refer to the mechanism by which events in fetal life can influence long-term health. There are three main mechanisms by which change occurs: (1) permanent structural change, as demonstrated for example by a reduction in beta cell mass, nephron number, or cardiac structure and function; (2) accelerated cellular aging, indicated by telomere shortening; (3) epigenetic programming of gene expression through changes in DNA methylation and/or histone modifications.

Metabolic memory is the phenomenon by which previous exposure to metabolic perturbations has long-lasting effects. This is best showed in T1D by the diabetes control and complications trial/epidemiology of diabetes interventions and complications (DCCT/EDIC) trials, whereby a period of intensive diabetes treatment with improved metabolic control resulted in decreased risk of microvascular complications a decade later, despite similar glycemic control for the previous decade. This metabolic memory is due to epigenetic changes causing altered signaling and transcriptional changes.

Diabetes genetics, immunology and environment

Factors that trigger autoimmunity and development of T1D are being investigated to find novel interventions that may prevent this process. Perceived requirement of micronutrient supplementation during pregnancy is common, one such example is iron supplementation. Colleagues in Finland found that in their cohort, increased newborn iron levels were associated with an increased odds ratio for developing T1D. Because increased reactive oxygen species (ROS) may cause β cell destruction, new agents reducing ROS may have a role in preventing the advancement of antibody positivity to T1D.

VIDIS symposium

Fresh pancreatic tissue from patients at diabetes diagnosis could help in understanding of the disease

process. RNA for all the genes involved in insulin production was found in the tissue samples, suggesting that the cellular machinery for producing insulin is still intact. Second, immunohistochemistry and polymerase chain reaction (PCR) analysis for RNA showed that enterovirus capsid protein 1 and hyper-expression of class 1 HLA molecules was detected in all T1D islet cells. Autoimmune diseases share many genetic and environmental determinants. Identifying combinations of genetic and environmental factors that interact may provide the ability to explain disease risk profile and pathogenesis.

Hot topics in the basic science arena

Data on mitochondrial damage as central to the pathogenesis of diabetic nephropathy were presented. Mitochondrial dysfunction is noted as early as 4 wk in animal models with fragmented mitochondria showed on electron microscopy both in animal and human models.

High concentrations of lipids and glucose cause endoplasmic reticulum (ER) stress, which results in aberrant insulin secretion with an increase in the proinsulin to insulin ratio. Pretreatment with IL-22 reduces ER stress and chemokine production, and restores the production of high-quality insulin secretion.

Prenatal perturbation affects fetal development and can cause long-term programming disturbances. Alcohol can affect this foetal programming; therefore it is crucial to increase public awareness regarding these effects.

Complications – macrovascular disease in diabetes in the young

In children, non-invasive measurements of cardiac function and arterial stiffness, e.g., carotid/aortic intima media thickness (IMT) and flow-mediated dilation (FMD) as a measure of vascular endothelial function are currently the best available markers of future cardiovascular disease. There seems to be a need to focus on other cardiovascular risk factors including lipid profiles, sodium intake and blood pressure, rather than just lowering of HbA1c to prevent cardiovascular diseases (CVD) in children with diabetes.

Atherosclerosis begins in childhood and in some cases may even start before birth. Results of the AddIT trial will help answer some questions regarding the use of statins in children with T1D, bearing in mind that this trial is measuring early markers of cardiovascular disease.

We are what we eat

High AGE diets result in hyperfiltration, an early finding in diabetic nephropathy. This provides further

evidence that highly processed foods, and cooking techniques (such as deep frying) which have high AGEs, should be avoided.

Using advanced sequencing techniques and bioinformatics it was found, that the exocrine signature from the pancreas is different, concluding that the community phenotype of the gut microbiome in patients with T1D is different from controls with potential implications for the pathogenesis of T1D.

Obesity is not only a result of poor eating habits and a sedentary lifestyle, but there is a strong genetic and biological component as most individuals who lose weight gain it all back. Body weight is regulated in the hypothalamus with involvement of several hormones. To maintain weight loss, individuals need to remain focussed, constantly vigilant of everything they eat and exercise daily.

Cutting edge technology

The rapid technological advances in the past decade have improved clinical management, with a reduced risk of severe hypoglycaemia. Pumps in association with continuous glucose monitoring (CGM), have significantly reduced overnight hypoglycaemia, but also improved blood glucose variability.

The three main components to any closed-loop system are a glucose sensor, a mechanism of insulin (and/or glucagon) delivery and the algorithm controlling the pump, each with its own limitations – the accuracy of the sensors, dermatologic complications, algorithms controlling insulin delivery, biologic variability of the insulin action and meal absorption. Most recent studies have been completed with ‘hybrid’ closed loop models.

New drugs in diabetes

SGLT2 (sodium glucose transport) inhibitors are important new tools for the management of diabetes with benefits beyond glycaemia, particularly by minimizing hyperfiltration to prevent early diabetic nephropathy. In T1D, SGLT2 inhibitors enabled lowered HbA1c, lower fasting glucose, less hypoglycaemia, and a lower requirement for insulin.

GLP1 agonists are well established in the treatment of adult T2D. In combination with basal insulin, there is added therapeutic advantage.

‘Smart insulin’ preparations using polymer-based nanotechnology that act as glucose sensors are currently limited to animal data but show promising preliminary results.

Protecting mental health in diabetes

The majority of research in mental health is based on depressive symptoms identified by validated screening,

rather than formal diagnosis of clinical depression. Barriers to screening are noted to include determining who is qualified to undertake screening, reluctance to screen because of family and professional concerns regarding stigma and burden. Depression is associated with poorer metabolic control, poorer quality of life, and greater rates of family conflict. Treatment options for comorbid depression include cognitive behavioral therapy, behavioral family systems therapy, and antidepressant medications.

In the Western Australian Childhood Diabetes Database the hazard ratio (HR) for any psychiatric disorder was 2.3 in those with childhood-onset T1D; the highest risk was for eating disorders (HR 5.1).

Fear of hypoglycaemia is associated with decreased quality of life. Fear of hypoglycaemia in children and youth has been associated with negative effects on glycemic control, with higher average HbA1c, and fear of hypos can impact the mental health in parents of children with T1D. Improvements in pump technology may reduce frequency of hypoglycaemia, whereas, the use of diabetes alert dogs although popular have very little objective data to accurately predict hypoglycaemia.

However, the incidence of severe hypoglycaemia was reported decreasing according to data from the Norwegian Childhood Diabetes Registry, consistent with results from other centers. From 2001–2013 the rates of severe hypoglycaemia have decreased from 14.4 to 4.2 per 100 patient-yr, with no significant change in HbA1c over the same time period.

Rights of individuals with diabetes

Children are not to be viewed as powerless objects of charity but as human beings with rights (UN Convention). Communities and nations can be empowered through social media, partnerships and international collaborations to promote the rights of children.

Adolescence has been referred to as a ‘culture bound syndrome’, a developmentally unique period. Adolescence with diabetes is then viewed as being at an intersection of socially construed disease with actual biological disease. It is a period of reckless and

mindless risk taking behavior. Technology can be used as an important secret weapon, which can aid them in making their decisions. Parents should be encouraged to give up control and transfer responsibility to the teenager over a period of time.

Care of patients with disability and diabetes is complex. The long-term goal is more than just minimisation of disorder-related harm, but must also include optimisation and adjustment of each individual at various stages in life.

Diabetes in indigenous people

The burden of diabetes in Indigenous Australians is enormous and the gap between Indigenous and non-Indigenous Australians unacceptably large. Indigenous Australians with diabetes are nine times more likely to die from CVD. Key issues relate to disparities in access to healthy food and health services, socioeconomic burdens, and the downstream effects of a displaced population treated with a Western understanding of disease processes rather than an Indigenous perspective of the same.

Increased incidence of T2D in indigenous children may be caused by genetic factors (ethnicity and family history), epigenetic factors related to exposures in utero, and also obesity and low physical activity. Social factors, including chronic stress, poverty and low socioeconomic status also need to be addressed as related factors.

Prenatal and antenatal strategies are aimed at improving early diagnosis and treatment of T2D, reducing access to sugary drinks and improving access to fruit and vegetables, as well as providing midwifery training about diabetes management. Postnatal strategies are focussed on improving the rates of breast feeding.

For the complete report, please go to the www.ISPAD.org.

The 42nd Annual ISPAD meeting will take place in Valencia, Spain from 26–29 October 2016. Details can be found at <http://www.ispad.org/>. ISPAD and the organizing committee welcome the international pediatric diabetes community to attend.