PS 001 Autoimmune diabetes

265

Vitamin D intake during childhood and advanced beta cell autoimmunity in young children with HLA-conferred susceptibility to type 1 diabetes

S.M. Virtanen[1,2], H.-M. Takkinen[2], L. Uusitalo[1,2], S. Niinistö[1], S. Ahonen[2], J. Nevalainen[3], M.G. Kenward[4], R. Veijola[5], J. Ilonen[6,7], O. Simell[8], M. Knip[9,10];
[1]Life Style and Participation, National Institute for Health and Welfare, Helsinki, [2]School of Health Sciences, University of Tampere, [3]Social Research, Statistics, University of Turku, Finland, [4]Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK, [5]Pediatrics, University of Oulu, [6]Virology, University of Eastern Finland, Kuopio, [7]Virology, University of Turku, [8]Pediatrics, University of Turku, [9]the Children's Hospital, University of Helsinki, [10]Pediatrics, University Hospital of Tampere, Finland.

Background: Evidence for the role of vitamin D during childhood in the development of beta-cell autoimmunity and clinical diabetes is inconsistent.
Materials and methods: Two hundred seventy-four children with repeated positivity for antibodies against islet cells (ICA), together with positivity for at least one of the other three antibodies analyzed or clinical type 1 diabetes (a composite endpoint of advanced beta-cell autoimmunity) were identified from a prospective birth cohort of 7787 infants with HLA-DQB1-conferred susceptibility to type 1 diabetes born in 1996-2004. Three-day food records were completed by the families and day care personnel at 3 to 12 month intervals. Four birth date, gender, area and genetic risk matched controls having been in the follow-up at least until the age when the case became a case were randomly selected for each case.
Results: The mean dietary intakes of vitamin D from diet and supplements for 3 and 6 month, 1, 2, 3, 4 and 6 year-olds were 10.4, 12.1, 11.1, 7.9, 5.9, 5.1 and 6.3 µg/day, respectively. Vitamin D intake either from food (OR 1.08, 95% CI 0.97-1.20), supplements (OR 0.96, 95% CI 0.86-1.07) or the total dietary intake (OR 0.96, 95% CI 0.83-1.11) were not associated with advanced beta-cell autoimmunity.
Conclusion: In relation to the nutrition recommendations the average intake of vitamin D was suboptimal among these children with HLA-conferred susceptibility to type 1 diabetes. The longitudinal vitamin D intake was not, however, related to the development of advanced beta-cell autoimmunity.
Clinical Trial Registration Number: NCT00223613

266

Serum levels of soluble receptors for advanced glycation end products decline at seroconversion to autoantibody positivity in prediabetic children

K.M. Salonen[1], S. Ryhänen[1], J.M. Forbes[2], J. Ilonen[3,4], P.-H. Groop[5,6], M. Knip[1,5];
[1]Children´s Hospital, University of Helsinki and Helsinki University Hospital, Finland, [2]Baker IDI Heart & Diabetes Institute, Melbourne, Australia, [3]Immunogenetics Laboratory, University of Turku, [4]Department of Clinical Microbiology, University of Eastern Finland, Kuopio, [5]Folkhälsan Research Center, Helsinki, [6]Department of Nephrology, Department of Medicine Helsinki University Central Hospital, Biomedicum Helsinki, Finland.

Background and aims: The receptor for advanced glycation end products (RAGE) is a multiligand receptor involved in inflammatory and immune responses. RAGE is suggested to play a role both in the pathogenesis of type 1 diabetes (T1D) and in the development of its complications. The circulating concentrations of soluble RAGE (sRAGE) may be reduced during acute autoimmune processes. This study set out to assess the dynamics of sRAGE during the preclinical T1D disease process.
Materials and methods: Serum levels of sRAGE were analyzed in 110 children who progressed to T1D during prospective observation. Samples analyzed were taken at four different time points: (1) before seroconversion to autoantibody positivity; (2) at the time of seroconversion to positivity for one autoantibody; (3) at the time of seroconversion to positivity for multiple ($\geq$ 2) autoantibodies; and (4) close to the diagnosis of T1D. Samples of 110 autoantibody-negative controls matched for age, sex, HLA-genotype and place of birth were analyzed for sRAGE at corresponding time points.

Results: The progressors had higher levels of sRAGE at all four time points, but the difference was significant only in the first and last sample [mean difference 172 pg/ml, p=0.01 and 164 pg/ml, p=0.02, respectively (t-test)]. There was a decline in the sRAGE levels in the progressors between the first sample and the second sample [mean sRAGE 1400 pg/ml vs. 1251 pg/ml, p=0.001 (paired t-test)]. A difference in the sRAGE concentrations was also seen when the first sample was compared to the third sample (mean sRAGE 1402 pg/ml vs. 1232 pg/ml, p<0.001). There was no such difference in sRAGE levels between the samples taken from the matched controls at corresponding time points. There were no significant differences between the sRAGE levels at seroconversion and the concentrations at T1D diagnosis.
Conclusion: Prediabetic children seem to have higher circulating concentrations of sRAGE when compared to controls. A reduction in the circulating sRAGE concentrations coincides with the appearance of diabetes-predictive autoantibodies in children progressing to overt T1D. Whether this reflects a damaging or attempted protective mechanism remains to be defined.

267

Screening for IA-2 and zinc transporter 8 antibodies identifies relatives of type 1 diabetic patients with a high and age-independent progression rate to clinical onset

E.V. Balti[1], S. Demeester[1], A. Van Dalem[1], O. Costa[1,2], H. Dorchy[3], S. Tenoutasse[3], T. Mouraux[3,4], C. De Block[5], P. Gillard[6], K. Decochez[1,7], J.M. Wenzlau[8], J.C. Hutton[8], D.G. Pipeleers[1], I. Weets[1,2], F.K. Gorus[1,2];
[1]Diabetes Research Center, Brussels Free University, [2]Department of Clinical Chemistry and Radio-immunology, University Hospital Brussels, [3]Diabetology Clinic, Queen Fabiola Children's University Hospital, Brussels, [4]Department of Pediatrics, University Hospital Mont-Godinne, Yvoir, [5]Department of Endocrinology, Diabetology and Metabolism, University of Antwerp, [6]Department of Endocrinology, University Hospital Leuven, [7]Department of Diabetology, University Hospital Brussels, Belgium, [8]Barbara Davis Center for Childhood Diabetes, University of Colorado at Denver, Aurora, USA.

Background and aims: In first-degree relatives of type 1 diabetic patients, we investigated whether diabetes risk assessment solely based on IA-2 and zinc transporter 8 antibody status (IA-2A, resp. ZnT8A) is as effective as screening for autoantibodies (Abs) against insulin (IAA), GAD (GADA) and IA-2 (with or without ZnT8A) in identifying children, adolescents and adults who rapidly progress to diabetes (within 5 years) in the perspective of constituting homogeneous risk groups for immune interventions before diabetes onset.
Materials and methods: Abs were determined by radiobinding assays during follow-up of 6444 siblings and offspring aged 0-39 years at inclusion and consecutively recruited by the Belgian Diabetes Registry.
Results: We identified 394 persistently IAA[+], GADA[+], IA-2A^{+} and/or ZnT8A^{+} relatives (6.1%). After a median follow-up time of 52 months, 132 relatives developed type 1 diabetes. In each age category tested (0-9 years, 10-19 years and 20-39 years) progression to diabetes was significantly quicker in the presence of IA-2A and/or ZnT8A than in their joint absence. The 5-year progression rate was age-independent if IA-2A and/or ZnT8A were present at baseline but decreased with age if only GADA and/or IAA were detected (*P* = 0.008). Screening for IA-2A and ZnT8A alone identified 74% of the rapid progressors (vs. 65% if positive for $\geq$2 Abs among IAA, GADA and IA-2A) and reduced the group of high-risk Ab[+] relatives to be followed by 63%. Positivity for IA-2A and/or ZnT8A was as sensitive as positivity for at least 2 out of 4 antibodies in individuals aged 10-39 years but less sensitive under age 10, an age group generally not considered for immune interventions until now.
Conclusion: Screening for IA-2A and ZnT8A alone allows to identify the majority of rapidly progressing prediabetic siblings and offspring regardless of age and is more cost-effective to select participants for intervention trials than conventional screening.