Influence of the dietary history on the prevention of celiac disease: continuation of the PreventCD study (PreventCD2).

Published: 03-02-2016
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Primary: to evaluate the effect of the intervention of PreventCD at age 18 years in terms of frequency of CD and CD autoimmunity.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malabsorption conditions
Study type	Observational invasive

Summary

ID

NL-OMON50621

Source
ToetsingOnline

Brief title
PreventCD2

Condition

- Malabsorption conditions

Synonym
gluten enteropathy, gluten intolerance

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: stichting STICOON

Intervention

Keyword: Coeliac disease, Gluten, High risk children, Puberty, Tolerance

Outcome measures

Primary outcome

Frequency of CD in the participants at the age of 18 years, according to the

ESPGHAN guidelines.

Secondary outcome

Secondary: to determine (1) the association of the baseline variables and (2)

the duration of breastfeeding, daily gluten intake and infections on the

development of CD at age 18 years; and to clarify, during and after puberty,

the intriguing differences observed before puberty between males and females,

especially in these with the highest risk for CD (HLA-DQ2 homozygotes)

Study description

Background summary

Rationale: Coeliac disease (CD) is a chronic disorder caused by intolerance to gluten and affects as much as 1-3% of the Europeans (5 million people). It is treated with a gluten free diet (GFD), but prevention would be even more beneficial. In 2007, the multicenter European PreventCD project was initiated, from now on referred to as PreventCD. The purpose of PREVENTCD is to investigate the influence of infant nutrition on the development of CD and related autoimmune phenomena, as well as how genetic, immunological, and environmental factors relate to this development (www.preventcd.com). The hypothesis of the food intervention study in PreventCD-1 was that it would be possible to induce tolerance for gluten in genetically predisposed children by introducing small quantities of gluten during the period of breastfeeding. The results (cohort age 3 to 6.6 years) have been published in October 2014 in the New England Journal of Medicine 1. The most important findings were that development of CD was not influenced by introducing small quantities of gluten at 4 months of age, and that it is not influenced by the presence or duration of breastfeeding. Moreover, we learned that CD develops already at a very young

age, more often in girls and more often in children homozygous for HLA-DQ2.

In PreventCD-2, the children have been followed to the age of 12 years to evaluate the effect of the gluten intervention in the initial randomized study (PREVENTCD-1)1. In PreventCD-2, (data at June 2019 (confidential unpublished results) a total of 699 from the 944 original cohort of children are included in the follow-up, 563 of them with TGA determinations during the last 3 years. Mean age 10,1 years (range 8,4-12,0), 52% of them boys. 135 Children had been diagnosed with CD and 158 small bowel biopsies had been performed. The mean age at CD diagnosis is 4,3 years (SD 2,2) and 53% of the cases had symptoms, being the most common abdominal pain (42.3%), diarrhoea (35.7%) and failure to thrive/abdominal distention (both 30%). The cumulative incidence of CD at 9 years of age is 16,9% with incidences at 3, 5 and 7 years of 5,1%, 10.4% and 15,4% respectively. CD development significantly more frequent in girls at all ages. The frequency of CD development was significantly higher in those children homozygous for HLA-DQ2 (DR3-DQ2/DR3-DQ2, DR3-DQ2/DR7-DQ2), with a cumulative incidence at 8 years of 33.2%. However, and intriguingly, this effect of HLA-DQ2 homozygosity is only present in girls and not in boys.As well as at the age of 3 years, the intervention with early introduction of gluten did not have a significant effect on the development of CD at the age of 8 years (figure 4), neither for boys or for girls. It is essential to increase the follow-up up to the age of 18 years to give insight in the natural history and risk for the disease in this unique high risk population for CD , among others to clarify, during and after puberty, the intriguing differences between males and females

Study objective

Primary: to evaluate the effect of the intervention of PreventCD at age 18 years in terms of frequency of CD and CD autoimmunity.

Study design

Observational study.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Participating families are well aware of the fact that their child has an increased risk to develop CD and have experience with participating in PreventCD. They are able to judge whether the burden of annually obtaining blood and faecal samples for PreventCD-2 is in balance with the burden from the work-up that their child would undergo whenever he/she is suspected to have CD. In PreventCD, approximately, 45% of the children diagnosed with CD were asymptomatic or had only mild symptoms. It is likely that also in PreventCD-2, we will detect CD before the start of clinical

manifestations, allowing timely initiation of a GFD and preventing adverse effects on the child*s growth, bone density, development, and health. Small bowel biopsies will only be performed when medically indicated and not just for the purpose of the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must already be participating in PreventCD-1. Inclusion criteria for PreventCD-1 were: the child had to have at least 1 first degree relative with CD, had to be positive for HLA-DQ2 and/or DQ8 and its parents/guardians had to give informed consent for the study.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: no informed consent.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-05-2016
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	03-02-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	20-01-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ISRCTN	ISRCTN74582487
CCMO	NL53741.058.15