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Editorial

Diabetes in Children and Adolescents: What is New?

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Introduction

Diabetes is one of the most common chronic diseases during childhood and adolescence [1]. In recent years, considerable progress has been made in the understanding of the epidemiology and pathogenesis of the different forms of diabetes and several advances have been made in the diagnosis and treatment of this condition.

Among the various forms of diabetes, the most frequent in the pediatric population is Type 1 Diabetes (T1D), characterized by an autoimmune destruction of the pancreatic β-cells [1]. However, during recent years, in parallel with the growing epidemic of childhood obesity, there has been the emergence of Type 2 Diabetes (T2D), a disease considered for long time as typical of adulthood [1]. Maturity Onset Diabetes of the Young (MODY) is another form of diabetes that may occur in children and adolescents. This term includes a group of disorders inherited in an autosomal dominant way, with onset before the age of 25, in the presence of family history of diabetes and in the absence of obesity and ketosis. This condition is due to a primary defect of β-cell function and insulin secretion [1]. Another form of diabetes that can affect to a lesser extent the pediatric age is neonatal diabetes, a monogenic condition, characterized by an onset of diabetes before the age of six months, and linked to defects in the development or function of pancreatic β-cells [1].

What is New in Terms of Epidemiology of Diabetes?

T1D represents 90% of all cases of diabetes during childhood and adolescence, with an increasing incidence at an annual rate of 3% during recent years [2]. Based on data published by the International Diabetes Federation (IDF), in the year 2015, in the world there were about 542,000 children with TID younger than 14 years; with 86,000 new diagnoses each year [3].

During recent years, in parallel with the growing epidemic of childhood obesity, there has also been the emergence of T2D. This type of diabetes is particularly common in the US and especially among obese adolescents belonging to ethnic minorities [4]. However, a growing number of cases of T2D are also reported in other parts of the world, such as Japan and Europe [4].

Recently, advances in genetics have also allowed a better identification and characterization of monogenic forms of diabetes, such as neonatal diabetes and MODY, which, although rare, require a proper diagnosis in order to implement an appropriate management [1].

What is New in Terms of Pathogenesis of Diabetes?

T1D is chronic T-cell mediated autoimmune disease, resulting from the interaction between various genetic and environmental factors [5]. Advances in genetics have led to the identification of several genes involved in the pathogenesis of T1D. HLA class-II alleles explain much of the genetic risk of T1D (about 30-50%). However, recent studies have shown that there are over 40 other genes (eg: Insulin genes, PTPN22, CTLA4, and IL2RA) that might contribute to the risk of developing T1D, although each individual allele has a small effect size in terms of overall risk [6]. Many chromosomal regions associated with T1D have been identified through Genome Wide Association Studies (GWAS), although further studies are needed to identify the genes corresponding to these regions and their function. Recent studies have underlined the importance of combining GWAS studies with gene expression profiles and analysis of protein networks in order to better understand the genetic component of T1D [7].

There is also recent evidence that changes in the immune phenotype could in part explain the increased incidence of T1D. In particular, cases of T1D diagnosed during more recent decades seem to be associated with a 'more mature and aggressive 'immune response compared to cases diagnosed in previous decades, as highlighted by a higher frequency and concentration of auto-antibodies such as IA-2 and ZnT8A, which usually appear during advanced stages of the autoimmune process [8].

From an epidemiological point of view, the increasing incidence of T1D has occurred too rapidly to be explained by changes in the genetic background and suggests a role for changes in environmental factors [9]. Numerous studies have analyzed factors such as viral infections, pre-, peri- and post-natal factors, which could represent targets for future preventive strategies [9]. Prenatal factors, such as excessive maternal weight gain during pregnancy, a high birth weight have emerged as factors predisposing to the development of T1D. Caesarean section has also been associated with a higher frequency of T1D when compared with spontaneous delivery, probably due to a different composition of the intestinal flora of the infant, which derives from different microorganisms depending on the delivery is vaginally or by caesarean section [10].

Among factors acting during early life, dietary components could have a role in then pathogenesis of T1D. This has led to the investigation of changes in feeding patterns in infants as a potential primary prevention strategy for T1D. The TRIGR trial has explored the effect of two different formulas for infants, a standard formula (80% milk protein and 20% hydrolyzed proteins) and an alternative formula based on hydrolyzed casein on autoantibody seroconversion in term infants at genetic risk for T1D [11]. Although in the original pilot study, performed in 230 infants, the intervention with the hydrolyzed formula was associated with a 50% reduction in the risk of seroconversion [11], more recent results from the 7-year follow-up of the trial have been disappointing, being unable to show any significant

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difference in terms of seroconversion between the two formulas [12]. In another birth cohort trial, the BABYDIET, a delayed introduction of gluten in the infant diet was investigated as a potential primary prevention strategy, but also in this case there was no beneficial effect in term of seroconversion [13].

Furthermore, over the last years there has been growing interest in the association between enterovirus infections, particularly Coxsackie virus B1, and the risk of developing T1D [14]. The mechanism through which enterovirus contribute to the risk of T1D are complex and involve the interaction between viruses, immune system, pancreatic cells and the patient's genotype.

Update on the Treatment of Diabetes

Over the last few decades many advances have been made to improve the treatment of T1D in children, with the aim of ensuring an optimal metabolic control and avoiding complications in the short and long term. These include the introduction of fast-acting insulin and long-acting analogues as part of a basal-bolus therapy, insulin pump therapy, and the introduction of a continuous glucose monitoring. Of increasing interest are studies, still in progress, aiming at the development of an 'artificial pancreas', which consists of a device that integrates an insulin pump, a system for monitoring glycemic and an algorithm, which adjusts the insulin infusion based on the blood glucose values [15]. A further area of intense research interest concern the evaluation of new therapies, such as immunotherapy, which should be implemented soon after diagnosis or even before the clinical diagnosis of T1D, to try to block the autoimmune process, and preserve the residual insulin production [16].

Management of pediatric T2D is based on lifestyle interventions, implemented when required with drugs such as metformin or insulin. There is not yet sufficient evidence to recommend other drugs, such as GLP-1 agonists, DPP-1 inhibitors for the management of T2D in youth [17].

Conclusions

Diabetes is a major medical condition, whose early diagnosis and prompt treatment are of paramount importance to reduce the morbidity and mortality associated with the disease. The epidemiological evidence of an increasing number of cases of T1D and T2D is alarming and highlights the importance of further studies to improve early diagnosis as well as prevention and treatment of this condition.

References

1. Craig ME, Jefferies C, Dabelea D, Balde N, Seth A, Donaghue KC. ISPAD Clinical Practice Consensus Guidelines 2014. Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatric Diabetes. 2014; 15 Suppl 20: 4-17.
2. Patterson CC, Dahlquist GG, Gyurus E, Green A, Soltesz G. Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. Lancet 2009; 373: 2027-2033.
3. International Diabetes Federation. IDF Diabetes, 7 ed. Brussels, Belgium: International Diabetes Federation, 2015.
4. D'Adamo E, Caprio S. Type 2 diabetes in youth: epidemiology and pathophysiology. Diabetes care 2011; 34 Suppl 2: S 161-165.
5. Todd JA. Etiology of type 1 diabetes. Immunity 2010; 32: 457-467.
6. Pociot F, Akolkar B, Concannon P, Erlich HA, Julier C, Morahan G, et al. Genetics of type 1 diabetes: what's next? Diabetes 2010; 59: 1561-1571.
7. Bergholdt R, Brorsson C, Palleja A, Berchtold LA, Floyel T, Bang-Berthelsen CH, et al. Identification of novel type 1 diabetes candidate genes by integrating genome-wide association data, protein-protein interactions, and human pancreatic islet gene expression. Diabetes 2012; 61: 954-962.
8. Long AE, Gillespie KM, Rokni S, Bingley PJ, Williams AJ. Rising incidence of type 1 diabetes is associated with altered immunophenotype at diagnosis. Diabetes 2012; 61: 683-686.
9. Vehik K, Dabelea D. The changing epidemiology of type 1 diabetes: why is it going through the roof? Diabetes Metab Res Rev 2011; 27: 3-13.
10. Bonifacio E, Warncke K, Winkler C, Wallner M, Ziegler AG. Cesarean section and interferon-induced helicase gene polymorphisms combine to increase childhood type 1 diabetes risk. Diabetes. 2011; 60: 3300-3306.
11. Knip M, Virtanen SM, Seppa K, Ilonen J, Savilahti E, Vaarala O, et al. Dietary intervention in infancy and later signs of β-cell autoimmunity. N Engl J Med 2010; 363: 1900-1908.
12. Knip M, Akerblom HK, Becker D, Dosch HM, Dupre J, Fraser W, et al. Hydrolyzed infant formula and early β-cell autoimmunity: a randomized clinical trial. JAMA 2014; 311: 2279-2287.
13. Hummel S, Pfluger M, Hummel M, Bonifacio E, Ziegler AG. Primary dietary intervention study to reduce the risk of islet autoimmunity in children at increased risk for type 1 diabetes: the BABYDIET study. Diabetes Care 2011; 34: 1301-1305.
14. Laitinen OH, Honkanen H, Pakkanen O, Oikarinen S, Hankaniemi MM, Huhtala H, et al. Coxsackie virus B1 is associated with induction of β-cell autoimmunity that portends type 1 diabetes. Diabetes 2014; 63:446-455.
15. Garvey K, Wolfsdorf JI. The Impact of Technology on Current Diabetes Management. Pediatr Clin North Am. 2015; 62: 873-888.
16. Nathan DM. Diabetes: Advances in Diagnosis and Treatment. Jama 2015; 314: 1052-1062.
17. Onge ES, Miller SA, Motycka C, DeBerry A. A review of the treatment of type 2 diabetes in children. Pediatr Pharmacol Ther. 2015; 20: 4-16.

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