

Epidemiology of food hypersensitivity in school children

Validation with double-blind placebo-controlled food challenges and biomarkers

The Obstructive Lung Disease in Northern Sweden (OLIN) Studies, Thesis XV

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Abstract

We investigated the incidence and remission of reported food hypersensitivity (FHS) in school-children from 8 to 12 years of age and the prevalence of hypersensitivity to milk, egg, cod and wheat in 12-year olds using reported data, clinical investigations and biomarkers. **Methods:** A population based cohort was recruited in 2006 from three municipalities in Northern Sweden. All children aged 7-8 years were invited to a parental questionnaire study and 2585 (96% of invited) participated. Children in two of the municipalities were invited to a skin prick test. At age 11-12 years, there was a follow-up of the cohort using the same methods, with the addition of a child interview and assessment of body mass index (BMI). At the follow-up, children reporting milk hypersensitivity were invited to structured interviews and children reporting complete elimination of milk, egg, cod or wheat were invited to a clinical examination and blood sampling. According to test results, they were categorized into FHS phenotypes; those with *current food allergy* underwent double-blind placebo-controlled food challenges (DBPCFCs) using our validated recipes. Before and after the DBPCFCs we analyzed cytokine mRNA expression in peripheral blood mononuclear cells with hallmark cytokines for the humoral allergy-promoting T helper (Th) 2 response, cellular cytotoxicity-promoting Th1 response-, regulatory Th3/Tr1- and inflammatory responses. Fecal inflammatory biomarkers were also analyzed. **Results:** Reported FHS increased from 21% at age 7-8 years to 26% at 11-12 years. The incidence (15%) and remission (33%) of reported FHS were high. Risk factors associated with incidence and remission were different for *milk hypersensitivity* and *hypersensitivity to foods other than milk*. The agreement between reported symptoms to milk, egg, cod, wheat, soy and peanut and sensitization to the culprit food was poor. At age 11-12 years, the prevalence of reported allergy to milk, egg, cod or wheat was 4.8% while the prevalence according to clinical evaluation was 1.4%. This was further halved when evaluated with DBPCFCs. The majority with reported allergy to milk, egg, cod and wheat was categorized as other FHS phenotypes, most commonly *probable lactose intolerance* (40%) and *outgrown food allergy* (19%). While reported milk hypersensitivity in the 11-12 year olds was 14.5%, only 3% were categorized as *current milk allergy*. *Current and outgrown milk allergy* was associated with other atopic disorders and lower BMI (OR 0.8). Before the challenges, the IL-13 and IL-10 mRNA expression was higher in children with a positive than a negative challenge outcome. **Conclusion:** Reported FHS was common in children in Northern Sweden and increased from 7-8 to 11-12 years of age. Both the incidence and remission of reported FHS were high. There was an 8-fold difference in the prevalence of allergy to milk, egg, cod or wheat when reported data was assessed by clinical examinations and DBPCFCs. Allergy to milk, egg, cod and wheat was uncommon in children completely avoiding these foods due to perceived FHS. Higher IL-13 and IL-10 mRNA expression preceded a positive challenge outcome.

Keywords: Food hypersensitivity, school children, epidemiology, food challenges, biomarkers

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