Effect of cow's milk exposure and maternal type 1 diabetes on cellular and humoral immunization to dietary insulin in infants at genetic risk for type 1 diabetes. Finnish Trial to Reduce IDDM in the Genetically at Risk Study Group.

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Abstract

Type 1 diabetes is considered to be a T-cell-mediated autoimmune disease in which insulin-producing beta-cells are destroyed. Immunity to insulin has been suggested to be one of the primary autoimmune mechanisms leading to islet cell destruction. We have previously shown that the first immunization to insulin occurs by exposure to bovine insulin (BI) in cow's milk (CM) formula. In this study, we analyzed the development of insulin-specific T-cell responses by proliferation test, emergence of insulin-binding antibodies by enzyme immunoassay, and insulin autoantibodies by radioimmunoassay in relation to CM exposure and family history of type 1 diabetes in infants with a first-degree relative with type 1 diabetes and increased genetic risk for the disease. The infants were randomized to receive either an adapted CM-based formula or a hydrolyzed casein (HC)-based formula after breast-feeding for the first 6-8 months of life. At the age of 3 months, both cellular and humoral responses to BI were higher in infants exposed to CM formula than in infants fully breast-fed (P = 0.015 and P = 0.007). IgG antibodies to BI were higher in infants who received CM formula than in infants who received HC formula at 3 months of age (P = 0.01), but no difference in T-cell responses was seen between the groups. T-cell responses to BI at 9 months of age (P = 0.05) and to human insulin at 12 (P = 0.014) and 24 months of age (P = 0.009) as well as IgG antibodies to BI at 24 months of age (P = 0.05) were lower in children with a diabetic mother than in children with a diabetic father or a sibling, suggesting possible tolerization to insulin by maternal insulin therapy. The priming of insulin-specific humoral and T-cell immunity occurs in early infancy by dietary insulin, and this phenomenon is influenced by maternal type 1 diabetes.

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