Influence of the dietary history in the prevention of coeliac disease : possibilities of induction of tolerance for gluten in genetically predisposed children. The dutch food intervention study

Published: 08-12-2006
Last updated: 09-05-2024

1. Development of a prevention strategy for CD in children from high risk families for the disease by induction of oral tolerance to gluten;2. Identification of the immunological mechanisms involved in initiating the aberrant response to gluten...

Ethical review	-
Status	Recruitment stopped
Health condition type	Malabsorption conditions
Study type	Interventional

Summary

ID

NL-OMON30313

Source
ToetsingOnline

Brief title
preventcd

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: Europese Unie,Eurospital, Italy,Numico,Phadia BmHg, Germany

Intervention

Keyword: coeliac disease, gluten, high risk children, tolerance

Outcome measures

Primary outcome

In the European project (1000 children), reduction of 50% of CD development in the intervention group at the age of 3 years (25 children with CD, expected 50).

Secondary outcome

- Understanding of the influence of early nutrition on the development of CD in relation to immunologic and genetic factors.

- If our strategy to develop tolerance for gluten happens to be effective: contribution to the development of new (evidence based) European guidelines for early infant feeding practices, aimed at the primary prevention of CD and related autoimmune diseases.

Study description

Background summary

Coeliac disease (CD) is a chronic disorder caused by hypersensitivity to some of the most common proteins (gluten) in the diet of the European population. CD affects as much as 1% of the Europeans (2.5 million people) and is the most common food intolerance in Europe. If recognised, CD patients have only limited

access to safe foods and there is not causal therapy available. The proposed study is part of the multicenter European project PREVENTCD, founded by the European Commission FP-6-2005-FOOD-4B; Proposal/Contract no.: 036383. The general objective of PREVENTCD is to significantly reduce the number of people suffering from CD in Europe, by developing primary prevention strategies for CD. This study represents the Dutch contribution to the dietary intervention study of PREVENTCD.
The hypothesis of the study is that it is possible to induce tolerance for gluten in genetically predisposed children through the introduction of small quantities of gluten during the period of breast-feeding.

Study objective

1. Development of a prevention strategy for CD in children from high risk families for the disease by induction of oral tolerance to gluten;
2. Identification of the immunological mechanisms involved in initiating the aberrant response to gluten introduction in the diet of infants genetically predisposed to CD;
3. Identification of the factors in the early dietary history involved in the aberrant response to gluten in children;

Study design

European, multicenter, double blind, prospective, randomised food intervention study

Intervention

The Dutch Coeliac Society (NCV) will invite to participate their members with CD expecting a newborn (child or sibling) during the next months. Informed consent to participate will be asked from the families by the local responsible physician.
Genotyping for the associated genetic factors associated with CD, including the strong associated HLA-DQ2 and/or DQ8 factors, will be determined in cord blood after birth.
The children bearing HLA-DQ2 and/or DQ8 will be blindly randomised to either a group for "tolerance induction for gluten" or to a "control" group. At least 6 months of breast-feeding will be STRONGLY encouraged for all the children.
At the age of 4 months tolerance induction will be attempted by the daily intake of 1g wheat flour (100 mg gluten) during 8 weeks while continuing breast-feeding. No gluten will be given in these 8 weeks to control infants, but 1g. lactose as a placebo intervention. Compliance will be assessed by visit or interview.
The infants will be strictly followed up. At 7 fixed time points 5ml blood will be obtained to allow for the screening of CD-specific antibodies, phenotypic characterization of 20 markers indicating lymphocyte activation and regulatory

T cell induction, and monitoring for the occurrence of gluten-specific T cell responses typical for CD.
Children with positive antibodies strongly indicating CD or with clinical suspicion of CD will
be offered a small bowel biopsy for the definitive diagnosis of CD.

Study burden and risks

Zie protocol pagpage 23 - 30
Possible burden for participants:
- Invited parents/guardians might feel anxiety when reading the letter inviting them to the study (annex 3), as it describes her/his child as having high risk for CD.
- Families, in which the child has increased values of the serological marker (AtTG) suggesting undiagnosed CD (aprox. 10%), are also likely to experience some anxiety when waiting for further examinations, thus this time period will be kept as short as possible.
- The small intestinal biopsy necessary for confirming or excluding CD is a well-established method for diagnosis and complications are extremely rare, however, during the procedure some discomfort isn*t uncommon. Biopsy will only be performed when medically indicated and NOT just for purpose of the study.
- A database system is used for the storage of all findings, e.g. results of blood sample analyses and replies in the questionnaires, which might worry some families. However, informed consent is required before inclusion of any child into the study and the database, only a small group of researchers have access to the database, and if the child and/or parents express a wish to end their participation their identity code will immediately be erased.
Advantages for participants:
- Detection of CD BEFORE the start of its clinical manifestations, allowing the prompt institution of a gluten-free diet and preventing the adverse long-term health implications of active CD.
- In the immunologically identified and diagnosed sub-group of individuals, the clinical manifestation will be detected at an early stage allowing the prompt institution of a gluten-free diet
- the children who, thanks to the study, can be classified as early as possible as not being prone to CD, will be spared the anxiety of vigilance and expectation toward the development of CD and
- the small group of children with signs of gluten sensitivity, as evidenced by the presence of CD antibodies in serum, but without evident small intestinal lesions, will benefit from the planned follow-up by a paediatric gastroenterologist.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Infant born during the study with a first degree relative (parent or sibling) with Coeliac Disease.
2. Family know by the NCV (Dutch coeliac disease association)
3. Informed consent for the study

Exclusion criteria

1. No informed consent for the study
2. Insufficient knowledge of the Dutch language. Parents-guardians unable to understand the information necessary to give informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2007
Enrollment:	150
Type:	Actual

Ethics review

Not available

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
CCMO	NL14647.000.06