Study On The Effectiveness Of Oral Administration Of Prolyl Endoprotease For Gluten Detoxification As A Means To Treat Coeliac Disease

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To determine if AN-PEP is capable of detoxifying gluten in vivo in patients diagnosed with coeliac disease

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal disorders
Study type	Interventional

Summary

ID

NL-OMON31647

Source
ToetsingOnline

Brief title
AN-PEP supportive treatment in coeliac disease

Condition

- Gastrointestinal disorders
- Autoimmune disorders

Synonym
Coeliac disease

Research involving
Human

Sponsors and support

Primary sponsor: DSM Food Specialties

Source(s) of monetary or material Support: DSM Food Specialties BV

Intervention

Keyword: AN-PEP, Coeliac Disease, Gluten Free Diet

Outcome measures

Primary outcome

To investigate in vivo AN-PEP activity, small intestinal biopsy material will

be analysed for the following:

* Histopathological changes according to the Modified Marsh criteria.

* The presence and activity of gluten reactive T cells isolated from biopsies.

* The immunophenotype of lymphocytes (IEL and LPL) isolated from biopsies.

To investigate in vivo AN-PEP activity, peripheral blood samples will be

analysed for the following:

* The presence and activity of gluten reactive T cells.

* The presence of coeliac disease specific antibodies (EMA, tTGA).

Secondary outcome

Not applicable

Study description

Background summary

Coeliac disease is a small intestinal disease caused by inflammatory T cell responses to proline-rich peptides derived from gluten molecules in wheat and related cereals. Due to the high proline content gluten peptides are resistant to degradation in the gastrointestinal tract. Oral supplementation with enzymes that can cut gluten has therefore been suggested as a potential treatment modality for coeliac disease. In the present study we wish to determine if

co-administration of such an enzyme to a gluten containing meal can prevent the occurrence of coeliac disease specific symptoms and be therefore a suitable alternative to a gluten-free diet. In particular we wish to determine if a prolyl endoprotease derived from the food grade organism Aspergillis niger (AN-PEP) is capable of detoxifying 8 grams of gluten in a commercial food product.

Study objective

To determine if AN-PEP is capable of detoxifying gluten in vivo in patients diagnosed with coeliac disease

Study design

Randomised double-blinded semi-cross-over design

This study includes three two-week periods.
1st Period: Patients are given a commercial food product containing 8 grams of gluten, to which AN-PEP has been added, once daily.
2nd Period: Wash-out period of fourteen days. During this period all patients will use gluten free diet.
3rd Period: Patients who are negative for coeliac disease symptoms during the 1st period will be randomised in two groups. The first group receives a commercial food product containing 8 grams of gluten, to which AN-PEP has been added, once daily. The second group receives the same product to which placebo has been added.

Intervention

Not applicable

Study burden and risks

Patients are expected to pay five visits to the out-patient clinic of the department of gastroenterology of the VU university medical center.
During three of the visits 12 spike-biopsies will be taken from the duodenum during oesophago-gastro-duodenoscopy. 5 blood samples (10ml) will be taken during all of the five visits.
Patients will be asked to fill in a questionnaire at the start of the study, at the end of the first period and at the start and end of the last period of the study, concerning the quality of life score.
During the first period patients will be asked to consume a gluten containing commercial food product to which AN-PEP has been added, once daily. In the third period of this study patients will be asked to consume the same food product to which AN-PEP or placebo has been added.

There are no known or expected risks associated with the ingestion of gluten during the course of the study other than the coeliac disease specific symptoms. In fact, a gluten challenge is used as part of the diagnostic procedure for coeliac disease. No adverse effects are expected with venous puncture.
Studies have shown that 6 to 10 mucosal biopsies (3 * 6 mg) can be taken without any side effects. No perforations have been described with this technique and there is no indication that this leads to major bleeding.
AN-PEP has been tested extensively in a toxicology program. No hypersensitivity reactions have been found in previous human feeding studies with this type of food grade enzymes.

Contacts

Public
DSM Food Specialties

P.O. Box 1
2600 MA Delft
Nederland
Scientific
DSM Food Specialties

P.O. Box 1
2600 MA Delft
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Confirmed diagnosis of coeliac disease (Marsh III B/C)
* Detectable coeliac disease specific antibodies (EMA, tTGA) at time of diagnosis.
* A strict gluten free diet for at least 1 year and normalised villous architecture (Marsh 0/I);
* Male and female, 18-70 years old;
* No detectable anti-endomysium and low anti-tissue transglutaminase (< 4 U/ml) prior to the start of the study;
* Patient is willing to undergo all protocol related assessments and visits (including up to 3 separate oesophago-gastro-duodenoscopies with multiple biopsies taken each time) from the duodenum descendents;
* Patient has read the information provided on the study and given written consent;
* Female participants at fertile age must use adequate contraception.

Exclusion criteria

* Use of any immunoregulatory drug within the last 6 months;
* Use of any anticoagulant drug;
* Clinically suspected bleeding tendency;
* Pregnancy or breast feeding;
* Presence of any concurrent active infection;
* IgA deficiency.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-05-2008

Enrollment:	14
Type:	Actual

Ethics review

Approved WMO Date:	26-03-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL21084.029.08